

Diabetes in children and young people (update):

diagnosis and management of type 1 and type 2 diabetes in children and young people

Clinical Guideline <...>

Appendices

December 2014

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Health and Care Excellence*

Disclaimer

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Appendix A: Recommendations from NICE clinical guideline 15 (2004) that have been deleted or changed

A.1 Recommendations to be deleted

The table shows recommendations from 2004 that NICE proposes deleting in the 2015 update. The right-hand column gives the replacement recommendation, or explains the reason for the deletion if there is no replacement recommendation.

Recommendation numbers in the table refer to the numbering in the NICE guideline.

Recommendation in 2004 guideline	Comment
Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document. (1.1.2.5)	This recommendation has been deleted because the new 2015 recommendations on DKA give detailed advice on the need for referral to hospital when DKA is suspected or confirmed, and DKA is always treated in hospital.
Children and young people with type 1 diabetes should be informed that the use of multiple daily insulin injection regimens or continuous subcutaneous insulin infusion (or insulin pump therapy) will not prolong the partial remission phase, although these forms of therapy may be appropriate for optimising glycaemic control, especially in young people. (1.1.3.2)	Replaced by: Take into account the personal and family circumstances of the child or young person with type 1 diabetes and discuss their personal preferences with them and their family members or carers (as appropriate) when choosing an insulin regimen. (1.2.19) Offer children and young people with type 1 diabetes multiple daily insulin injection regimens from diagnosis. If a multiple daily insulin injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). (1.2.20)
Children and young people with newly diagnosed type 1 diabetes should be offered a structured programme of education covering the aims of insulin therapy, delivery of insulin, self-monitoring of blood glucose, the effects of diet, physical activity and intercurrent illness on glycaemic control, and the detection and management of hypoglycaemia. (1.1.4.1)	Replaced by: Offer children and young people with type 1 diabetes and their family members or carers (as appropriate) a continuing programme of education from diagnosis. Ensure that the programme includes the following core topics: <ul style="list-style-type: none"> • insulin therapy, including its aims, how it works and its mode of delivery • blood glucose monitoring, including targets for blood glucose control (blood glucose and HbA1c levels) • the effects of diet, physical activity and intercurrent illness on blood glucose control • managing intercurrent illness ('sick-day

Recommendation in 2004 guideline	Comment
	<p>rules', including monitoring of blood ketones [beta-hydroxybutyrate])</p> <ul style="list-style-type: none"> • detecting and managing hypoglycaemia, hyperglycaemia and ketosis. (1.2.1) <p>Tailor the education programme to each child or young person with type 1 diabetes and their family members or carers (as appropriate), taking account of issues such as:</p> <ul style="list-style-type: none"> • personal preferences • emotional wellbeing • age and maturity • cultural considerations • existing knowledge • current and future social circumstances • life goals. (1.2.2)
<p>Children and young people with type 1 diabetes and their families should be offered timely and ongoing opportunities to access information about the development, management and effects of type 1 diabetes. The information provided should be accurate and consistent and it should support informed decision-making. (1.2.1.1)</p>	<p>Replaced by:</p> <p>Offer children and young people with type 1 diabetes and their family members or carers (as appropriate) a continuing programme of education from diagnosis. Ensure that the programme includes the following core topics:</p> <ul style="list-style-type: none"> • insulin therapy, including its aims, how it works and its mode of delivery • blood glucose monitoring, including targets for blood glucose control (blood glucose and HbA1c levels) • the effects of diet, physical activity and intercurrent illness on blood glucose control • managing intercurrent illness ('sick-day rules', including monitoring of blood ketones [beta-hydroxybutyrate]) • detecting and managing hypoglycaemia, hyperglycaemia and ketosis. (1.2.1)
<p>Children and young people with type 1 diabetes and their families should be offered opportunities to discuss particular issues and to ask questions at each clinic visit. (1.2.1.2)</p>	<p>Replaced by:</p> <p>Encourage children and young people with type 1 diabetes and their family members or carers (as appropriate) to discuss any concerns or raise any questions they have with their diabetes team. (1.2.5)</p>
<p>The method of delivering education and content will depend on the individual and should be appropriate for the child's or young person's age, maturity, culture, wishes and existing knowledge within the family. (1.2.1.3)</p>	<p>Replaced by:</p> <p>Tailor the education programme to each child or young person with type 1 diabetes and their family members or carers (as appropriate), taking account of issues such as:</p> <ul style="list-style-type: none"> • personal preferences • emotional wellbeing • age and maturity • cultural considerations • existing knowledge

Recommendation in 2004 guideline	Comment
	<ul style="list-style-type: none"> • current and future social circumstances • life goals. (1.2.2)
<p>Pre-school and primary school children with type 1 diabetes should be offered the most appropriate individualised regimens to optimise their glycaemic control. (1.2.2.1)</p>	<p>Replaced by: Offer children and young people with type 1 diabetes multiple daily insulin injection regimens from diagnosis. If a multiple daily insulin injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). (1.2.20)</p>
<p>Young people with type 1 diabetes should be offered multiple daily injection regimens to help optimise their glycaemic control. (1.2.2.2)</p>	<p>Replaced by: Offer children and young people with type 1 diabetes multiple daily insulin injection regimens from diagnosis. If a multiple daily insulin injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). (1.2.20)</p>
<p>Multiple daily injection regimens should be offered only as part of a package of care that involves continuing education, dietary management, instruction on the use of insulin delivery systems and blood glucose monitoring, emotional and behavioural support, and medical, nursing and dietetic expertise in paediatric diabetes, because this improves glycaemic control. (1.2.2.3)</p>	<p>The contents of this recommendation are covered by new recommendations throughout the guideline.</p>
<p>Children and young people using multiple daily injection regimens should be informed that they may experience an initial increase in the risk of hypoglycaemia and short-term weight gain. (1.2.2.4)</p>	<p>This recommendation has been deleted because the GDG considered that multiple daily injection regimens improve blood glucose control so reference to hypoglycaemia was no longer appropriate. The group did not identify evidence to indicate that weight gain is an important adverse event.</p>
<p>Young people who do not achieve satisfactory glycaemic control with multiple daily injection regimens should be offered additional support and, if appropriate, alternative insulin therapy (once-, twice- or three-times daily mixed insulin regimens or continuous subcutaneous insulin infusion using an insulin pump). (1.2.2.6)</p>	<p>Replaced by: If a child or young person with type 1 diabetes does not achieve satisfactory blood glucose control:</p> <ul style="list-style-type: none"> • offer appropriate additional support such as increased contact frequency with their diabetes team, and • if necessary, offer an alternative insulin regimen (multiple daily injections, continuous subcutaneous insulin infusion using an insulin pump or once-, twice- or three-times daily mixed insulin injections). (1.2.31)
<p>Young people with type 1 diabetes who have</p>	<p>Replaced by:</p>

Recommendation in 2004 guideline	Comment
<p>difficulty adhering to multiple daily injection regimens should be offered twice-daily injection regimens. (1.2.2.7)</p>	<p>Take into account the personal and family circumstances of the child or young person with type 1 diabetes and discuss their personal preferences with them and their family members or carers (as appropriate) when choosing an insulin regimen. (1.2.19)</p> <p>Offer children and young people with type 1 diabetes multiple daily insulin injection regimens from diagnosis. If a multiple daily insulin injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). (1.2.20)</p>
<p>Continuous subcutaneous insulin infusion (or insulin pump therapy) is recommended as an option for people with type 1 diabetes provided that:</p> <ul style="list-style-type: none"> • multiple-dose insulin therapy (including, where appropriate, the use of insulin glargine) has failed; and • those receiving the treatment have the commitment and competence to use the therapy effectively. (1.2.2.8) 	<p>Replaced by:</p> <p>Take into account the personal and family circumstances of the child or young person with type 1 diabetes and discuss their personal preferences with them and their family members or carers (as appropriate) when choosing an insulin regimen. (1.2.19)</p> <p>Offer children and young people with type 1 diabetes multiple daily insulin injection regimens from diagnosis. If a multiple daily insulin injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). (1.2.20)</p>
<p>Continuous subcutaneous insulin infusion therapy should be initiated only by a trained specialist team, which should normally comprise a physician with a specialist interest in insulin pump therapy, a diabetes specialist nurse and a dietitian. (1.2.2.9)</p>	<p>Replaced by:</p> <p>Offer children and young people with type 1 diabetes multiple daily insulin injection regimens from diagnosis. If a multiple daily insulin injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). (1.2.20)</p>
<p>Established users of continuous subcutaneous insulin infusion therapy should have their insulin management reviewed by their specialist team so that a decision can be made about whether a trial or a switch to multiple-dose insulin incorporating insulin glargine would be appropriate. (1.2.2.11)</p>	<p>Replaced by:</p> <p>Offer children and young people with type 1 diabetes multiple daily insulin injection regimens from diagnosis. If a multiple daily insulin injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). (1.2.20)</p>
<p>Children and young people with type 1 diabetes</p>	<p>The part of the recommendation referring to</p>

Recommendation in 2004 guideline	Comment
<p>should be offered the most appropriate insulin preparations (rapid-acting insulin analogues, short-acting insulins, intermediate-acting insulins, long-acting insulin analogues or biphasic insulins) according to their individual needs and the instructions in the patient information leaflet supplied with the product, with the aim of obtaining an HbA1c level of less than 7.5% without frequent disabling hypoglycaemia and maximising quality of life. (1.2.3.1)</p>	<p>patient information leaflets has been deleted, as the GDG felt that healthcare professionals would be expected to take account of this information regardless. In addition, the text on HbA1c target levels has been deleted, as this is covered by the new 2015 recommendations on HbA1c target levels.</p> <p>The GDG considered that the remainder of the 2004 recommendation was no longer relevant. There is already a recommendation about providing rapid-acting insulin analogues from the 2004 guideline (1.2.30), and children and young people using multiple daily insulin or mixed insulin regimens would invariably receive specific preparations according their needs.</p>
<p>Children and young people with type 1 diabetes who use insulin preparations containing intermediate-acting insulin should be informed that these preparations should be mixed before use according to the instructions in the patient information leaflet supplied with the product. (1.2.3.4)</p>	<p>This recommendation has been deleted because mixing of insulins by the patient is no longer part of clinical practice.</p>
<p>Children and young people with type 1 diabetes and their families should be informed that the target for long-term glycaemic control is an HbA1c level of less than 7.5% without frequent disabling hypoglycaemia and that their care package should be designed to attempt to achieve this.(1.2.6.1)</p>	<p>Replaced by:</p> <p>Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that an HbA1c target level of 48 mmol/mol (6.5%) or lower is ideal to minimise the risk of long-term complications. (1.2.68)</p> <p>Explain to children and young people with type 1 diabetes who have an HbA1c level above the ideal target of 48 mmol/mol (6.5%) and their family members or carers (as appropriate) that any reduction in HbA1c level reduces the risk of long-term complications. (1.2.69)</p> <p>Agree an individualised lowest achievable HbA1c target with each child or young person with type 1 diabetes and their family members or carers (as appropriate), taking into account factors such as daily activities, individual life goals, complications, comorbidities and the risk of hypoglycaemia. (1.2.70)</p> <p>Support children and young people with type 1 diabetes and their family members or carers (as appropriate) to achieve and maintain their individual agreed HbA1c target level. (1.2.71)</p>
<p>Current HbA1c measurements should be made available in outpatient clinics because their availability can lead to immediate changes in insulin therapy and/or diet and so reduce the need for follow-up appointments. (1.2.6.3)</p>	<p>The GDG considered that this recommendation was no longer necessary because it is no longer difficult to get the results of HbA1c tests promptly in practice.</p>
<p>Children and young people with type 1 diabetes and their families should be informed that aiming to achieve low levels of HbA1c can lead to increased risks of hypoglycaemia and that high</p>	<p>Replaced by:</p> <p>Explain the benefits of safely achieving and maintaining the lowest attainable HbA1c to children and young people with type 1 diabetes</p>

Recommendation in 2004 guideline	Comment
levels of HbA1c can lead to increased risks of long-term microvascular complications. (1.2.6.4)	and their family members or carers (as appropriate). (1.2.67)
Children and young people with HbA1c levels consistently above 9.5% should be offered additional support by their diabetes care teams to help them improve their glycaemic control because they are at increased risk of developing diabetic ketoacidosis and long-term complications.(1.2.6.5)	<p>Replaced by:</p> <p>Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that an HbA1c target level of 48 mmol/mol (6.5%) or lower is ideal to minimise the risk of long-term complications. (1.2.68)</p> <p>Explain to children and young people with type 1 diabetes who have an HbA1c level above the ideal target of 48 mmol/mol (6.5%) and their family members or carers (as appropriate) that any reduction in HbA1c level reduces the risk of long-term complications. (1.2.69)</p> <p>Support children and young people with type 1 diabetes and their family members or carers (as appropriate) to achieve and maintain their individual agreed HbA1c target level. (1.2.71)</p>
Children and young people with type 1 diabetes should be encouraged to use blood glucose measurements for short-term monitoring of glycaemic control because this is associated with reduced levels of glycated haemoglobin. Urine glucose monitoring is not recommended because it is less effective and is associated with lower patient satisfaction.(1.2.6.6)	<p>Replaced by:</p> <p>Advise children and young people with type 1 diabetes and their family members or carers (as appropriate) to routinely perform at least 5 capillary blood glucose tests per day. (1.2.59)</p>
Children and young people with type 1 diabetes and their families should be informed that the optimal targets for short-term glycaemic control are a pre-prandial blood glucose level of 4–8 mmol/litre and a post-prandial blood glucose level of less than 10 mmol/litre. (1.2.6.7)	<p>Replaced by:</p> <p>Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that the optimal target ranges for short-term blood glucose control are:</p> <ul style="list-style-type: none"> • fasting blood glucose level of 4–7 mmol/litre (or 5–7 mmol/litre for young people intending to drive the following morning) • a blood glucose level of 4–7 mmol/litre before meals • a blood glucose level of 5–9 mmol/litre after meals. (1.2.55)
Children and young people with type 1 diabetes and their families should be encouraged to perform frequent blood glucose monitoring as part of a continuing package of care that includes dietary management, continued education and regular contact with their diabetes care teams. (1.2.6.8)	<p>Replaced by:</p> <p>Advise children and young people with type 1 diabetes and their family members or carers (as appropriate) to routinely perform at least 5 capillary blood glucose tests per day. (1.2.59)</p> <p>Advise children and young people with type 1 diabetes and their family members or carers (as appropriate) that more frequent testing may be needed in some circumstances, for example during intercurrent illness. (1.2.60)</p>

Recommendation in 2004 guideline	Comment
<p>Children and young people with type 1 diabetes who are trying to optimise their glycaemic control and/or have intercurrent illness should be encouraged to measure their blood glucose levels more than four times per day. (1.2.6.12)</p>	<p>Replaced by: Advise children and young people with type 1 diabetes and their family members or carers (as appropriate) to routinely perform at least 5 capillary blood glucose tests per day. (1.2.59)</p> <p>Advise children and young people with type 1 diabetes and their family members or carers (as appropriate) that more frequent testing may be needed in some circumstances, for example during intercurrent illness. (1.2.60)</p>
<p>Children and young people with type 1 diabetes who have persistent problems with hypoglycaemia unawareness or repeated hypoglycaemia or hyperglycaemia should be offered continuous glucose monitoring systems. (1.2.6.14)</p>	<p>Replaced by: Offer ongoing unblinded ('real-time') continuous glucose monitoring with alarms to children and young people with type 1 diabetes who have:</p> <ul style="list-style-type: none"> • frequent severe hypoglycaemia or • impaired awareness of hypoglycaemia associated with adverse consequences (for example, seizures or anxiety). (1.2.63) <p>Consider intermittent (unblinded ['real-time'] or blinded ['retrospective']) continuous glucose monitoring to help improve blood glucose control in children and young people who continue to have hyperglycaemia despite insulin adjustment and additional support. (1.2.65)</p>
<p>Children and young people with type 1 diabetes should be offered blood glucose monitors with memories (as opposed to monitors without memories) because these are associated with improved patient satisfaction. (1.2.6.15)</p>	<p>This recommendation has been deleted because blood glucose monitors now routinely have memory functions.</p>
<p>Children and young people with type 1 diabetes should be encouraged to develop a good working knowledge of nutrition and how it affects their diabetes. (1.2.7.3)</p>	<p>Replaced by: Support children and young people with type 1 diabetes and their family members or carers (as appropriate) to develop a good working knowledge of nutrition and how it affects their diabetes. (1.2.34)</p>
<p>Children and young people with type 1 diabetes and their families should be informed of the importance of healthy eating in reducing the risk of cardiovascular disease (including foods with a low glycaemic index, fruit and vegetables, and types and amounts of fats), and means of making appropriate nutritional changes in the period after diagnosis and according to need and interest at intervals thereafter. (1.2.7.4)</p>	<p>Replaced by: Explain regularly to children and young people with type 1 diabetes and their family members or carers (as appropriate) how healthy eating (including eating foods with a low glycaemic index, fruit and vegetables, and appropriate types and amounts of fats) can reduce their risk of cardiovascular disease, and support them to adjust their food choices accordingly. (1.2.35)</p>
<p>Children and young people with type 1 diabetes should be encouraged to consider eating a bedtime snack. The nutritional composition and timing of all snacks should be discussed with the diabetes care team. (1.2.7.5)</p>	<p>Replaced by: Encourage children and young people with type 1 diabetes and their family members or carers (as appropriate) to discuss the nutritional composition and timing of snacks with the diabetes team. (1.2.40)</p>
<p>Children and young people using multiple daily injection regimens should be offered education</p>	<p>Replaced by: Offer children and young people with type 1</p>

Recommendation in 2004 guideline	Comment
<p>about insulin and dietary management as part of their diabetes care package, to enable them to adjust their insulin dose to reflect their carbohydrate intake. (1.2.7.6)</p>	<p>diabetes and their family members or carers (as appropriate) a continuing programme of education from diagnosis. Ensure that the programme includes the following core topics:</p> <ul style="list-style-type: none"> • insulin therapy, including its aims, how it works and its mode of delivery • blood glucose monitoring, including targets for blood glucose control (blood glucose and HbA1c levels) • the effects of diet, physical activity and intercurrent illness on blood glucose control • managing intercurrent illness ('sick-day rules', including monitoring of blood ketones [beta-hydroxybutyrate]) • detecting and managing hypoglycaemia, hyperglycaemia and ketosis. (1.2.1) <p>Offer level 3 carbohydrate-counting education from diagnosis to children and young people with type 1 diabetes who are using multiple daily injections or insulin pump therapy, and to their family members or carers (as appropriate), and repeat the offer at intervals thereafter. (1.2.37)</p>
<p>Children and young people with type 1 diabetes, their parents and other carers should be informed that exercise should be undertaken with caution if blood glucose levels are greater than 17 mmol/litre in the presence of ketosis. (1.2.8.9)</p>	<p>Replaced by:</p> <p>When DKA is suspected in a child or young person with known diabetes (see recommendation 1.4.4) measure the blood ketones (beta-hydroxybutyrate), using a near-patient method if available. If the level is elevated, immediately send them to a hospital with acute paediatric facilities. (1.4.5)</p> <p>When DKA is suspected in a child or young person with known diabetes (see recommendation 1.4.4) and it is not possible to measure the blood ketones (beta-hydroxybutyrate) using a near-patient method, immediately send them to a hospital with acute paediatric facilities. (1.4.6)</p>
<p>Parents and, where appropriate, school nurses and other carers should be offered education on the administration of glucagon.(1.3.1.7)</p>	<p>This recommendation has been deleted as it was no longer relevant in light of amendments to other recommendations from the 2004 guideline.</p>
<p>Young people with type 1 diabetes should be offered alcohol education programmes.(1.2.9.2)</p>	<p>Replaced by:</p> <p>Offer children and young people with type 1 diabetes and their family members or carers (as appropriate) a continuing programme of education from diagnosis. Ensure that the programme includes the following core topics:</p> <ul style="list-style-type: none"> • insulin therapy, including its aims, how it works and its mode of delivery • blood glucose monitoring, including targets for blood glucose control (blood glucose and HbA1c levels) • the effects of diet, physical activity and

Recommendation in 2004 guideline	Comment
	<p>intercurrent illness on blood glucose control</p> <ul style="list-style-type: none"> • managing intercurrent illness ('sick-day rules', including monitoring of blood ketones [beta-hydroxybutyrate]) • detecting and managing hypoglycaemia, hyperglycaemia and ketosis. (1.2.1) <p>Tailor the education programme to each child or young person with type 1 diabetes and their family members or carers (as appropriate), taking account of issues such as:</p> <ul style="list-style-type: none"> • personal preferences • emotional wellbeing • age and maturity • cultural considerations • existing knowledge • current and future social circumstances • life goals. (1.2.2)
<p>Parents and, where appropriate, school nurses and other carers should be offered education on the administration of glucagon.(1.3.1.7)</p>	<p>This recommendation has been deleted as it was no longer relevant in light of amendments to other recommendations from the 2004 guideline.</p>
<p>Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes. (1.3.2.1)</p>	<p>This recommendation is no longer necessary as the recognition and management of DKA has now been covered in detail by the 2015 update.</p>
<p>Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward. (1.3.2.2)</p>	<p>Replaced by:</p> <p>Children and young people with DKA should be cared for in a facility that can provide the level of monitoring and care for DKA specified in section 1.4 of this guideline. (1.4.16)</p> <p>Children and young people with DKA should be cared for either on a high-dependency unit, or on a general paediatric ward with one-to-one nursing, if:</p> <ul style="list-style-type: none"> • they are younger than 2 years or • they have severe DKA (blood pH below 7.1). (1.4.17)
<p>Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit. (1.3.2.3)</p>	<p>Replaced by:</p> <p>Children and young people with DKA should be cared for in a facility that can provide the level of monitoring and care for DKA specified in in section 1.4 of this guideline. (1.4.16)</p> <p>Children and young people with DKA should be cared for either on a high-dependency unit, or on a general paediatric ward with one-to-one nursing, if:</p> <ul style="list-style-type: none"> • they are younger than 2 years or • they have severe DKA (blood pH below 7.1). (1.4.17)
<p>Children with diabetic ketoacidosis who are</p>	<p>Replaced by:</p>

Recommendation in 2004 guideline	Comment
<p>younger than 2 years of age should be managed in a paediatric intensive care unit. (1.3.2.4)</p>	<p>Children and young people with DKA should be cared for in a facility that can provide the level of monitoring and care for DKA specified in in section 1.4 of this guideline. (1.4.16)</p> <p>Children and young people with DKA should be cared for either on a high-dependency unit, or on a general paediatric ward with one-to-one nursing, if:</p> <ul style="list-style-type: none"> • they are younger than 2 years or • they have severe DKA (blood pH below 7.1). (1.4.17)
<p>Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose. (1.3.2.5)</p>	<p>Replaced by: Treat DKA with oral fluids and subcutaneous insulin only if the child or young person is alert, not nauseated or vomiting, and not clinically dehydrated. (1.4.22)</p>
<p>Children and young people with type 1 diabetes and their families should be offered clear guidance and protocols ('sick-day rules') for the management of type 1 diabetes during intercurrent illness. (1.3.4.1)</p>	<p>Replaced by: Provide each child and young person with type 1 diabetes and their family members or carers (as appropriate) with clear individualised oral and written advice ('sick-day rules') about managing type 1 diabetes during intercurrent illness or episodes of hyperglycaemia, including:</p> <ul style="list-style-type: none"> • monitoring blood glucose • monitoring blood ketones (beta-hydroxybutyrate) • adjusting their insulin regimen • food and fluid intake • when to seek further advice or help. <p>Revisit the advice with the child or young person and their family members or carers (as appropriate) at least annually. (1.2.54)</p>
<p>Children and young people with type 1 diabetes should have short-acting insulin or rapid-acting insulin analogues and blood and/or urine ketone testing strips available for use during intercurrent illness. (1.3.4.2)</p>	<p>Replaced by: Provide children and young people with type 1 diabetes with rapid-acting insulin analogues for use during intercurrent illness or episodes of hyperglycaemia. (1.2.30)</p> <p>Provide each child and young person with type 1 diabetes and their family members or carers (as appropriate) with clear individualised oral and written advice ('sick-day rules') about managing type 1 diabetes during intercurrent illness or episodes of hyperglycaemia, including:</p> <ul style="list-style-type: none"> • monitoring blood glucose • monitoring blood ketones (beta-hydroxybutyrate) • adjusting their insulin regimen • food and fluid intake

Recommendation in 2004 guideline	Comment
	<ul style="list-style-type: none"> • when to seek further advice or help. Revisit the advice with the child or young person and their family members or carers (as appropriate) at least annually. (1.2.54) Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that it is important to ensure that blood ketone testing strips are not used after the specified ('use-by') date. (1.2.74)
Routine screening for elevated blood lipid levels and/or neurological function is not recommended for children and young people with type 1 diabetes. (1.3.5.2)	The GDG considered that monitoring for dyslipidaemia or neurological function in children and young people with type 1 diabetes is not part of current practice and so a recommendation was unnecessary.
Parents of pre-school children with type 1 diabetes should be informed that persistent hypoglycaemia, in particular in association with seizures, is associated with a small but definite risk of long-term neurocognitive dysfunction.(1.4.4.1)	This recommendation has been deleted because advice on preventing and treating hypoglycaemia was considered more important. Assessment for cognitive difficulties is still covered by the following 2004 recommendation: Diabetes teams should consider referring children and young people with type 1 diabetes who have frequent hypoglycaemia and/or recurrent seizures for assessment of cognitive function, particularly if these occur at a young age. (1.2.85)
Children and young people with type 1 diabetes, especially young people using multiple daily injection regimens, should be offered structured behavioural intervention strategies because these may improve psychological well-being and glycaemic control. (1.4.7.2)	Replaced by: Offer specific family-based behavioural interventions, such as behavioural family systems therapy, if there are difficulties with diabetes-related family conflict. (1.2.100) Consider a programme of behavioural intervention therapy for children and young people with type 1 diabetes in whom there are concerns about psychological wellbeing in order to improve: <ul style="list-style-type: none"> • health-related quality of life - for example, counselling or cognitive behavioural therapy (CBT), including CBT focused on quality of life • adherence to diabetes treatment - for example, motivational interviewing or multi-systemic therapy • glycaemic control in children and young people with high HbA1c levels (HbA1c above 69 mmol/mol (above 8.5%)) - for example, multi-systemic therapy • self-esteem - for example, support strategies such as mentoring • depression - for example, motivational interviewing. (1.2.101)
Young people with type 1 diabetes should be offered specific support strategies, such as mentoring and self-monitoring of blood glucose levels supported by problem solving, to improve	Replaced by: Consider a programme of behavioural intervention therapy for children and young people with type 1 diabetes in whom there are

Recommendation in 2004 guideline	Comment
their self-esteem and glycaemic control. (1.4.7.3)	<p>concerns about psychological wellbeing in order to improve:</p> <ul style="list-style-type: none"> health-related quality of life - for example, counselling or cognitive behavioural therapy (CBT), including CBT focused on quality of life adherence to diabetes treatment - for example, motivational interviewing or multi-systemic therapy glycaemic control in children and young people with high HbA1c levels (HbA1c above 69 mmol/mol (above 8.5%)) - for example, multi-systemic therapy self-esteem - for example, support strategies such as mentoring depression - for example, motivational interviewing. (1.2.101)
Families of children and young people with type 1 diabetes should be offered specific support strategies (such as behavioural family systems therapy) to reduce diabetes-related conflict between family members. (1.4.7.4)	<p>Replaced by: Offer specific family-based behavioural interventions, such as behavioural family systems therapy, if there are difficulties with diabetes-related family conflict. (1.2.100)</p>
Teaching staff should be informed about the potential effects of type 1 diabetes on cognitive function and educational attainment (1.5.1.3)	<p>This recommendation has been deleted because it was considered more important to assess children and young people at increased risk of cognitive function disorders than to raise concerns about all children and young people with type 1 diabetes. This is covered in the following 2004 recommendation: Diabetes teams should consider referring children and young people with type 1 diabetes who have frequent hypoglycaemia and/or recurrent seizures for assessment of cognitive function, particularly if these occur at a young age. (1.2.85)</p>

A.2 Amended recommendation wording (change to meaning)

Recommendations are labelled **[2004, amended 2015]** if the evidence has not been reviewed but:

- changes have been made to the recommendation wording that change the meaning or
- NICE has made editorial changes to the original wording to clarify the action to be taken or
- the recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.

Recommendation numbers in the table refer to the numbering in the NICE guideline.

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
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Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<p>The diagnosis of type 1 diabetes in children and young people should be based on the criteria specified in the 1999 World Health Organization report on the diagnosis and classification of diabetes mellitus.[1]</p> <p>The symptoms and signs of type 1 diabetes include: hyperglycaemia (random blood glucose more than 11 mmol/litre), polyuria, polydipsia and weight loss. (1.1.1.1)</p>	<p>Be aware that the characteristics of type 1 diabetes include:</p> <ul style="list-style-type: none"> • hyperglycaemia (random plasma glucose more than 11 mmol/litre) • polyuria • polydipsia • weight loss. (1.1.1) <p>Confirm type 1 diabetes in children and young people using the criteria specified in the 2006 World Health Organization report on the diagnosis and classification of diabetes mellitus. (1.1.3)</p>	<p>The WHO updated their report on the diagnosis and classification of diabetes in 2006.</p> <p>In addition, this recommendation has been split into 2 recommendations to make it easier to understand.</p> <p>‘Symptoms and signs’ has been replaced with ‘characteristics’ as the GDG felt this was a more accurate term for the list of conditions in this recommendation.</p>
<p>Children and young people with suspected type 1 diabetes should be offered immediate (same day) referral to a multidisciplinary paediatric diabetes care team that has the competencies needed to confirm diagnosis and to provide immediate care. (1.1.1.2)</p>	<p>Refer children and young people with suspected type 1 diabetes immediately (on the same day) to a multidisciplinary paediatric diabetes care team with the competencies needed to confirm diagnosis and to provide immediate care. (1.1.2)</p>	<p>The action was changed from ‘offer’ to ‘refer’, as the 2012 NICE guidelines manual used to develop this update has a specific definition of the word ‘offer’ that was not used when the original 2004 guideline was published.</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<p>Consideration should be given to the possibility of other types of diabetes (such as early-onset type 2 diabetes, other insulin resistance syndromes, maturity-onset diabetes in the young and molecular/enzymatic abnormalities) in children and young people with suspected type 1 diabetes who:</p> <ul style="list-style-type: none"> • have a strong family history of diabetes • are obese at presentation • are of black or Asian origin • have an insulin requirement of less than 0.5 units/kg body weight/day outside a partial remission phase • have no insulin requirement • rarely or never produce ketone bodies in the urine (ketonuria) during episodes of hyperglycaemia • show evidence of insulin resistance (for example, acanthosis nigricans) • have associated features, such as eye disease, deafness, or another systemic illness or syndrome. (1.1.1.3) 	<p>Think about the possibility of type 2 diabetes in children and young people with suspected diabetes who:</p> <ul style="list-style-type: none"> • have a strong family history of diabetes • are obese at presentation • are of black or Asian family origin • have no insulin requirement, or have an insulin requirement of less than 0.5 units/kg body weight/day after the partial remission phase • show evidence of insulin resistance (for example, acanthosis nigricans). (1.1.5) <p>Think about the possibility of types of diabetes other than types 1 or 2 (such as other insulin resistance syndromes, maturity-onset diabetes in the young and molecular/enzymatic abnormalities) in children and young people with suspected diabetes who have any of the following features:</p> <ul style="list-style-type: none"> • rarely or never produce ketone bodies in the urine (ketonuria) during episodes of hyperglycaemia • have associated features, such as retinitis pigmentosa, deafness, or another systemic illness or syndrome. (1.1.6) 	<p>This recommendation has been split into two, as the GDG felt that type 2 diabetes should be considered separately from the rarer conditions now that it is covered in this guideline. In addition, not all of the factors listed applied to type 2 diabetes or to the rarer conditions. Because of this, the GDG felt that separating them into two lists makes it clearer which factors apply to which condition. In the second recommendation, 'eye disease' has been replaced with 'retinitis pigmentosa', as the GDG felt that 'eye disease' was not specific enough and could be mistaken for diabetic retinopathy.</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<p>Young people with type 1 diabetes should be encouraged to attend clinics on a regular basis (three or four times per year) because regular attendance is associated with good glycaemic control. (1.5.2.1)</p>	<p>Encourage young people with type 1 diabetes to attend clinic 4 times a year because regular contact is associated with good blood glucose control. (1.2.3)</p>	<p>The recommended number of contacts has been updated to reflect the Paediatric Diabetes Best Practice Tariff Criteria. In addition, 4 clinic attendances is standard in current clinical practice.</p>
<p>Children and young people with type 1 diabetes and their families should be informed that, as for other children, regular dental examinations^[2] and eye examinations (every 2 years) are recommended. (1.3.5.4)</p>	<p>Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that like others they are advised to have</p> <ul style="list-style-type: none"> • regular dental examinations (see the NICE guideline on dental recall) • an eye examination by an optician every 2 years. (1.2.4) 	<p>An explanation has been added to the bullet on eye examination to make it clear this refers to standard eye tests rather than retinopathy monitoring. In addition, 'recommended' has been changed to 'advised to have' as part of the editorial changes to make this sentence active.</p>
<p>Children and young people with type 1 diabetes and their families should be informed that the Department of Health⁷ recommends immunisation against pneumococcal infection for children and young people with diabetes over the age of 2 months. (1.2.11.2)</p>	<p>Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that the Department of Health's Green Book recommends immunisation against pneumococcal infection for children and young people with diabetes who need insulin or oral hypoglycaemic medicines. (1.2.17)</p>	<p>This recommendation has been updated to reflect guidance from the Department of Health's Green Book.</p>
<p>Children and young people with newly diagnosed type 1 diabetes</p>	<p>Explain to children and young people with newly diagnosed type 1 diabetes and their</p>	<p>This recommendation</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<p>should be informed that they may experience a partial remission phase (or 'honeymoon period') during which a low dosage of insulin (0.5 units/kg body weight/day) may be sufficient to maintain an HbA1c level of less than 7%. (1.1.3.1)</p>	<p>family members or carers (as appropriate) that they may experience a partial remission phase (a 'honeymoon period') during which a low dosage of insulin (0.5 units/kg body weight/day) may be sufficient to maintain an HbA1c level of less than 48 mmol/mol (6.5%). (1.2.25)</p>	<p>ion has been expanded to include family members or carers (as appropriate), as they may also be involved in the child or young person's treatment. In addition, the target HbA1c level has been updated to match the new recommendations on HbA1c target levels.</p>
<p>Children and young people with type 1 diabetes using insulin injection regimens should be offered needles that are of an appropriate length for their body fat (short needles are appropriate for children and young people with less body fat; longer needles are appropriate for children and young people with more body fat). (1.2.4.2)</p>	<p>Provide children and young people with type 1 with insulin injection needles that are of an appropriate length for their body fat. (1.2.27)</p>	<p>The information on what needle length is appropriate for a child has been deleted from this recommendation, as the GDG felt that this was well known and did not need defining in the recommendation.</p>
<p>Children and young people with type 1 diabetes should be offered:</p> <ul style="list-style-type: none"> • annual foot care reviews • investigation of the state of injection sites at each clinic visit. (1.3.5.3) 	<p>Offer children and young people with type 1 diabetes a review of injection sites at each clinic visit. (1.2.29)</p>	<p>The text on foot care has been removed from this recommendation, as it is covered by the new NICE guideline on diabetic foot care.</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<p>Children and young people with type 1 diabetes and their families should be informed that they have the same basic nutritional requirements as other children and young people. The food choices of children and young people should provide sufficient energy and nutrients for optimal growth and development, with total daily energy intake being distributed as follows:</p> <ul style="list-style-type: none"> • carbohydrates – more than 50% • protein – 10–15% • fat – 30–35%. <p>The consumption of five portions of fruit and vegetables per day is also recommended. Neonates, infants and pre-school children require individualised dietary assessment to determine their energy needs. (1.2.7.2)</p>	<p>Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that children and young people with type 1 diabetes have the same basic nutritional requirements as other children and young people. Children and young people's food should provide sufficient energy and nutrients for optimal growth and development. (1.2.36)</p>	<p>The text on total daily energy intake distribution and eating 5 portions of fruit and vegetables per day has been removed from this recommendation, as the 2015 recommendation 1.2.41 covers this. In addition, the specific energy intake levels were removed, as these are applicable to all children and not just those with type 1 diabetes.</p>
<p>Children and young people with type 1 diabetes should have their height and weight measured and plotted on an appropriate growth chart and their body mass index calculated at each clinic visit. The purpose of measuring and plotting height and weight and calculating body mass index is to check for normal growth and/or significant changes in weight because these may reflect changing glycaemic control. (1.3.5.5)</p>	<p>At each clinic visit for children and young people with type 1 diabetes:</p> <ul style="list-style-type: none"> • measure height and weight and plot on an appropriate growth chart • calculate body mass index. <p>Check for normal growth and/or significant changes in weight because these may reflect changing blood glucose control. (1.2.45)</p>	<p>This recommendation has been heavily edited for clarity, and the second part of the recommendation has been rewritten to make it easier to follow.</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<p>Children and young people with type 1 diabetes and their families should be informed about the effects of exercise on blood glucose levels and about strategies for preventing exercise-induced hypoglycaemia during and/or after physical activity. (1.2.8.4)</p>	<p>Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) about the effects of exercise on blood glucose levels and about strategies for avoiding hypo- or hyperglycaemia during or after physical activity. (1.2.49)</p>	<p>The term 'exercise-induced' has been removed from this recommendation, as the GDG felt that the cause of hypoglycaemia did not need stating here. In addition, hyperglycaemia caused by exercise has been added to this recommendation, as this is also a complication that children and young people with type 1 diabetes and their family members or carers (as appropriate) should be aware of. In addition, this recommendation has been expanded to include family members or carers (as appropriate), as they may also be involved in the child or young person's treatment.</p>
<p>Children and young people with type 1 diabetes should be offered testing of their HbA1c levels two to four times per year (more frequent testing may be appropriate if there is concern about poor glycaemic control).</p>	<p>Offer children and young people with type 1 diabetes measurement of their HbA1c level 4 times a year (more frequent testing may be appropriate if there is concern about poor blood glucose control). (1.2.72)</p>	<p>The recommended number of measurements has been updated to reflect the</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
(1.2.6.2)		Paediatric Diabetes Best Practice Tariff Criteria. In addition, 4 measurements a year is standard in current clinical practice.
Children and young people with type 1 diabetes, their parents and other carers should be informed that they should always have access to an immediate source of carbohydrate (glucose or sucrose) and blood glucose monitoring equipment for immediate confirmation and safe management of hypoglycaemia. (1.3.1.1)	Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that they should always have access to an immediate source of fast-acting glucose and blood glucose monitoring equipment for immediate confirmation and safe management of hypoglycaemia. (1.2.77)	The type of carbohydrate suitable for safe management of hypoglycaemia has been changed from 'glucose or sucrose' to 'fast-acting glucose', as the GDG felt this was what was recommended in current practice.

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<p>Parents and, where appropriate, school nurses and other carers should have access to glucagon for subcutaneous or intramuscular use in an emergency, especially when there is a high risk of severe hypoglycaemia. (1.3.1.6)</p>	<p>Family members or carers and, where appropriate, school nurses and other carers should be trained and equipped to give intramuscular glucagon for severe hypoglycaemia in an emergency. (1.2.78)</p>	<p>Subcutaneous glucagon has been removed from this recommendation, as the GDG did not think this was used in current practice. The recommendation has been reworded to make it clear that intramuscular glucagon would only be given for severe hypoglycaemia. In addition, 'have access' has been replaced with 'trained and equipped', as the GDG felt that this was an important point that was left out of the original recommendation.</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<p>Children and young people with mild to moderate hypoglycaemia should be treated as follows.</p> <ul style="list-style-type: none"> • Take immediate action. • The first line of treatment should be the consumption of rapidly absorbed simple carbohydrate (for example, 10–20 g carbohydrate given by mouth). • The simple carbohydrate should raise blood glucose levels within 5–15 minutes. • Carbohydrate given in liquid form may be taken more easily. • It may be appropriate to give small amounts of rapidly absorbed simple carbohydrate frequently because hypoglycaemia may cause vomiting. • As symptoms improve or normoglycaemia is restored additional complex long-acting carbohydrate should be given orally to maintain blood glucose levels unless a snack or meal is imminent. • Additional complex long-acting carbohydrate is not required for children and young people using continuous subcutaneous insulin infusion. • Blood glucose levels should be rechecked within 15 minutes. (1.3.1.4) 	<p>Immediately treat mild to moderate hypoglycaemia in children and young people as follows.</p> <ul style="list-style-type: none"> • Give fast-acting glucose (for example, 10-20 g) by mouth (liquid carbohydrate may be taken more easily than solid). • Be aware that fast-acting glucose may need to be given in frequent small amounts, because hypoglycaemia can cause vomiting. • Recheck blood glucose levels within 15 minutes (fast-acting glucose should raise blood glucose levels within 5-15 minutes). • As symptoms improve or normoglycaemia is restored, give oral complex long-acting carbohydrate to maintain blood glucose levels, unless the child or young person is: <ul style="list-style-type: none"> ○ about to have a snack or meal ○ receiving a continuous subcutaneous insulin infusion. (1.2.79) 	<p>This recommendation has been reworded and reordered to make it easier to understand. In addition, the type of carbohydrate suitable for safe management of hypoglycaemia has been changed from 'glucose or sucrose' to 'fast-acting glucose', as the GDG felt this was what was recommended in current practice.</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<p>Children and young people with severe hypoglycaemia should be treated as follows.</p> <ul style="list-style-type: none"> • In a hospital setting, 10% intravenous glucose should be used when rapid intravenous access is possible (up to 500 mg/kg body weight – 10% glucose is 100 mg/ml). • Outside hospital, or where intravenous access is not practicable, intramuscular glucagon or concentrated oral glucose solution (e.g. Hypostop) may be used. • Children and young people over 8 years old (or body weight more than 25 kg) should be given 1 mg glucagon. • Children under 8 years old (or body weight less than 25 kg) should be given 500 micrograms of glucagon. • Blood glucose levels should respond within 10 minutes. • As symptoms improve or normoglycaemia is restored, in children and young people who are sufficiently awake, additional complex long-acting carbohydrate should be given orally to maintain blood glucose levels. 	<p>Treat severe hypoglycaemia in children and young people who are in hospital and in whom rapid intravenous access is possible by giving 10% intravenous glucose. Give a maximum dose of 500 mg/kg body weight (equivalent to a maximum of 5 ml/kg). (1.2.80)</p> <ul style="list-style-type: none"> • Treat severe hypoglycaemia in children and young people who are not in hospital or who do not have rapid intravenous access available as follows. • Use intramuscular glucagon or concentrated oral glucose solution (for example Glucogel®). Do not use oral glucose solution if the level of consciousness is reduced as this could be dangerous. • If using intramuscular glucagon: <ul style="list-style-type: none"> ○ give children and young people over 8 years old (or who weigh more than 25 kg) 1 mg glucagon. ○ give children under 8 years old (or who weigh less than 25 kg) 500 micrograms of glucagon. 	<p>This recommendation has been reworded, reordered, and split into 2 separate recommendations to make it easier to understand.</p> <p>In addition, the action in the section on intramuscular glucagon and concentrated oral glucose solution has changed from 'may be used' to 'Use'. This is because the GDG felt that these 2 were the only standard treatment options rather than 2 options out of several, as was suggested by the original wording.</p> <p>The reference to 'Hypostop' has been changed to 'Glucogel', as the GDG felt that this was the preparation commonly used in clinical practice.</p> <p>A warning on using oral glucose solution in children with reduced levels of consciousness has been added, as the GDG felt that</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<ul style="list-style-type: none"> Some children and young people may continue to have reduced consciousness for several hours after a severe hypoglycaemic episode, and repeat blood glucose measurements will be required to determine whether further glucose is necessary. Medical assistance should be sought for children and young people whose blood glucose levels fail to respond and those in whom symptoms persist for more than 10 minutes. (1.3.1.5) 	<ul style="list-style-type: none"> Seek medical assistance if blood glucose levels do not respond or symptoms persist for more than 10 minutes. As symptoms improve or normoglycaemia is restored, and once the child or young person is sufficiently awake, give oral complex long-acting carbohydrate to maintain blood glucose levels. Recheck the blood glucose repeatedly in children and young people who have persistently reduced consciousness after a severe hypoglycaemic episode, to determine whether further glucose is needed. (1.2.81) 	
<p>Young people with type 1 diabetes should be informed about the specific effects of alcohol consumption on glycaemic control, particularly the risk of (nocturnal) hypoglycaemia. (1.2.9.1)</p>	<p>Explain to young people with type 1 diabetes the effects of alcohol consumption on blood glucose control, and in particular that there is an increased risk of hypoglycaemia including hypoglycaemia while sleeping. (1.2.82)</p>	<p>The term 'nocturnal hypoglycaemia' has been changed to 'hypoglycaemia while sleeping', as the GDG did not think the original term was common in clinical practice.</p>
<p>Non-adherence to therapy should be considered in children and young people with type 1 diabetes who have poor glycaemic control, especially in adolescence. (1.4.6.1)</p>	<p>Think about the possibility of non-adherence to therapy in children and young people with type 1 diabetes who have poor blood glucose control, especially in adolescence. (1.2.86)</p>	<p>The action was changed from 'consider' to 'think about', as the 2012 NICE guidelines manual used to develop this update has a specific definition of the word 'consider' that was not used when the original 2004 guideline was published.</p>
<p>Diabetes care teams should be aware that children and young people with type 1 diabetes have a greater risk of emotional and behavioural problems than other children and young people.</p>	<p>Diabetes teams should be aware that children and young people with type 1 diabetes have a greater risk of emotional and behavioural difficulties. (1.2.93)</p>	<p>This recommendation has been amended, as the original suggested</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
(1.4.1.1)		that children and young people with type 1 diabetes have a greater risk of emotional and behavioural problems than all other children and young people, which is not the case.
Young people with 'brittle diabetes' (that is, those who present with frequent episodes of diabetic ketoacidosis over a relatively short time) should have their emotional and psychological well-being assessed. (1.4.6.3)	Assess the emotional and psychological well-being of young people with type 1 diabetes who present with frequent episodes of diabetic ketoacidosis. (1.2.95)	The term 'brittle diabetes' has been removed from this recommendation, as the GDG felt that this term was no longer commonly used in clinical practice.
Children and young people with type 1 diabetes and their families should be offered timely and ongoing access to mental health professionals because they may experience psychological disturbances (such as anxiety, depression, behavioural and conduct disorders and family conflict) that can impact on the management of diabetes and well-being. (1.4.7.5)	Offer children and young people with type 1 diabetes and their family members or carers (as appropriate) timely and ongoing access to mental health professionals because they may experience psychological problems (such as anxiety, depression, behavioural and conduct disorders and family conflict) that can impact on the management of diabetes and well-being. See also the NICE guidelines on depression in children and young people and antisocial behaviour and conduct disorders in children and young people. (1.2.97)	A cross-reference to the NICE guidelines on depression in children and young people and antisocial behaviour and conduct disorders in children and young people has been added for information.
Diabetes care teams should be aware that children and young people with type 1 diabetes, in particular young women, have an increased risk of eating disorders. (1.4.3.1)	Diabetes teams should be aware that children and young people with type 1 diabetes, in particular young women, have an increased risk of eating disorders. See also the NICE guideline on eating disorders. (1.2.105)	A cross-reference to the NICE guideline on eating disorders has been added for information.
Diabetes care teams should be aware that children and young	Be aware that children and young people with type 1 diabetes who have eating disorders	The terms 'persistent

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<p>people with type 1 diabetes who have eating disorders may have associated problems of persistent hyperglycaemia, recurrent hypoglycaemia and/or symptoms associated with gastric paresis. (1.4.3.2)</p>	<p>may have associated difficulties with</p> <ul style="list-style-type: none"> • poor blood glucose control (both hyperglycaemia and hypoglycaemia) • symptoms of gastroparesis. (1.2.106) 	<p>hyperglycaemia' and 'recurrent hypoglycaemia' have been replaced with the text on poor blood glucose control, covering both hyperglycaemia and hypoglycaemia. This is because the GDG felt that these two complications are both indicative of 'poor blood glucose control', so it would be simpler to use this phrase in the recommendation.</p> <p>In addition, the phrase 'symptoms associated with gastric paresis' has been changed, as the GDG felt that the use of 'associated' made this recommendation vague. 'gastric paresis' has been changed to 'gastroparesis', as this is the term currently used in practice.</p>
<p>Children and young people with type 1 diabetes in whom eating</p>	<p>For children and young people with type 1 diabetes in whom eating disorders are</p>	<p>This recommendat</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<p>disorders are identified by their diabetes care team should be offered joint management involving their diabetes care team and child mental health professionals. (1.4.3.3)</p>	<p>identified, offer joint management involving their diabetes team and child mental health professionals. (1.2.107)</p>	<p>ion has been amended as healthcare professionals outside of the diabetes team (such as GPs) can also identify eating disorders.</p>
<p>Children and young people with type 1 diabetes and their families should be informed that, as for other children, regular dental examinations[3] and eye examinations (every 2 years) are recommended. (1.3.5.4)</p>	<p>Explain to children and young people with type 2 diabetes and their family members or carers (as appropriate) that like others they are advised to have:</p> <ul style="list-style-type: none"> • regular dental examinations[4] • an eye examination by an optician every 2 years. (1.3.3) 	<p>An explanation has been added to the bullet on eye examination to make it clear this refers to standard eye tests rather than retinopathy monitoring. 'recommended' has been changed to 'advised to have' as part of the editorial changes to make this sentence active. In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<p>Children and young people with type 1 diabetes and their families should be offered information about the existence of and means of contacting local and/or national diabetes support groups and organisations, and the potential benefits of membership. This should be done in the time following diagnosis and periodically thereafter. (1.5.1.1)</p>	<p>Give children and young people with type 2 diabetes and their family members or carers (as appropriate) information about local and/or national diabetes support groups and organisations, and the potential benefits of membership. Give this information after diagnosis and regularly afterwards. (1.3.5)</p>	<p>NICE has made editorial changes to the original wording to clarify the action to be taken (no change to meaning): a verb has been added, or the verb used has been changed.</p> <p>In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.</p>
<p>Children and young people with type 1 diabetes and their families should be advised how to obtain information about benefits in relation to government disability support. (1.5.1.4)</p>	<p>Explain to children and young people with type 2 diabetes and their family members or carers (as appropriate) how to find information about possible benefits from government disability support. (1.3.6)</p>	<p>The word 'possible' has been added, as the benefits available to children and young people with type 2 diabetes can be different to those available to children and young people with type 1 diabetes.</p> <p>In addition, this recommendation originally only applied</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
		to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.
<p>Children and young people with type 1 diabetes and their families should be informed that the Department of Health[5] recommends annual immunisation against influenza for children and young people with diabetes over the age of 6 months. (1.2.11.1)</p>	<p>Explain to children and young people with type 2 diabetes and their family members or carers (as appropriate) that the Department of Health's Green Book recommends annual immunisation against influenza for children and young people with diabetes. (1.3.12)</p>	<p>These recommendations originally only applied to type 1 diabetes in children and young people, but have been included in the section of this guideline on type 2 diabetes as they are applicable to this population.</p> <p>In addition, 'over 6 months' has been taken out of this recommendation, as type 2 diabetes normally only occurs in young people or adults, and never in children under 6 months.</p>
<p>Children and young people with type 1 diabetes and their families should be informed that the Department of Health⁷ recommends immunisation</p>	<p>Explain to children and young people with type 2 diabetes and their family members or carers (as appropriate) that the Department of Health's Green Book recommends immunisation against pneumococcal infection</p>	<p>This recommendation has been updated to reflect</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<p>against pneumococcal infection for children and young people with diabetes over the age of 2 months. (1.2.11.2)</p>	<p>for children and young people with diabetes who need insulin or oral hypoglycaemia medicines. (1.3.13)</p>	<p>guidance from the Department of Health's Green Book.</p> <p>In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.</p> <p>In addition, 'over the age of 2 months' has been taken out of this recommendation, as type 2 diabetes normally only occurs in young people or adults, and never in children under 2 months.</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
<p>Children and young people with type 1 diabetes should have their height and weight measured and plotted on an appropriate growth chart and their body mass index calculated at each clinic visit. The purpose of measuring and plotting height and weight and calculating body mass index is to check for normal growth and/or significant changes in weight because these may reflect changing glycaemic control. (1.3.5.5)</p>	<p>At each clinic visit for children and young people with type 2 diabetes:</p> <ul style="list-style-type: none"> • measure height and weight and plot on an appropriate growth chart • calculate body mass index. <p>Check for normal growth and/or significant changes in weight because these may reflect changing blood glucose control. (1.3.20)</p>	<p>This recommendation has been heavily edited for clarity, and the second part of the recommendation has been rewritten to make it easier to follow.</p> <p>In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.</p>
<p>Diabetes care teams should be aware that children and young people with type 1 diabetes have a greater risk of emotional and behavioural problems than other children and young people. (1.4.1.1)</p>	<p>Diabetes teams should be aware that children and young people with type 2 diabetes have a greater risk of emotional and behavioural difficulties. (1.3.31)</p>	<p>This recommendation has been amended, as the original suggested that children and young people with diabetes have a greater risk of emotional and behavioural problems than all other children and young people, which is not the case.</p> <p>In addition, this</p>

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
		recommendation originally only applied to type 1 diabetes in children and young people, but has been amended to include type 2 diabetes as it is applicable to this population.
Children with type 1 diabetes who are younger than 2 years of age and children and young people who have social or emotional difficulties, or who live a long way from hospital should be offered inpatient initial management. (1.1.2.6)	Offer initial inpatient management to children with diabetes who are aged under 2 years. (1.5.5) Think about initial inpatient management for children and young people with diabetes if there are social or emotional factors that would make home-based management inappropriate, or if they live a long distance from the hospital. (1.5.6)	This recommendation has been split into 2 recommendations to make the differences in care for the 2 populations clearer. In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been amended to include type 2 diabetes as it is applicable to this population.
	1.2.21, 1.2.23, 1.2.24	The terms 'preprandial' and 'postprandial' have been changed to 'pre-meal', 'before meals', and 'after meals' when appropriate, as the GDG felt that these

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
		terms are simpler and more commonly used.
	1.2.21, 1.2.22, 1.2.23, 1.2.24, 1.2.25, 1.2.39, 1.2.50	These recommendations have been expanded to include family members or carers (as appropriate), as they may also be involved in the child or young person's treatment.
	1.2.6, 1.2.22, 1.2.33, 1.2.92, 1.2.96, 1.2.109, 1.4.64, 1.5.7, 1.5.12	NICE has made editorial changes to the original wording to clarify the action to be taken (no change to meaning): a verb has been added, or the verb used has been changed.
	1.3.7, 1.3.8, 1.3.9, 1.3.10, 1.3.11, 1.3.16, 1.3.21, 1.3.29, 1.3.30, 1.3.32, 1.3.34, 1.3.35, 1.3.36, 1.3.37, 1.3.38, 1.5.1, 1.5.2, 1.5.3, 1.5.4, 1.5.5, 1.5.6, 1.5.8, 1.5.9, 1.5.10	These recommendations originally only applied to type 1 diabetes in children and young people, but have been included in the section of this guideline on type 2 diabetes as they are applicable to this population.

a[1] World Health Organization (1999)

Recommendation in 2004 guideline	Recommendation in current guideline	Reason for change
a[2]	Dental recall: Recall interval between routine dental examinations. NICE clinical guideline 19 (2004).	
a[3]	Dental recall: Recall interval between routine dental examinations. NICE clinical guideline 19 (2004).	
a[4]	Dental recall: Recall interval between routine dental examinations (2004) NICE guideline CG19	
a[5]	Salisbury, D. M. and Department of Health, Welsh Office, Scottish Office Department of Health, DHSS (Northern Ireland): 1996. Update for pneumococcal vaccination.	

A.3 Changes to recommendation wording for clarification only (no change to meaning)

Recommendation numbers in the table refer to the numbering in the NICE guideline.

Recommendation numbers in current guideline	Comment
All recommendations except those labelled [new 2015]	Recommendations have been edited into the direct style (in line with current NICE style for recommendations in clinical guidelines) where possible. Yellow highlighting has not been applied to these changes. Where applicable, terminology has been made consistent within the guideline and with terminology that will be used in other updates of NICE guidelines on diabetes (diabetes in pregnancy [publication expected February 2015], type 1 diabetes and type 2 diabetes [publication expected August 2015]) – for example, ‘impaired awareness of hypoglycaemia’ rather than ‘hypoglycaemia unawareness’; ‘blood glucose control’ rather than ‘glycaemic control’.
1.2.9	This recommendation has been updated to use modern disability terminology.
1.2.22	(CSII or insulin pump) is specified for clarity (original wording did not mention insulin pumps).
1.2.97, 1.3.35	The term ‘psychological disturbances’ has been rephrased to ‘psychological problems’ to avoid putting a negative emphasis on mental health conditions.
1.2.98, 1.3.36	The term ‘assessment of psychological dysfunction’ has been rephrased to ‘psychological assessment’ to avoid putting a negative emphasis on mental health assessment and treatment.
1.2.21, 1.2.22, 1.2.23, 1.2.76, 1.2.79, 1.2.80, 1.2.81, 1.2.87, 1.2.88, 1.2.95	Type 1 diabetes is specified for clarity (original wording had ‘diabetes’ or did not specify diabetes at all).

Appendix B: 2015 update scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Diabetes in children and young people: diagnosis and management of type 1 and type 2 diabetes in children and young people

1.1 Short title

Diabetes in children and young people

2 The remit

This is an update of [Type 1 diabetes](#) (NICE clinical guideline 15). See section 4.3.1 for details of which sections will be updated for children and young people. We will also carry out an editorial review of all recommendations to ensure that they comply with NICE's duties under equalities legislation.

This update is being undertaken as part of the guideline review cycle.

The guideline is also being extended to cover type 2 diabetes in children and young people.

This is the scope for 1 of 4 NICE clinical guidelines being developed that address diabetes care. Included below is a summary of the content for each guideline and of the NICE steering committee.

Guideline 1 – Diabetes in children and young people (developed by the National Collaborating Centre for Women's and Children's Health)

This guideline will update [Type 1 diabetes in children, young people and adults](#) (NICE clinical guideline 15). It will cover the diagnosis and management of type 1 and type 2 diabetes in children and young people (younger than 18 years). It will include: structured education programmes, behavioural interventions to improve adherence, glucose monitoring strategies, ketone

monitoring, insulin regimens for type 1 diabetes and metformin monotherapy for type 2 diabetes.

Guideline 2 – Diabetes in pregnancy (developed by the National Collaborating Centre for Women’s and Children’s Health)

This guideline will update [Diabetes in pregnancy](#) (NICE clinical guideline 63). It will cover women of reproductive age who have pre-existing diabetes or who develop diabetes during pregnancy and it will also cover their newborn babies. It will include: target glucose ranges in the preconception period and during pregnancy, glucose monitoring strategies during pregnancy, screening, diagnosis and treatment of gestational diabetes, and postnatal testing for type 2 diabetes.

Guideline 3 – Type 1 diabetes in adults (developed by the National Clinical Guideline Centre)

This guideline will update [Type 1 diabetes in children, young people and adults](#) (NICE clinical guideline 15). It will cover adults (18 years or older) with type 1 diabetes. It will include: tests to differentiate type 1 diabetes from type 2 diabetes, structured education programmes, clinical monitoring of glucose control, insulin regimens, ketone monitoring, dietary advice on carbohydrate counting and glycaemic index, and treatment and monitoring of specific complications.

Guideline 4 –Type 2 diabetes in adults (developed by the Internal Clinical Guidelines Programme, Centre for Clinical Practice, NICE)

This guideline will update [Type 2 diabetes](#) (NICE clinical guideline 66) and [Type 2 diabetes: newer agents](#) (NICE clinical guideline 87). It will cover adults (18 years or older) with type 2 diabetes. It will include: pharmacological management of blood glucose levels, target values for blood glucose control, self-monitoring of blood glucose levels for blood glucose control, antithrombotic therapy and drug therapy for erectile dysfunction.

NICE steering committee

NICE has set up a steering committee to oversee the production of these clinical guidelines. The group, which includes the Guideline Development Groups' chairs, together with staff from the 3 guidance-producing centres and NICE, will identify and act on any gaps or overlaps across the different guidance topics to ensure that the final guidelines are complementary and consistent. It is intended that the guidance-producing centres will share systematic reviews and cross-refer to recommendations in the other guidelines where appropriate. This update is being undertaken as part of the guideline review cycle.

3 Clinical need for the guideline

3.1 *Epidemiology*

3.1.1 Type 1 diabetes

- a) Type 1 diabetes is an autoimmune disorder resulting in the destruction of insulin-producing cells in the pancreas. It is predominantly diagnosed in children and young people and inevitably needs insulin replacement treatment.
- b) Around 26,500 children and young people in the UK are estimated to have type 1 diabetes needing insulin replacement therapy.
- c) Most children and young people diagnosed with type 1 diabetes do not have a family member with the condition, although there may be related disorders such as thyroid or rheumatoid disease in the family. However, a family history of type 1 diabetes does increase a child's risk of developing type 1 diabetes. For children with an identical twin with type 1 diabetes, the risk of developing the disorder is 1 in 3, for children with a father with type 1 diabetes the risk is 1 in 16, and for children with a mother with type 1 diabetes the risk is 1 in 40. By comparison, the population risk is roughly 1 in 500, although this varies with geographical location.

- d) Children and young people with type 1 diabetes have poorer glucose control and the higher rates of acute metabolic complications such as diabetic ketoacidosis in comparison with children and young people with type 2 diabetes. Nine per cent of children and young people with diabetes experienced at least 1 episode of diabetic ketoacidosis in 2009–2010.
- e) Systems of surveillance for the early detection of complications in children and young people with type 1 diabetes are important, as is effective management of late complications when they occur.
- f) Good blood glucose control is known to prevent or delay the long-term complications of both type 1 and type 2 diabetes.

3.1.2 Type 2 diabetes

- g) In 2011, around 300 children and young people in the UK had a confirmed diagnosis of type 2 diabetes.
- h) Type 2 diabetes is initially an insulin-resistant state, the primary treatment for which is weight loss and exercise. Pharmacological measures to increase insulin sensitivity or to increase insulin release can be added to lifestyle interventions, but insulin may be needed because of the continuing failure of insulin secretion. Like type 1 diabetes, type 2 diabetes has a significant impact on lifestyle in the short term, and is associated with major long-term complications and reduced life expectancy.
- i) Obesity is the most common risk factor for type 2 diabetes. Type 2 diabetes is more common in people of South Asian, Chinese, black African and African–Caribbean origin. In Europeans, type 2 diabetes in children is associated with the most severe degrees of obesity.
- j) People from the most deprived socioeconomic backgrounds are 2.5 times more likely than average to have type 2 diabetes at any given age.

3.2 Current practice

- a) Fewer than 20% of children and young people with diabetes receive the basic care recommended by NICE guidelines.
- b) Current standard care for children and young people with diabetes includes patient education, dietary advice, psychological support and management of complications.
- c) Standard care for children and young people with type 1 diabetes also includes insulin therapy.
- d) For children and young people with type 2 diabetes, first-line care often includes advice on the need for weight loss and the importance of adopting a healthy lifestyle. Metformin may also be used to improve glycaemic control by increasing insulin sensitivity. If good glycaemic control is not achieved then additional insulin or other agents may be needed.
- e) The aim of patient education is to enable children and young people and their parents or carers to live a normal life and minimise the risk of complications. It includes advice on diet, improving glycaemic control and how complications are managed.
- f) Management of hypoglycaemia depends on its severity. Hospital care may be needed if the child or young person is unresponsive or unconscious, but some children and young people can be cared for at home.
- g) It is considered good practice that children and young people with diabetes receive an integrated package of care and that this is delivered by a multidisciplinary care team with expertise in paediatric diabetes, including its clinical, educational, dietetic, lifestyle and psychological management.
- h) Children and young people with type 1 diabetes are monitored for growth and pubertal development, blood pressure, injection site

complications, thyroid disease and coeliac disease. Long-term glycaemic control is monitored using haemoglobin A_{1c} (HbA_{1c}). From the age of 12 years they are also monitored for retinopathy and nephropathy by the measurement of microalbuminuria. Rare associated conditions (juvenile cataracts, necrobiosis lipoidica, rheumatoid disease and Addison's disease, among others) may also be considered.

- i) Children and young people with type 1 or type 2 diabetes receive annual foot care reviews from the age of 12 years. Minor problems (ingrown toenails or verrucas) are common and may be treated by a chiropodist. Serious foot problems are very rare in children and young people.
- j) Psychological and social issues are also important to consider at each clinic visit, and treatment or advice is given where necessary.
- k) There is a process of transition so that from the age of 13 years, young people are prepared for eventual transfer to adult care. This includes agreed protocols and joint clinics if possible. Young people are given time to familiarise themselves with this process and it is only completed when they are ready to move to adult services. The timing of transition depends on the young person's physical development, emotional maturity, stability of health, other life changes and local circumstances.
- l) Since the publication of [Type 1 diabetes](#) (NICE clinical guideline 15), new evidence has been published (or is anticipated) to warrant reconsideration of the following areas of care for children and young people with type 1 diabetes:
 - structured education programmes
 - behavioural interventions to improve adherence
 - insulin regimens (multiple daily injections versus mixed insulin injections)
 - strategies for glucose and ketone monitoring

- dietetic advice
 - recognition and management of diabetic ketoacidosis
 - recognition of complications and comorbidities.
- m) Consideration is also being given to the following areas of care for children and young people with type 2 diabetes based on clinical priorities and likely availability of evidence:
- structured education programmes
 - behavioural interventions to improve adherence
 - dietetic advice
 - weight management
 - metformin monotherapy
 - targets for HbA_{1c}
 - recognition and management of diabetic ketoacidosis
 - recognition of complications and comorbidities.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

- a) Children and young people (younger than 18 years) with type 1 diabetes.

- b) Children and young people (younger than 18 years) with type 2 diabetes (new 2012).
- c) Where the evidence supports it, the following subgroups will be given special consideration:
 - children and young people with an ethnicity associated with a high prevalence of diabetes
 - disabilities (including learning disabilities)
 - children and young people with comorbidities (medical or psychological conditions)
 - children and young people with poor educational achievement.

4.1.2 Groups that will not be covered

- a) Young women with diabetes who wish to conceive or who are pregnant.
- b) Children and young people with other forms of diabetes mellitus (for example, monogenic diabetes and cystic fibrosis-related diabetes) (new 2012).
- c) Adults (aged 18 years and older) with type 1 diabetes.
- d) Adults (aged 18 years and older) with type 2 diabetes.

4.2 Healthcare setting

All settings in which NHS care is received or commissioned.

The guideline will address the support and advice that the NHS should offer to crèches, nurseries, schools and other institutions.

The guideline will also be relevant to the work, but will not cover the practice, of:

- social services and the voluntary sector

- services supplied by secondary and tertiary specialties for late complications of diabetes (for example, renal, cardiology, urology and ophthalmology services) to which patients have been referred
- the education sector.

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

Areas from the original guideline that will be updated

- a) The role of c-peptide and antibody testing in the diagnosis of type 1 and type 2 diabetes.
- b) Structured education programmes for children and young people with type 1 diabetes.
- c) Behavioural interventions to improve adherence in children and young people with type 1 diabetes.
- d) Multiple daily injections versus mixed insulin injections in children and young people with type 1 diabetes.
- e) HbA_{1c} targets for children and young people with type 1 diabetes.
- f) Glucose monitoring strategies in children and young people with type 1 diabetes, including:
 - blood glucose targets
 - frequency of intermittent testing (finger-prick read by meter)
 - continuous glucose monitoring with retrospective (intermittent) versus real-time (long-term) adjustment of treatment.

- g) Blood ketone monitoring compared with urine ketone monitoring in children and young people with type 1 diabetes.
- h) Dietetic advice, including carbohydrate counting and glycaemic index, for children and young people with type 1 diabetes.
- i) Recognition and management of diabetic ketoacidosis in children and young people with type 1 diabetes:
 - recognition based on symptoms, signs and biochemical abnormalities
 - immediate management at presentation (for example, maintenance of airway, breathing and circulation or the potential need for a nasogastric tube to prevent pulmonary aspiration)
 - clinical assessment and investigations at presentation to guide management
 - fluid management, including:
 - assessment of dehydration
 - route of administration
 - rate and volume of administration
 - choice of fluid
 - other additives (for example, glucose, potassium and bicarbonate)
 - insulin therapy, including:
 - timing
 - route of administration
 - dosage
 - anticoagulant prophylaxis to prevent venous thrombosis
 - clinical monitoring (to assess the response to treatment and to look for evidence of cerebral oedema), including:
 - general observations (for example, heart and respiratory rate and blood pressure)
 - body weight
 - hydration status

- fluid balance
 - neurological observations
 - electrocardiographic (ECG) monitoring
 - laboratory monitoring (to assess the response to treatment and to look for evidence of hypokalaemia), including:
 - blood glucose
 - blood or urine ketones
 - serum urea and electrolytes
 - acid/base status.
- j) Recognition of complications and comorbidities in children and young people with type 1 diabetes (retinopathy and nephropathy).

Areas not in the original guideline that will be included in the update

- k) Structured education programmes for children and young people with type 2 diabetes.
- l) Behavioural interventions to improve adherence in children and young people with type 2 diabetes.
- m) Dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes.
- n) Weight management in children and young people with type 2 diabetes who are overweight or obese to improve glycaemic control.
- o) Metformin monotherapy for children and young people with type 2 diabetes.
- p) HbA_{1c} targets for children and young people with type 2 diabetes.
- q) Recognition and management of diabetic ketoacidosis in children and young people with type 2 diabetes (the specific aspects to be

covered for this area will be the same as those in section 4.3.1, point h)).

- r) Recognition of complications and comorbidities in children and young people with type 2 diabetes (hypertension, dyslipidaemia, retinopathy and nephropathy).

4.3.2 Clinical issues that will not be covered

Areas from the original guideline that will not be updated

The following areas addressed in [Type 1 diabetes](#) (NICE clinical guideline 15) will not be updated (the existing recommendations will remain as current guidance):

- a) All aspects of diagnosis and initial management in children and young people other than those listed in section 4.3.1, including:
- location of initial management after diagnosis
 - advice on the natural history of type 1 diabetes.
- b) All aspects of ongoing management other than those listed in section 4.3.1, including:
- insulin preparations, including new short- and long-acting insulins
 - methods of delivering insulin
 - metformin in addition to insulin for type 1 diabetes
 - exercise
 - advice on alcohol, smoking and recreational drugs
 - long-distance travel
 - immunisation.
- c) All aspects of complications and associated conditions other than those listed in section 4.3.1, including:
- hypoglycaemia
 - care during surgery

- monitoring for complications and comorbidities of type 1 diabetes other than those specified.
- d) All aspects of psychological and social issues other than those listed in section 4.3.1, including:
- emotional and behavioural problems, anxiety, depression and eating disorders
 - cognitive disorders
 - behavioural and conduct disorders
 - psychosocial support
 - adolescence.
- e) Continuity of care, including:
- communication between organisations
 - transition from paediatric to adult care.

Areas not covered by the original guideline or the update

- f) Management of hypoglycaemia unawareness in children and young people with type 1 diabetes.
- g) Glycaemic monitoring strategies for children and young people with type 2 diabetes.
- h) Treatment for children and young people with type 2 diabetes in whom glycaemic control is not maintained with metformin.
- i) Bariatric surgery for children and young people with type 2 diabetes.
- j) Monitoring for complications and comorbidities of type 2 diabetes other than those specified in section 4.3.1.
- k) Management of complications and comorbidities of type 1 or type 2 diabetes.

- l) Contraceptive, pre-pregnancy and conception advice for children and young people with type 1 or type 2 diabetes.
- m) Foot care for children and young people with type 1 or type 2 diabetes.

4.4 Main outcomes

- a) Glycaemic control.
- b) Any adverse effects of interventions used to manage type 1 or type 2 diabetes.
- c) Health-related quality of life (validated questionnaire), for example, diabetes-specific health-related quality of life.
- d) Complications of diabetes.
- e) Mortality.
- f) Psychological outcomes.
- g) Patient satisfaction.

4.5 Review questions

These are draft review questions and the final questions will be agreed by the Guideline Development Group during development.

Type 1 diabetes

- What is the effectiveness of c-peptide and antibody tests to distinguish type 1 and type 2 diabetes?
- What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?
- What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 1 diabetes?

- What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?
- What is the optimal HbA_{1c} target for children and young people with type 1 diabetes?
- What are the optimal blood glucose targets for children and young people with type 1 diabetes?
- How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?
- What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?
- What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis?
- What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?
- What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?
- What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?
- What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?
- What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?
- At what rate should children and young people with diabetic ketoacidosis be rehydrated?
- What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

- When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?
- How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?
- What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?
- Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:
 - general observations (for example, heart and respiratory rate and blood pressure)
 - body weight
 - hydration status
 - fluid balance
 - neurological observations
 - ECG monitoring?
- Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:
 - blood glucose
 - blood or urine ketones
 - serum urea or electrolytes
 - acid/base status?
- What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?
- What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?

Type 2 diabetes

- What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?

- What is the effectiveness of behavioural interventions to promote engagement with clinical services in children and young people with type 2 diabetes?
- What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 2 diabetes?
- What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?
- Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA_{1c}?
- What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?
- What is the optimal HbA_{1c} target for children and young people with type 2 diabetes?
- What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?
- What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?
- What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?
- At what rate should children and young people with diabetic ketoacidosis be rehydrated?
- What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?
- When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?
- How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

- What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?
- Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:
 - general observations (for example, heart and respiratory rate and blood pressure)
 - body weight
 - hydration status
 - fluid balance
 - neurological observations
 - ECG monitoring?
- Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:
 - blood glucose
 - blood or urine ketones
 - serum urea or electrolytes
 - acid/base status?
- What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?
- What is the optimal monitoring strategy for identifying dyslipidaemia in children and young people with type 2 diabetes?
- What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?
- What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

4.6 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and

analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see 'Further information').

4.7 Status

Scope

This is the final scope.

Timing

The development of the guideline recommendations will begin in October 2012.

5 Related NICE guidance

5.1 Published guidance

Related NICE guidance

- [Preventing type 2 diabetes: risk identification and interventions for individuals at high risk](#). NICE public health guidance 38 (2012).
- [Anxiety](#). NICE clinical guideline 113 (2011).
- [Preventing type 2 diabetes: population and community interventions](#). NICE public health guidance 35 (2011).
- [Depression with a chronic physical health problem](#). NICE clinical guideline 91 (2010).
- [Type 2 diabetes](#). NICE clinical guideline 87 (2009).
- [Coeliac disease](#). NICE clinical guideline 86 (2009).
- [Medicines adherence](#). NICE clinical guideline 76 (2009).
- [Promoting physical activity for children and young people](#). NICE public health guidance 17 (2009).
- [Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus](#). NICE technology appraisal guidance 151 (2008).

- [Obesity](#). NICE clinical guideline 43 (2006).
- [Four commonly used methods to increase physical activity](#). NICE public health guidance 2 (2006).
- [Type 2 diabetes: footcare](#). NICE clinical guideline 10 (2004).
- [Guidance on the use of patient-education models for diabetes](#). NICE technology appraisal guidance 60 (2003).
- [Guidance on the use of long-acting insulin analogues for the treatment of diabetes – insulin glargine](#). NICE technology appraisal guidance 53 (2002).

5.2 Guidance under development

NICE is currently developing the following related guidance (details available from the NICE website):

- Obesity – working with local communities. NICE public health guidance. Publication expected November 2012.
- Overweight and obese children and young people – lifestyle weight management services. NICE public health guidance. Publication expected October 2013.
- Type 1 diabetes in adults (update). NICE clinical guideline. Publication expected July 2014.
- Type 2 diabetes in adults (update). NICE clinical guideline. Publication expected July 2014.
- Diabetes in pregnancy (update). NICE clinical guideline. Publication expected June 2014.
- Lipid modification (update). NICE clinical guideline. Publication date to be confirmed.
- Buccal insulin for the management of type 1 diabetes. NICE technology appraisal guidance. Publication date to be confirmed.

6 Further information

Information on the guideline development process is provided in the following documents, available from the NICE website:

- [‘How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS’](#)
- [‘The guidelines manual’](#).

Information on the progress of the guideline will also be available from the [NICE website](#).

Appendix C: Stakeholder organisations

C.1 Original (2004) stakeholder organisations

A. Menarini Diagnostics Ltd
Abbott Laboratories Limited (BASF/Knoll)
Afiya Trust
African and Caribbean Diabetes Association
Ambulance Service Association
Association of British Clinical Diabetologists
Association of British Health-Care Industries
Association of Clinical Biochemists
Association of the British Pharmaceuticals Industry
AstraZeneca UK Ltd
Atkins Nutritional Inc
Aventis Pasteur MSD
Aventis Pharma
Blood Pressure Association
Bournemouth Diabetes and Endocrine Centre
British Association of Prosthetists and Orthotists
British Association of Sport and Exercise Sciences
British Dietetic Association
British Geriatrics Society Special Interest Group in Diabetes
British Hypertension Society
British In Vitro Diagnostics Association
British Medical Association
British National Formulary
British Psychological Society
British Society for Paediatric Endocrinology and Diabetes
British Society of Periodontology
BUPA
Chartered Society of Physiotherapy
Cheshire West PCT and Ellesmere Port & Neston PCT Diabetes NSF LIT
Commission for Health Improvement

College of Optometrists
Coloplast Limited
Community District Nurses Association
ConvaTec
Department of Health
Depression Alliance
Diabetes UK
Eli Lilly and Company Ltd
Faculty of Dental Surgery
Faculty of Public Health
Fibroid Network Charity
General Medical Council
Health Development Agency
Heart UK
Institute of Sport and Recreation Management
Insulin Dependent Diabetes Trust
Johnson & Johnson Medical
Kidney Alliance
LifeScan
Limbless Association
Long Term Medical Conditions Alliance
Maternity Health Links
Medicines and Healthcare products Regulatory Agency
Medtronic Limited
Merck Sharp & Dohme
National Association of Theatre Nurses
Type 1 diabetes
National Council for Disabled People, Black, Minority and Ethnic Community
National Public Health Service
Newcastle PCT
NHS Information Authority
NHS Quality Improvement Scotland
Norfolk and Norwich University Hospital NHS Trust

Novo Nordisk Limited
Ortho Biotech
Patient Involvement Unit for NICE
Pfizer Limited
Prodigy
Provalis Diagnostics Ltd
Roche Diagnostics Limited
Royal College of Anaesthetists
Royal College of General Practitioners
Royal College of General Practitioners Wales
Royal College of Midwives
Royal College of Nursing
Royal College of Ophthalmologists
Royal College of Paediatrics and Child Health
Royal College of Pathologists
Royal College of Physicians of London
Royal College of Psychiatrists
Royal College of Surgeons of England
Royal National Institute of the Blind
Royal Pharmaceutical Society of Great Britain
Scottish Intercollegiate Guidelines Network
Sheffield Teaching Hospitals NHS Trust
Society of Chiropodists and Podiatrists
The Royal Society of Medicine
Tissue Viability Nurses Association
Tissue Viability Society
TOAST (The Obesity Awareness and Solutions Trust)
UK National Screening Committee
UK Pain Society
UK Thalassaemia Society
Welsh Assembly Government (formerly National Assembly for Wales)
Westmeria Healthcare Ltd
Guideline Development Group membership and acknowledgements

C.2 2015 update

The final published guideline will include a list of registered stakeholder organisations for the 2015 update.

Appendix D: Declarations of interest

D.1 2015 update

All GDG members' interests were recorded on declaration forms provided by NICE. The forms covered consultancies, fee-paid work, share holdings, fellowships and support from the healthcare industry. GDG members' interests are listed in this section. Note that the GDG chair, members and expert advisers were appointed under NICE's April 2007 Code of Practice for Declaring and Dealing with Conflicts of Interest.

This appendix includes all interests declared on or before 28 November 2014.

Table 1: GDG members' declarations of interest

GDG member	Interest
Jerry Wales (Chair)	<p><u>Non-personal pecuniary</u> Sheffield Children's Hospital Foundation Trust clinical research faculty received funding from Merck Sharp & Dohme (MSD) and Parexel via the Medicines for Children Research Network (MCRN) for Jerry Wales's participation in research into the pharmacokinetics of novel medications for type 2 diabetes (both projects yet to start), from Novo Nordisk for Jerry Wales's participation in a Paediatric Investigation Protocol for a new long-acting insulin for type 1 diabetes (historical declaration only, no ongoing interests), and from 9 companies manufacturing medications or equipment for diabetes (Abbott, Bayer, LifeScan (Johnson and Johnson), Lilly, Novo Nordisk, Owen Mumford, Roche, Sanofi, and Ypsomed) to support the Yorkshire Regional Paediatric Diabetes Network meeting 2011 (historical declaration only, no ongoing interests)</p> <p><u>Personal non-pecuniary</u> Member of the British Society for Paediatric Endocrinology and Diabetes (BSPED), Diabetes UK, the European Society for Paediatric Endocrinology (ESPE) and the International Society for Pediatric and Adolescent Diabetes (ISPAD); published and lectured on bariatric surgery in young people; joint chief investigator on a project funded by Diabetes UK but receives no money directly and has no managerial responsibility for the budget</p>
Francesca Annan	<p><u>Personal pecuniary</u> Received funding from Eli Lilly for speaking at the Eli Lilly National Paediatric Diabetes Meeting in May 2014 on topics related to the management of diabetes that were not specific to the scope of the guideline (fat and protein counting and exercise); invited chair at International Diabetes Federation (IDF) World Congress, Dubai 2011 and received funding from Novo Nordisk, Roche and Sanofi towards travel and accommodation expenses; received funding to cover travel and accommodation expenses from the ISPAD to attend and speak as an expert panel member</p>

GDG member	Interest
	<p>on the management of diabetes at the 40th ISPAD conference in Toronto, Canada in September 2014; invited speaker at the ISPAD annual meeting 2012 and received funding from Roche towards accommodation expenses; invited speaker (on the topic of exercise and diabetes management) at the Juvenile Diabetes Research Foundation (JDRF) 'Type 1 diabetes discovery weekend' and received funding from JDRF towards travel expenses, the conference was supported by industry sponsorship; received educational grant (£250) from Novo Nordisk to cover the cost of ISPAD conference registration fee, the conference was supported by industry sponsorship</p> <p><u>Non-personal pecuniary</u></p> <p>Co-applicant for the following Health Technology Assessment (HTA) funded trials: Child and Adolescent Structured Competencies Approach to Diabetes Education (CASCADE), randomised controlled trial (RCT) of continuous subcutaneous insulin infusion compared to multiple daily injection regimens in children and young people at diagnosis of type 1 diabetes (Subcutaneous Insulin, Pumps or Injections (SCIPI)); organised an educational meeting on the topic of 'exercise in diabetes'. Funds were received from Novo Nordisk to cover the costs of food and the venue. Francesca Annan did not receive these funds directly</p> <p><u>Personal non-pecuniary</u></p> <p>Member of British Dietetic Association, Diabetes Management & Education Group (DMEG), Diabetes UK, ISPAD, Sports Dietitians UK; regular teaching commitments related to nutritional management of diabetes, and exercise and diabetes at University of York, University of Warwick, Coventry University, Birmingham Children's Hospital; contributed to ISPAD guidelines on nutritional management and exercise; wrote articles on exercise and diabetes management and nutritional management of diabetes for Complete Nutrition and Diabetes Care for Children & Young People; presentations at national and international meetings on exercise and diabetes management; reviewed patient information content of Diabetes UK publications and pharmaceutical company literature (Lilly and Roche); chair of Paediatric Sub Group of Diabetes Management and Education Group (a specialist group of The British Dietetic Association) from April 2013; member of the writing group for ISPAD consensus guidelines</p>
Jo Dalton	<p><u>Personal pecuniary</u></p> <p>Current post as paediatric diabetes specialist nurse funded by a diabetes charity within the Royal London Hospital</p> <p><u>Personal non-pecuniary</u></p> <p>Member of the guideline development group (GDG) for the 2004 NICE guideline on type 1 diabetes in children and young people; member of the Royal College of Nursing (RCN), ISPAD, Primary Care Diabetes Society (PCDS), professional member of Diabetes UK, attended a study day funded by Medtronic on a topic that is not specific to the guideline scope (continuous subcutaneous insulin infusion therapy); registered for a symposium funded by Novo Nordisk in Leicester on paediatric diabetes in October 2014 but did not attend</p>

GDG member	Interest
Jacqueline Double	<p><u>Personal pecuniary</u> Honorarium from NHS Diabetes as Chair of national Parent Reference Group; invited speaker at 2 Friends For Life conferences and received free travel and food, the conferences were supported by industry sponsorship; received funding to cover travel expenses to attend a meeting in Australia funded by a number of commercial sources; gave a presentation at an IDF meeting in Melbourne. Travel expenses were paid by the organisation</p> <p><u>Personal family interest</u> Husband received funding to cover travel expenses from Children with Diabetes (a US not-for-profit organisation) to attend a Family Conference in the USA</p> <p><u>Personal non-pecuniary</u> Spoke for NHS Technology Adoption Centre (NTAC) and NHS Diabetes; ran workshops on schools, advocacy and mother's emotional needs; member of Diabetes UK and JDRF; director of INPUT (a patient-run organisation that advocates for access to insulin pumps and diabetes technology in the UK) until December 2012; member of UK Children with Diabetes Advocacy Group</p>
Sarah Eaton	<p><u>Non-personal pecuniary</u> Member of conference planning team for conferences organised by Diabetes UK and the Universities of York and Huddersfield. The conferences are sponsored by a number of pharmaceutical companies but Sarah Eaton does not receive any funding personally and is not responsible for management of the funds</p> <p><u>Personal non-pecuniary</u> Attended GP education meetings funded by Ashfield In2 Focus, Bayer Healthcare, Boehringer Ingelheim, HRA Pharma, Napp Pharmaceuticals, Pfizer, Reckit Benckiser; professional member of Diabetes UK, volunteer for Diabetes UK children's care events; member of team (also involving Diabetes UK, University of Huddersfield and University of York) planning a conference on new developments in diabetes management in primary care</p>
Julie Edge (Chair of the diabetic ketoacidosis (DKA) subgroup)	<p><u>Personal pecuniary</u> Honoraria for writing on type 1 diabetes for the British National Formulary for Children; honoraria for writing on type 1 diabetes for Practical Diabetes; attended the ISPAD annual meeting in Gothenburg as invited speaker and received expenses (travel, registration, 3 nights' hotel accommodation and one evening meal) from ISPAD; received funding from the IDF to cover the cost of travel and accommodation expenses incurred when attending their meeting in Melbourne; received funding from the Australia Paediatric Society to cover registration and travel expenses to speak on the topic of cerebral oedema in children and young people with DKA at their Diabetes Meeting, the event was funded by a number of commercial sources; received funding from Diabetes UK to cover travel expenses to attend their Diabetes UK conference</p> <p><u>Non-personal pecuniary</u> Julie Edge holds managerial responsibility for departmental funding from Oxford Medical Diagnostics for a research project on a device not directly linked to any of the topics in</p>

GDG member	Interest
	<p>the scope, from Aventis, Novo Nordisk, and Roche for sponsorship of educational meetings, and from the British Heart Foundation, Diabetes UK, JDRF, National Institute for Health Research Comprehensive Clinical Research Network (NIHR CCRN) via the Comprehensive Local Research Networks (CLRN) and Thames Valley Diabetes Research Network (TVRN) for the following research projects for which Julie Edge is the local principle investigator: Adolescent Type 1 Diabetes Cardio-Renal Intervention Trial (AdDIT); Diabetes Genome Anatomy Project (DGAP); and studies about insulin for diabetes including an RCT of continuous subcutaneous insulin infusion compared to multiple daily injection regimens in children and young people at diagnosis of type 1 diabetes (SCIPI); holds managerial responsibility for departmental funding from Advanced Therapeutics, Animas/LifeScan (part of Johnson and Johnson), Glucomen, Lilly, Novo Nordisk and Roche for sponsorship of educational meetings in 2013; holds managerial responsibility for departmental funding from Advanced Therapeutics, Aventis, Novo Nordisk and Roche for sponsorship of educational meetings in 2014; received funding from Novo Nordisk to cover travel expenses to attend and speak at a symposium (also funded by Novo Nordisk) in Leicester on paediatric diabetes in October 2014</p> <p><u>Personal non-pecuniary</u></p> <p>Involved over many years in research on the management of DKA; lectured and prepared guidelines on DKA; member of Association of Children's Diabetes Clinicians (ACDC), BSPED, Diabetes UK and ISPAD; member of the writing group for ISPAD consensus guidelines; attended a half-day training course organised by Medtronic about continuous intravenous insulin therapy pumps; author of a paper looking at the timing of insulin therapy which was included in the guideline systematic review for the same topic; joint author on a paper looking at the rate of fluid administration which was included in the guideline systematic review for the same topic</p>
Nikhil Gokani	<p><u>Personal pecuniary</u></p> <p>Payment received for systematic reviewing work not directly linked to any of the topics in the guideline scope</p> <p><u>Personal non-pecuniary</u></p> <p>Supporting member of Diabetes UK and member of its groups and committees; contingent PhD candidate in public health and law; member of the National Diabetes Audit Partnership Board; member of Royal College of Physicians (RCP) joint specialty committee on endocrinology and diabetes</p>
William Lamb	<p><u>Personal pecuniary</u></p> <p>Honoraria from Practical Diabetes for writing an article about adolescent diabetes and from Medtronic Ltd for lecturing on continuous glucose monitoring; honoraria from eMedicine.com (part of Medscape from WebMD) for writing and updating articles about diabetes and DKA; attended an educational meeting organised by Francesca Annan on the topic of exercise in diabetes, the meeting was sponsored by Novo Nordisk and travel expenses were paid by the conference organisers; received payment for medico-legal</p>

GDG member	Interest
	<p>work (expert testimony and a report) in a case pertaining to paediatric diabetes care that was not specific to the scope of the guideline (neglect); received funding to cover travel expenses to speak at a conference on diabetes and exercise, the conference was sponsored by a number of insulin pump manufacturers; received funding from university employer to cover travel expenses to speak at a training course on the use of insulin pumps, the course was sponsored by a number of insulin pump manufacturers</p> <p><u>Personal non-pecuniary</u></p> <p>Professional member of Diabetes UK; member of ACDC, BSPED and ISPAD; volunteer for Diabetes UK and JDRF; associate editor of Clinical Diabetes; attended meetings supported by various industry sponsors unknown to William Lamb as part of continuing professional development. Spoke at JDRF 'Type 1 diabetes discovery weekend', the event was supported by industry sponsorship but William Lamb received no funding</p>
Carol Metcalfe	<p><u>Personal pecuniary</u></p> <p>Received funding from Novo Nordisk to attend the Diabetes UK annual Professional Conference in March 2014 and from Eli Lilly to attend the Eli Lilly National Paediatric Diabetes Meeting in May 2014; received funding from Roche to cover accommodation costs while attending a study day (also funded by Roche) on a topic that is not specific to the guideline scope (continuous subcutaneous insulin infusion therapy); received funding from Novo Nordisk to cover accommodation expenses while attending a symposium (also funded by Novo Nordisk) in Leicester on paediatric diabetes in October 2014</p>
Claire Pesterfield	<p><u>Non-personal pecuniary</u></p> <p>Addenbrookes Charitable Trust will receive honoraria from Abbott, Animas, Roche and Medtronic for Claire Pesterfield presenting clinical case studies regarding diabetes care and preparing 2 articles for publication (1 about an education event (sports day) for Diabetes Care of Children and Young People and the other about management of neonatal diabetes for Diabetes Management)</p> <p><u>Personal non-pecuniary</u></p> <p>Volunteer for Diabetes UK; IDF young leader programme mentor; wrote article about parental attitudes to a closed-loop blood glucose trial for Diabetes Technology and Therapeutics (2010); co-founder and director of Team Blood Glucose, a not-for-profit social enterprise that provides peer support and education resources to encourage people with or at risk of diabetes to participate in exercise</p>

Table 2: NCC-WCH staff members' declarations of interest

Staff member	Interest
Sarah Bailey	No interests declared
Frauke Becker	No interests declared
Zosia Beckles	No interests declared
Rupert Franklin	No interests declared
Yelan Guo	No interests declared
Paul Jacklin	No interests declared

Staff member	Interest
Sadia Janjua	No interests declared
Juliet Kenny	No interests declared
Hugh McGuire	No interests declared
Paul Mitchell	No interests declared
Moira Mugglestone	No interests declared
M Stephen Murphy	No interests declared
Su Park	No interests declared
Nitara Prasannan	No interests declared
Wendy Riches	No interests declared
Grammati Sarri	No interests declared
Cristina Visintin	No interests declared
Amy Wang	No interests declared
Katie Webster	No interests declared

Table 3: Expert advisers' declarations of interest

Expert adviser	Interest
Katharine Barnard	<u>Personal pecuniary interest</u> Honorarium from Animas to attend advisory board meetings in January and July 2014 for the CHOICE study – the study looks at treatment satisfaction with insulin pump therapy; honorarium from Johnson and Johnson to provide expert advice on impact of diabetes-related devices (until October 2014); honorarium from Novo Nordisk to attend advisory board meetings for the DAWN2 study – the study looks at psychosocial attitudes of adults and family members with type 1 diabetes (until March 2014); honorarium from Roche Diagnostics to act as Global Advisory Board member (ongoing) providing advice on the topic of psychosocial impact of devices for adults with type 1 diabetes; honorarium from Sanofi to attend one-off meeting on behavioural aspects of diabetes (February 2014)
Andrew Durward	No interests declared

Appendix E: Review protocols

E.1 Diagnosis

Review question: What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?

The systematic review for this question was conducted by the guidance-producing centre for the guideline 'Type 1 diabetes in adults'. The style of the review protocol differs slightly from the style used elsewhere in this guideline.

Diagnosis	
Review question for update	What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes? Note that the evidence review was prepared by the guidance-producing centre for type 1 diabetes in adults who used the following as a working version of the review

Diagnosis	
	question for compatibility with the evidence review for the adult's guideline <i>In young people with diabetes, what is the best marker (C-peptides plus or minus antibodies) to distinguish between a diagnosis of type 1 diabetes, type 2 diabetes and other forms of diabetes?</i>
Objectives	<p>The aim of this review is to determine whether the presence of C-peptides and/or antibodies in people with diabetes distinguishes between type 1 diabetes, type 2 diabetes, and other forms of diabetes, in order to make an accurate diagnosis. Also what titre or concentration of each of these markers is present and distinguishes the types.</p> <ul style="list-style-type: none"> • What is the best test or combination of tests to give you the highest level of certainty in discriminating type 1 diabetes from type 2 diabetes? <p>When does uncertainty exist, and what should be done when uncertainty exists?</p>
Population	<p>Young people with all types of diabetes</p> <ul style="list-style-type: none"> • young people is defined as aged at least 11 years and younger than 18 years • diabetes types are: type 1 diabetes, type 2 diabetes, latent autoimmune diabetes of adulthood (LADA) and maturity onset diabetes of the young (MODY)
Subgroups	<p>The following groups will be considered separately if data are available:</p> <ul style="list-style-type: none"> • young people
Diagnostic tests	<p>C-peptide:</p> <ul style="list-style-type: none"> • plasma C-peptide (stimulated) • urinary C-peptide • urinary C-peptide:creatinine ratio <p>Antibody tests:</p> <ul style="list-style-type: none"> • anti-islet cell antibody (ICA) • anti-glutamic acid decarboxylase 65 antibody or anti-glutamic acid decarboxylase antibody (GADA) • insulinoma-associated (IA-2 / ICA512) autoantibody • other (zinc transporter 8 (ZnT8), islet-specific glucose-6-phosphatase catalytic subunit (IGRP), anti-ZnT8)
Outcomes	<ul style="list-style-type: none"> • Presence of marker (number or percentage of participants with marker) • Concentration of marker (ug/ml) • Change in marker over time (number or percentage of participants with marker) • Change in concentration of marker over time (ug/ml)
Importance of outcomes	<p>Critical outcomes</p> <ul style="list-style-type: none"> • Not relevant
Study design	All study types
Population size and directness	<p>Studies will be excluded if any of the following apply.</p> <ul style="list-style-type: none"> • The population is mixed, with no young people subgroup analyses. Mixed populations excluded are: <ul style="list-style-type: none"> ◦ children and young people ◦ children, young people and adults • The population is exclusively children (age < 11 years) • They are validation studies • They are treatment studies • They are pre-diabetes populations (we are not going to look at studies that use markers as predictors of the future development of diabetes) • They are detecting markers in relatives of people with diabetes

Diagnosis	
	<p>Sample size restrictions. We will exclude studies if any of the following apply.</p> <ul style="list-style-type: none"> • Adults and young people with sample size of $N < 50$ if we retrieve > 20 studies that have been conducted in young people and adults separately • Young people with a sample size of $N < 50$ if there are > 20 young people studies retrieved
Setting	All settings (as per scope)
Search strategy	Search will be restricted to studies published since the original guideline for type 1 diabetes in adults (2003). If only a few studies are found, then we will extend the search to all years
Review strategy	<p>Appraisal of methodological quality/evidence synthesis</p> <ul style="list-style-type: none"> • The methodological quality of each study will be assessed using NICE checklists and a narrative synthesis of the evidence will be provided
Notes	<p>If no/insufficient evidence is found we will (in order of preference):</p> <ul style="list-style-type: none"> • consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • move to GDG consensus

Diagnosis – health economic evidence	
Objectives	To identify economic studies relevant to the review question set out above
Criteria	Populations, interventions and comparators as specified in the individual review protocol above. Must be a relevant economic study design (cost-utility analysis, cost-benefit analysis, cost effectiveness analysis, cost-consequence analysis, comparative cost analysis)
Search strategy	An economic study search was undertaken using population specific terms and an economic study filter
Review strategy	<p>Each study is assessed using the NICE economic evaluation checklist - NICE guidelines manual (2009 edition)</p> <p>Inclusion/exclusion criteria</p> <ul style="list-style-type: none"> • If a study is rated as both 'Directly applicable' and 'Minor limitations' (using the NICE economic evaluation checklist) then it should be included in the guideline. An evidence table should be completed and it should be included in the economic profile • If a study is rated as either 'Not applicable' or 'Very serious limitations' then it should be excluded from the guideline. It should not be included in the economic profile and there is no need to include an evidence table • If a study is rated as 'Partially applicable' and/or 'Potentially serious limitations' then there is discretion over whether it should be included. The health economist should make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the GDG if required. The ultimate aim being to include studies that are helpful for decision making in the context of the guideline and current NHS setting. Where exclusions occur on this basis, this should be noted in the relevant section of the guideline with references. <p>Also exclude:</p> <ul style="list-style-type: none"> • unpublished reports unless submitted as part of a call for evidence • abstract-only studies • letters • editorials • reviews of economic evaluations • foreign language articles <p>Where there is discretion</p> <p>The health economist should be guided by the following hierarchies.</p> <p><i>Setting:</i></p> <ul style="list-style-type: none"> • UK NHS • OECD countries with predominantly public health insurance systems (for example, France, Germany, and Sweden) • OECD countries with predominantly private health insurance systems (for example, the USA, and Switzerland) • Non-OECD settings (always 'Not applicable') <p><i>Economic study type:</i></p> <ul style="list-style-type: none"> • cost-utility analysis • other type of full economic evaluation (cost-benefit analysis, cost effectiveness analysis, cost-consequence analysis) • comparative cost analysis • non-comparative cost analyses including cost of illness studies (always 'Not applicable') <p><i>Year of analysis:</i></p> <ul style="list-style-type: none"> • the more recent the study, the more applicable it is <p><i>Quality and relevance of effectiveness data used in the economic analysis:</i></p>

Diagnosis – health economic evidence	
	<ul style="list-style-type: none"> the more closely the effectiveness data used in the economic analysis matches with the studies included for the review of clinical evidence the more useful the analysis will be to decision making for the guideline
Notes	Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered

E.2 Type 1 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

Type 1 diabetes – education		
Existing recommendation(s) in 2004 guideline	<p>Children and young people with newly diagnosed type 1 diabetes should be offered a structured programme of education covering the aims of insulin therapy, delivery of insulin, self-monitoring of blood glucose, the effects of diet, physical activity and intercurrent illness on glycaemic control, and the detection and management of hypoglycaemia.</p> <p>Children and young people with type 1 diabetes and their families should be offered timely and ongoing opportunities to access information about the development, management and effects of type 1 diabetes. The information provided should be accurate and consistent and it should support informed decision-making.</p> <p>Children and young people with type 1 diabetes and their families should be offered opportunities to discuss particular issues and to ask questions at each clinic visit.</p> <p>The method of delivering education and content will depend on the individual and should be appropriate for the child's or young person's age, maturity, culture, wishes and existing knowledge within the family.</p> <p>Particular care should be given to communication and the provision of information when children and young people with type 1 diabetes and/or their parents have special needs, such as those associated with physical and sensory disabilities, or difficulties in speaking or reading English.</p>	<p>The 2004 guideline includes recommendations about education at diagnosis and as part of ongoing management for type 1 diabetes</p> <p>An external adviser has been appointed to advise the GDG on technical aspects of clinical research relating to behavioural interventions and the interface with education programmes</p>
Review question for update	What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?	
Objectives	To determine the effectiveness of structured education programmes in improving outcomes for children and young people with	The ISPAD Clinical Practice Consensus Guidelines 2009 are available at

Type 1 diabetes – education		
	<p>type 1 diabetes. Structured education programmes deliver information to the child or young person, or their family, with the intention of improving outcomes and using a process which includes (see ISPAD Clinical Practice Consensus Guidelines 2009, Chapter 5 (Diabetes education in children and adolescents)):</p> <ul style="list-style-type: none"> • a structured, agreed, written curriculum • use of trained educators • quality assurance • audit 	<p>http://www.ispad.org/content/ispad-clinical-practice-consensus-guidelines-2009</p>
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) only	<p>Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion</p> <p>The next step might be to include systematic reviews of RCTs and nonrandomised comparative studies (but not individual nonrandomised studies)</p>
Status	Published articles indexed since the searches for the 2004 guideline were completed	<p>This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles)</p>
Population	Children and young people with type 1 diabetes	<p>The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years</p> <p>This review question will focus solely on 'patient' education (that is, education of healthcare professionals will be excluded)</p>
Intervention or index test	Structured education programmes specific to type 1 diabetes (education aimed at children and young people or their families)	<p>A useful reference (systematic review) for educational and behavioural interventions is AHQR 2008 (Evidence report 166 http://www.ahrq.gov/clinic/tp/diabetdp.htm)</p> <p>Possible search terms (based on AHRQ 2008 systematic review plus GDG suggestions):</p> <ul style="list-style-type: none"> • education • game • information • instruction • intervention • knowledge

Type 1 diabetes – education		
		<ul style="list-style-type: none"> • management • multimedia • online • self-help • skills • teach • train • patient care • phone • video <p>This review should cover: all settings (diabetes clinics, schools, etc), while recognising that recommendations will be limited to the clinical practice context all forms of delivery of education (for example, one-to-one, brief, face-to-face, and remote (telemedicine, including text messaging))</p> <p>Names of studies that might be relevant (not to be used as search terms): KICK-OFF (based on DAFNE) the 'German model' (see separate list of useful references)</p>
Comparator or reference standard	Alternative models of structured education Usual care	Usual care in this context usually includes unstructured, informal education, provision of information leaflets or multimedia
Clinical outcomes	<p>Physical outcomes</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ◦ HbA1c (minimum follow-up 6 months after completion of primary intervention) • Severe hypoglycaemic episodes • Diabetic ketoacidosis (DKA; number of episodes) • Adherence to diabetes management (including self-management) • Adherence to education intervention <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> • Health-related quality of life • Children and young people's and families' satisfaction with intervention (education intervention) • Risk-taking behaviours (such as smoking; this is of such importance that it has been included as an exceptional eighth outcome for data extraction) 	<p>The priority outcomes selected by the GDG are different to those for the review question on general behavioural interventions because psychosocial outcomes are more relevant there</p> <p>The GDG initially identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required. The minimum duration of follow-up was subsequently relaxed to cover follow-up from baseline (rather than completion of the primary intervention) to allow inclusion of clinically relevant evidence</p> <p>HbA1c minimally important difference (MID) is 0.5 percentage</p>

Type 1 diabetes – education		
		<p>points (5.5 mmol/mol)</p> <p>Severe hypoglycaemic episodes defined according to either of the following criteria.</p> <p>International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose)</p> <p>ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)</p> <p>No long-term interventions needed to be prioritised as outcomes because HbA1c will determine these</p>
Health economic outcomes	<p>This question was prioritised for health economic analysis</p> <p>Health-related quality of life and quality adjusted life years (QALYs)</p> <p>Adherence to education intervention</p>	<p>It will only be necessary to consider the cost effectiveness of structured education programmes if there is some evidence of benefit. If education programmes have a mixture of harms and benefits then a QALY approach could facilitate the appropriate trade-off. There may also be a need to model longer-term QALY gains or losses from intermediate trial or study outcomes (for example, changes in weight)</p>
Other criteria for inclusion/exclusion of studies	None	<p>Studies that evaluate education programmes for healthcare professionals will be excluded (see above)</p> <p>Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this (although the availability of such studies is not expected). Note that there are age-specific structured education programmes (mainly for young people)</p> <p>Subgroup analysis according to the presence of associated conditions</p>

Type 1 diabetes – education		
		such as autism spectrum disorder or learning difficulties, and according to language and culture-specific interventions would be useful if the evidence allows this
Search strategies	See separate document	NCC-WCH technical team to search the PsycINFO bibliographic database for this review question (in addition to the standard bibliographic databases)
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The notes above relating to subgroup analysis by associated conditions, language and cultural considerations reflect the importance of equalities issues in this question

E.3 Type 1 diabetes – behavioural interventions

Review question: What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 1 diabetes?

Type 1 diabetes – behavioural interventions		
Existing recommendation(s) in 2004 guideline	<p>Behavioural and conduct disorders Children and young people with type 1 diabetes who have behavioural or conduct disorders, and their families, should be offered access to appropriate mental health professionals.</p> <p>Non-adherence Non-adherence to therapy should be considered in children and young people with type 1 diabetes who have poor glycaemic control, especially in adolescence.</p> <p>Non-adherence to therapy should be considered in children and young people with established type 1 diabetes who present with diabetic ketoacidosis, especially if the diabetic ketoacidosis is recurrent.</p> <p>Young people with 'brittle diabetes' (that is, those who present with frequent episodes of diabetic ketoacidosis over a relatively short time) should have their emotional and psychological well-being assessed.</p> <p>The issue of non-adherence to therapy should be raised with children and young people and their families in a sensitive manner.</p> <p>Psychosocial support Diabetes care teams should be aware that poor psychosocial support has a negative impact on a variety of outcomes of type 1 diabetes in children and young people, including glycaemic control and self-esteem.</p> <p>Children and young people with type 1 diabetes, especially young people using multiple daily injection regimens, should be offered structured behavioural intervention strategies because these may improve psychological well-being and glycaemic control.</p> <p>Young people with type 1 diabetes should be offered specific support strategies, such as mentoring and self-monitoring of blood glucose levels supported by problem solving, to improve their self-esteem and glycaemic control.</p>	<p>The 2004 guideline does not make specific recommendations about behavioural interventions to improve outcomes in children and young people with type 1 diabetes, but it includes the recommendations listed which refer to related topics on behavioural and conduct disorders, non-adherence, psychosocial support, and adolescence</p> <p>An external adviser has been appointed to advise the GDG on technical aspects of clinical research relating to behavioural interventions and the interface with education programmes</p> <p>This recommendation and the one below are particularly relevant to this review question and the GDG will have the opportunity to change the recommendations or add new recommendations if appropriate</p>

Type 1 diabetes – behavioural interventions		
	<p>Families of children and young people with type 1 diabetes should be offered specific support strategies (such as behavioural family systems therapy) to reduce diabetes-related conflict between family members.</p> <p>Children and young people with type 1 diabetes and their families should be offered timely and ongoing access to mental health professionals because they may experience psychological disturbances (such as anxiety, depression, behavioural and conduct disorders and family conflict) that can impact on the management of diabetes and well-being.</p> <p>Diabetes care teams should have appropriate access to mental health professionals to support them in the assessment of psychological dysfunction and the delivery of psychosocial support.</p> <p>Adolescence Diabetes care teams should be aware that adolescence can be a period of worsening glycaemic control, which may in part be due to non-adherence to therapy.</p>	
Review question for update	What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 1 diabetes?	
Objectives	<p>To determine the effectiveness of behavioural interventions in improving outcomes for children and young people with type 1 diabetes. The question is sufficiently broad to cover interventions aimed at families and healthcare professionals as well as those aimed at the child or young person. The GDG prioritised behavioural interventions that should be addressed in this question as follows.</p> <ul style="list-style-type: none"> • Family therapy (including behavioural family systems therapy (BFST)): this is always delivered to one family unit but it can include separate sessions with different members (individuals/groups) within the unit • Cognitive behavioural therapy (CBT): this can be delivered one-to-one or in groups. The intervention focuses on recognising specific triggers for maladaptive behaviour and bringing about changes to behaviour • Motivational interviewing: this can be delivered one-to-one or in groups. The intervention focuses on general exploration of ambivalence around maladaptive behaviours and what the person wants to do or should do. The 	

Type 1 diabetes – behavioural interventions		
	<p>intervention develops insight into maladaptive behaviour</p> <ul style="list-style-type: none"> • Counselling: this is delivered one-to-one but the content of interventions termed counselling may vary • Mentoring: this can be delivered one-to-one or in groups. The mentor is typically older than the person receiving mentoring or is influential in the community • Peer support: this can be delivered one-to-one or in groups. The intervention typically involves people of similar age to the person receiving peer support 	
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) only	<p>Study designs other than RCTs will be considered for any of the prioritised interventions only if no RCT evidence is identified for inclusion for that intervention</p> <p>The next step might be to include systematic reviews of RCTs and nonrandomised comparative studies (but not individual nonrandomised studies)</p>
Status	Published articles indexed since the searches for the 2004 guideline were completed	<p>This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles)</p> <p>The aim is to retain general recommendations that have not become outdated and to add specific recommendations about behavioural interventions if relevant</p>
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	<p>Behavioural interventions specific to the management of type 1 diabetes in children and young people (this could involve interventions aimed at families and healthcare professionals as well as those aimed at the child or young person)</p> <ul style="list-style-type: none"> • Family therapy (include only validated therapies such as BFST – expert adviser to advise in relation to search results); it is likely that RCTs will be available for this type of intervention • CBT; it is likely that RCTs will be available for this type of intervention 	<p>Use the terms specific to the prioritised behavioural interventions when conducting the searches for this question</p> <p>Useful reference (systematic review) for educational and behavioural interventions is AHQR 2008 (Evidence report 166 http://www.ahrq.gov/clinic/tp/diabetes.htm)</p> <p>The following search terms from the</p>

Type 1 diabetes – behavioural interventions	
<ul style="list-style-type: none"> • Motivational interviewing; it is possible that RCTs will be available for this intervention, although it is more likely to have been used in young people and adults rather than children • Counselling; it is possible that RCTs will be available for this type of intervention • Mentoring; there may be no RCTs evaluating this type of intervention • Peer support; there may be no RCTs evaluating this type of intervention 	<p>AHRQ 2008 systematic review were considered by the GDG and expert adviser as part of the prioritisation of behavioural interventions for this question but they were not selected for the reasons given and they should not be used as search terms for this question:</p> <ul style="list-style-type: none"> • adherence (an outcome not an intervention) • behavioural therapy (poorly defined so not a priority) • biofeedback (more relevant to the question relating to education programmes) • cognitive therapy (not a priority because it focuses on awareness of behaviour but not changing behaviour) • conjoint therapy (refers to any two therapies joined together) • educational therapy (will be addressed in the education question) • psychological interventions (not specific) • psychological therapy (not specific) • solution-focused therapy (not specific – refers to any therapy that focuses on solutions rather than problems; several of the prioritised interventions are solution-focused) • therapy (not specific) <p>This review should cover:</p> <ul style="list-style-type: none"> • all settings (diabetes clinics, schools, etc), while recognising that recommendations will be limited to the clinical practice context • all forms of delivery of the prioritised behavioural interventions (for example, one-to-one, brief, face-to-face, and remote (telemedicine)) <p>Names of studies that might be relevant (not to be used as search terms):</p> <ul style="list-style-type: none"> • DEPICTED (motivational interviewing and agenda-setting for healthcare professionals) • CASCADE (incomplete but expected to report during the guideline development period) • FACTS (see, for example, the Diabetes UK and Juvenile Diabetes Foundation websites)

Type 1 diabetes – behavioural interventions		
Comparator or reference standard	<p>An alternative behavioural intervention listed above</p> <p>An alternative and well defined behavioural intervention not listed above (expert adviser to advise on what is well defined in relation to search results)</p> <p>Any other intervention aimed at changing a specific behaviour, a range of behaviours, or psychosocial adjustment to diabetes self-management</p> <p>Usual care (this will be the most common comparator)</p>	<p>Usual care in this context usually includes education, no therapy, provision of information leaflets or multimedia (DVDs, CDs, websites, apps)</p>
Clinical outcomes	<p>Physical outcomes</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ◦ HbA1c (minimum follow-up 6 months after completion of primary intervention) • Adherence to diabetes management (the scope requires this; to include self-management) • Adverse events (for example, severe hypoglycaemic episodes, diabetic ketoacidosis (DKA) or self-harm) <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> • Health-related quality of life • Children and young people's and families' satisfaction with intervention • Depression or anxiety • School performance or attendance (this will be very important for this question) • Risk-taking behaviours (such as smoking; this is of such importance that it has been included as an exceptional eighth outcome for data extraction) 	<p>The GDG initially identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required. The minimum duration of follow-up was subsequently relaxed to cover follow-up from baseline (rather than completion of the primary intervention) to allow inclusion of clinically relevant evidence</p> <p>The GDG noted that change in body mass index (BMI) standard deviation score (SDS) would be more important than DKA for the corresponding question for type 2 diabetes</p> <p>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</p> <p>Severe hypoglycaemic episodes defined according to either of the following criteria.</p> <ul style="list-style-type: none"> • International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose) • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)

Type 1 diabetes – behavioural interventions		
		No long-term interventions needed to be prioritised as outcomes because HbA1c will determine these
Health economic outcomes	<p>This question was not prioritised for health economic analysis</p> <p>Health-related quality of life and quality adjusted life years (QALYs)</p> <p>Adherence to treatment</p> <p>It may be possible attach a QALY to various long-term complications – this could be a longer list than the seven outcomes considered for the GRADE profiles</p>	<p>This question was rated as a medium (but not high) priority for health economic analysis, but it could be considered if resources allow, especially as there are parallels with the question on structured education packages, which was selected as a high priority for health economic analysis</p> <p>GDG to note that, although mortality is not prioritised as a clinical outcome, health economic modelling incorporating data on mortality might be relevant through the link between hyperglycaemia and mortality</p> <p>It would only be necessary to consider the cost effectiveness of behavioural interventions if there were some evidence of clinical benefit. If behavioural interventions have a mixture of harms and benefits then a QALY approach could facilitate the appropriate trade-off. There may also be a need to model longer-term QALY gains or losses from intermediate trial or study outcomes (for example, changes in weight)</p>
Other criteria for inclusion/exclusion of studies	None	<p>Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this (although the availability of such studies is not expected). Subgroup analysis by ages within these groups would also be useful if it is feasible</p> <p>Evidence tables should document who delivered the intervention(s), the frequency of contact with healthcare or other relevant professionals to deliver the intervention(s), and process evaluation information</p>
Search strategies	See separate document	NCC-WCH technical team to search the PsycINFO bibliographic database for this review question (in addition to the standard bibliographic databases)
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided</p>	

Type 1 diabetes – behavioural interventions		
	following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	

E.4 Type 1 diabetes – multiple daily injections

Review question: What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

Type 1 diabetes – multiple daily injections		
Existing recommendation(s) in 2004 guideline	<p>Pre-school and primary school children with type 1 diabetes should be offered the most appropriate individualised regimens to optimise their glycaemic control.</p> <p>Young people with type 1 diabetes should be offered multiple daily injection regimens to help optimise their glycaemic control.</p> <p>Young people who do not achieve satisfactory glycaemic control with multiple daily injection regimens should be offered additional support and, if appropriate, alternative insulin therapy (once-, twice- or three-times daily mixed insulin regimens or continuous subcutaneous insulin infusion using an insulin pump).</p> <p>Young people with type 1 diabetes who have difficulty adhering to multiple daily injection regimens should be offered twice-daily injection regimens.</p>	<p>The 2004 guideline contains the following definitions:</p> <ul style="list-style-type: none"> • pre-school children – children aged 1 year or older, and younger than 5 years • primary school children – children aged 5 years or older, and younger than 11 years • young people – people aged 11 years or older, and younger than 18 years
Review question for update	What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?	
Objectives	To establish the effectiveness of different insulin regimens in children and young people with type 1 diabetes	
Language	English	
Study design	<p>Systematic reviews and randomised controlled trials (RCTs) only</p> <p>Comparative observation studies (including cohort and case-control studies)</p>	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion
Status	Published articles (no limitation on year of publication)	Although this is an update of part of a review question considered in the 2004 guideline, no date limit will be applied to searches to ensure that all relevant articles are identified and allow extraction of data in the form of GRADE profiles
Population	Children and young people with type 1 diabetes	<p>The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years</p> <p>Exclude studies involving children</p>

Type 1 diabetes – multiple daily injections		
		<p>or young people with type 2 diabetes unless the results for children and young people with type 1 diabetes are reported separately</p>
Intervention or index test	Multiple daily injections of insulin, with or without carbohydrate counting	<p>The definition of multiple daily injections will be four or more injections per day using unmixed insulin (meaning insulins that are not mixed in the syringe)</p> <p>The 2004 guideline defines multiple daily injections as follows: the person has injections of short-acting insulin or rapid-acting insulin analogue before meals, together with one or more separate daily injections of intermediate-acting insulin or long-acting insulin analogue</p> <p>Evidence tables should record additional care received (carbohydrate counting, advice, monitoring, etc)</p> <p>Any articles in which four or more injections were given but it was not clear from the title or abstract whether mixed or unmixed insulin was used should be ordered and discussed with the GDG</p> <p>The GDG noted that studies in which short-term intensive insulin treatment is used from diagnosis are not relevant for this question</p> <p>Report the following types of studies separately:</p> <ul style="list-style-type: none"> • those in which all participants are studied from diagnosis • those in which all participants receive a change in treatment simultaneously • those in which selected children and young people receive a change in treatment (for example, because usual treatment has failed)
Comparator or reference standard	Fewer than four injections or occasions of injecting per day. Predominantly mixed insulin regimens – combinations of insulins with different durations of action given in a single injection – also includes regimens where such insulins are given in separate injections but at the same time. Two injections given at the same time will count	The definition of a mixed insulin regimen will be one in which fewer than four injections per day using mixed insulin (meaning insulin with different durations of action mixed in the syringe) are administered

Type 1 diabetes – multiple daily injections		
	<p>as one mixed injection</p> <p>25:75 and 30:70 mixes are currently available in the UK, but studies involving other mixes (for example, 40:60) or free-mixed insulin are also eligible for inclusion</p>	<p>The 2004 guideline defines fewer than four injections per day as follows: injections of short-acting insulin or rapid-acting insulin analogue mixed with intermediate-acting insulin. The insulin preparations may be mixed by the patient at the time of injection</p> <p>For example, mixtures of 25-30% short-acting analogue with an intermediate insulin (such as Humalog mix25)</p> <p>Any articles in which fewer than four injections were given but it was not clear from the title or abstract whether mixed or unmixed insulin was used should be ordered and discussed with the GDG</p>
Clinical outcomes	<p>Physical outcomes</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ○ HbA1c (minimum follow-up 6 months) ○ Severe hypoglycaemic episodes ○ Diabetic ketoacidosis (DKA; number of episodes) • Adherence to diabetes management (including self-management) • Changes in body mass index (BMI) standard deviation score (SDS) <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> • Health-related quality of life • Children and young people's and families' satisfaction with intervention 	<p>The GDG considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes</p> <p>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</p> <p>Severe hypoglycaemic episodes defined according to either of the following criteria.</p> <ul style="list-style-type: none"> • International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose) • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or

Type 1 diabetes – multiple daily injections		
		<p>unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)</p> <p>BMI SDS minimally important difference is 0.5 for weight-loss interventions and 0 for all other interventions</p>
Health economics outcomes	<p>This question was prioritised for health economic analysis</p> <p>Health-related quality of life (measured using quality adjusted life years (QALYs))</p> <p>Adherence to diabetes management (including self-management)</p> <p>It may be possible attach a QALY weight to various long-term complications – this could be a longer list than the seven outcomes considered for GRADE profiles</p>	
Other criteria for inclusion/exclusion of studies	Exclude studies with <10 participants in total	Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this
Search strategies	See separate document	
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p> <p>Evidence tables and an evidence profile will be used to summarise the evidence</p>	Results will be pooled using meta-analysis if possible
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

E.5 Type 1 diabetes – HbA1c targets

Review question: What is the optimal haemoglobin A1c (HbA1c) target for children and young people with type 1 diabetes?

Type 1 diabetes – HbA1c targets		
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes and their families should be informed that the target for long-term glycaemic control is an HbA1c level of less than 7.5% without frequent disabling hypoglycaemia and that their care package should be designed to attempt to achieve this.	
Review question for update	What is the optimal HbA1c target for children and young people with type 1 diabetes?	
Objectives	To determine the optimal HbA1c target value in terms of minimising the risk of long-term complications without incurring an increased risk of hypoglycaemic episodes as an adverse effect	<p>The threshold of 7.5% in the 2004 guideline recommendations comes from the Diabetes Control and Complications Trial (DCCT); the lower HbA1c the lower the risk of complications, and there is no lower limit at which the risk stops reducing; but at very low levels of HbA1c the risk of hypoglycaemia is unacceptable (for type 1 diabetes the risk of hypoglycaemia is great)</p> <p>This review question should, therefore, consider studies that focus on hypoglycaemia risk related to HbA1c</p>
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) Comparative observational studies (including cohort and case-control studies)	<p>Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion</p> <p>No RCTs that report results specific to children and young people are expected. Only consider studies involving adults if no RCTs or observational studies report data for children and young, and then only by cross-referring to the type 1 diabetes in adults guideline in which HbA1c targets are being updated</p>
Status	Published articles indexed since the searches for the 2004 guideline were completed	This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles). Note that newer studies will be more relevant to current diabetes management
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger

Type 1 diabetes – HbA1c targets		
		<p>than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years</p> <p>Note, however, that inclusion/exclusion of studies will be based on time at diagnosis and application of HbA1c targets, whereas long-term follow-up into adulthood will be relevant for this question</p>
Intervention	Specified target value for HbA1c or HbA1c values achieved (recorded)	Comparisons might, for example, relate to differences between clinics
Comparator or reference standard	Comparisons to be made between outcomes according to target values for HbA1c and/or HbA1c values achieved (recorded)	
Clinical outcomes	<p>Physical outcomes</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ○ Severe hypoglycaemic episodes (frequency) ○ Nocturnal hypoglycaemic episodes (frequency) ○ Any hypoglycaemic episode (however defined; frequency) • Contact with the diabetes care team as a measure of healthcare utilisation <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> • Health-related quality of life • Children and young people's and families' satisfaction with intervention (acceptability and comfort associated with testing, and anxiety or stress associated with trying to meet specific targets would be reflected here, but these were not expected to be reported frequently enough to warrant consideration as separate outcomes) 	<ul style="list-style-type: none"> • The GDG used the review protocol for the question related to blood glucose monitoring for type 1 diabetes as the starting point for the outcomes to be considered for this question • • Outcomes related to hypoglycaemia were prioritised for inclusion because the risk of hypoglycaemia is important with type 1 diabetes; this contrasts with the corresponding protocol for HbA1c targets for type 2 diabetes where the risk of long-term complications is more important • • The GDG identified a minimum follow-up period of 4 months after completion of the primary intervention for all prioritised outcomes). Include further follow-up if reported, for example, if a top-up intervention is required • • Severe hypoglycaemic episodes defined according to either of the following criteria. • International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose) • ISPAD 2000 grade 2 or 3 – the

Type 1 diabetes – HbA1c targets		
		child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)
Health economic outcomes	This question was not prioritised for health economic analysis	
Other criteria for inclusion/exclusion of studies	None	
Search strategies	See separate document	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	

E.6 Type 1 diabetes – blood glucose targets

Review question: What are the optimal blood glucose targets for children and young people with type 1 diabetes?

Type 1 diabetes – blood glucose targets		
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes and their families should be informed that the optimal targets for short-term glycaemic control are a pre-prandial blood glucose level of 4–8 mmol/litre and a post-prandial blood glucose level of less than 10 mmol/litre.	Depending on the evidence identified in the update, the GDG might want to consider lowering the recommended upper limits for blood glucose
Review question for update	What are the optimal blood glucose targets for children and young people with type 1 diabetes?	
Objectives	To determine the optimal blood glucose target range in terms of minimising the HbA1c level (as a surrogate for long-term complications) without incurring hypoglycaemia as an adverse effect. This question should include consideration of the timing of testing, for example, before or after meals	
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) Comparative observational studies (including cohort and case-control studies)	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion There is a 2011 Cochrane review protocol for 'Intensive glucose control versus conventional glucose control for type 1 diabetes mellitus'
Status	Published articles indexed since the searches for the 2004 guideline were completed	This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles)
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention	Specified target ranges for blood glucose or blood glucose values achieved (recorded)	It may be useful to include the following organisations (which

Type 1 diabetes – blood glucose targets		
		<p>have published blood glucose targets) as search terms:</p> <ul style="list-style-type: none"> • American Diabetes Association (ADA) • Australasian Paediatric Endocrine Group (APEG) • International Society for Pediatric and Adolescent Diabetes (ISPAD) <p>The GDG may be interested in:</p> <ul style="list-style-type: none"> • recommending more intensive blood glucose control than the 2004 guideline (for example, reducing the upper limit of the target range, and/or narrowing the target range) • considering the timing and frequency of monitoring relative to meals, etc • setting different targets depending on the insulin regimen used and for different age groups
Comparator or reference standard	Comparisons to be made between outcomes according to target ranges for blood glucose and/or blood glucose values achieved (recorded)	
Clinical outcomes	<p>Physical outcomes</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ○ HbA1c (minimum follow-up 6 months) ○ Severe hypoglycaemic episodes ○ Nocturnal hypoglycaemic episodes ○ Diabetic ketoacidosis (DKA; number of episodes) • Contact with the diabetes care team as a measure of healthcare utilisation <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> • Health-related quality of life • Children and young people's and families' satisfaction with intervention (acceptability and comfort associated with testing, and anxiety or stress associated with trying to meet specific targets would be reflected here, but these were not expected to be reported frequently enough to warrant consideration as separate outcomes) 	<p>The GDG identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required</p> <p>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</p> <p>Severe hypoglycaemic episodes defined according to either of the following criteria.</p>

Type 1 diabetes – blood glucose targets		
		<ul style="list-style-type: none"> • International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose) • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)
Health economic outcomes	This question was not prioritised for health economic analysis	
Other criteria for inclusion/exclusion of studies	None	
Search strategies	See separate document	
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p> <p>Evidence tables and an evidence profile will be used to summarise the evidence</p>	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	

E.7 Type 1 diabetes – blood glucose monitoring

Review questions:

How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?

What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?

What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?

Type 1 diabetes – blood glucose monitoring – frequency of finger prick testing		
Existing recommendation(s) in 2004 guideline	<p>Children and young people with type 1 diabetes and their families should be encouraged to perform frequent blood glucose monitoring as part of a continuing package of care that includes dietary management, continued education and regular contact with their diabetes care teams.</p> <p>Children and young people with type 1 diabetes who are trying to optimise their glycaemic control and/or have intercurrent illness should be encouraged to measure their blood glucose levels more than four times per day.</p> <p>Children and young people with type 1 diabetes should be encouraged to monitor their blood glucose levels before and after exercise so that they can:</p> <ul style="list-style-type: none"> • identify when changes in insulin or food intake are necessary • learn the glycaemic response to different exercise conditions • be aware of exercise-induced hypoglycaemia • be aware that hypoglycaemia may occur several hours • after prolonged exercise. <p>Young people with type 1 diabetes who drink alcohol should be informed that they should:</p> <ul style="list-style-type: none"> • eat food containing carbohydrate before and after drinking • monitor their blood glucose levels regularly and aim to keep the levels within the recommended range by • eating food containing carbohydrate. <p>Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no</p>	The GDG commented that 5 tests a day or more is considered to be good practice and so this should be the comparison for RCTs (5 or more per day compared with 4 or fewer)

Type 1 diabetes – blood glucose monitoring – frequency of finger prick testing		
	tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.	
Review question for update	How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?	
Objectives	To identify the optimal frequency of capillary blood glucose testing (at any site) in children and young people with type 1 diabetes. The question is designed to identify which frequency (or range of frequencies) of testing is associated with optimal glycaemic control and thus a reduced risk of long-term complications	Notes from GDG: <ul style="list-style-type: none"> • frequent blood glucose testing helps to mitigate against hypoglycaemia unawareness • blood glucose level- anxiety is related to excessive testing • excessive testing can be more expensive than continuous glucose monitoring, and so clinicians often use excessive testing as a rationale for requesting funding for continuous monitoring systems
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) and observational studies	Studies that may be of interest: <ul style="list-style-type: none"> • Hvidovre (name of a town in Denmark – pan-European audit) • Hanas (Swedish author) may also be relevant • DPV study (German) • Type 1 exchange study (USA)
Status	Published articles (no limitation on year of publication)	The original guideline did not consider non-comparative, observational studies and so no date limit will be applied to searches
Population	Children and young people with type 1 diabetes	
Intervention or index test	RCTs: 5 or more finger-prick tests per day Observational studies: frequency varies with lower limit of 0 tests per day and no upper limit	<ul style="list-style-type: none"> • It is not expected that there will be RCTs that fully answer this question and so no restriction in study design will be applied to the literature searches. This reflects the following considerations: • there are unlimited possibilities in terms of the frequency of testing • it might be difficult ethically to randomise any participants to just a few tests • including observational studies will allow consideration of no testing at all, which would never be recommended practice
Comparator or reference standard	RCTs: 4 or fewer finger-prick tests per day Observational studies: different frequencies of testing	
Clinical	Physical outcomes	The GDG selected 7 outcomes and

Type 1 diabetes – blood glucose monitoring – frequency of finger prick testing		
outcomes	<ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ○ HbA1c (minimum follow-up 6 months) ○ Severe hypoglycaemic episodes ○ Nocturnal hypoglycaemic episodes ○ Diabetic ketoacidosis (DKA; number of episodes) • Adherence to diabetes management (including self-management) <p>Psycho-social outcomes</p> <ul style="list-style-type: none"> • Health-related quality of life • Children and young people's and families' satisfaction with intervention (impact of pain to be reflected here) 	<p>agreed to use them across the three questions relating to blood glucose monitoring (with the exception of DKA which is used in this question but is replaced in the CGMS questions by mean blood glucose levels):</p> <ul style="list-style-type: none"> • frequency of finger-prick (capillary) testing, • sustained use of continuous subcutaneous glucose monitoring with real-time adjustment of insulin treatment versus intermittent use of continuous subcutaneous glucose monitoring with retrospective adjustment of insulin treatment, and • finger-prick (capillary) testing versus continuous subcutaneous glucose monitoring <p>Continuous subcutaneous glucose monitoring may be associated with very good control (low HbA1c) yet may also occur as part of the management of type 1 diabetes in children and young people with poor long-term control</p> <p>The GDG considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes</p> <p>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</p> <p>Severe hypoglycaemic episodes defined according to either of the following criteria.</p> <ul style="list-style-type: none"> • International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose) • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or

Type 1 diabetes – blood glucose monitoring – frequency of finger prick testing		
		in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)
Health economics outcomes	This question was prioritised for health economic analysis Health-related quality of life (measured using quality adjusted life years (QALYs)) In particular, risk of complications or accidents resulting from mild or severe hypoglycaemic episodes	The GDG's view was that commissioners ration testing strips because they are expensive and so this becomes a barrier to implementation
Other criteria for inclusion/exclusion of studies	None	Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this (frequency of testing is likely to depend on age)
Search strategies	See separate document	A single search for evidence will be undertaken across the three questions relating to blood glucose monitoring
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	School regulations can be a barrier to uptake, which creates variations in practice The GDG noted that it can be helpful if spare pens, meters and strips are available in schools

Type 1 diabetes – blood glucose monitoring – finger prick testing versus continuous glucose monitoring		
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes who have persistent problems with hypoglycaemia unawareness or repeated hypoglycaemia or hyperglycaemia should be offered continuous glucose monitoring systems. Children and young people with type 1 diabetes should be offered blood glucose monitors with memories (as opposed to monitors without memories) because these are associated with improved patient satisfaction. Research recommendation Research is needed to evaluate the clinical effectiveness of the routine use of invasive and noninvasive continuous glucose monitoring systems for optimising glycaemic control in children and young people with type 1 diabetes.	Update needs to be clear about which children and young people would benefit from using continuous glucose monitoring systems Devices without memories are no longer available and so this recommendation may be obsolete now
Review	What is the effectiveness of finger-prick blood	Continuous glucose monitoring

Type 1 diabetes – blood glucose monitoring – finger prick testing versus continuous glucose monitoring		
question for update	glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?	<p>can be used daily or just at night. Monitoring devices are often supplied by the diabetes care team for short-term use (4-5 days) for trouble-shooting multiple daily injection regimens, for example, to get an idea of when hypoglycaemia occurs (often at night). More recently, they have been made available to the child or young person for long-term use</p> <p>The child or young person may not see the results that are recorded – the results may be transmitted to the diabetes care team and analysed retrospectively</p> <p>This question covers all forms of finger-prick testing and continuous glucose monitoring</p>
Objectives	To identify the circumstances in which children and young people with type 1 diabetes should be offered continuous subcutaneous glucose monitoring in addition to capillary blood testing (finger-prick testing).	<p>NICE has confirmed that evidence relating to insulin pumps that perform a continuous glucose monitoring function can be considered in this review (alongside evidence relating to standalone continuous glucose monitoring devices). The guideline will not be able to make any specific recommendations in relation to insulin pumps and the review should avoid commenting on individual insulin pumps. The guideline will be able to cross-refer to the NICE technology appraisal (TA) 151 on insulin pump therapy for diabetes where appropriate (see http://publications.nice.org.uk/continuous-subcutaneous-insulin-infusion-for-the-treatment-of-diabetes-mellitus-ta151)</p>
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) only	<p>A 2012 Cochrane review 'Continuous glucose monitoring systems for type 1 diabetes mellitus' contains seven RCTs published since 2004</p> <p>The following studies might be relevant to this question:</p> <ul style="list-style-type: none"> • Pickup 2011 (meta-analysis based on individual patient data – see BMJ 2011;343:d3805 doi: 10.1136/bmj.d3805) • Bergenstal 2010 (multicentre

Type 1 diabetes – blood glucose monitoring – finger prick testing versus continuous glucose monitoring		
		<p>RCT – see N Engl J Med 2010;363:311-20 doi: 10.1056/NEJMoa1002853)</p> <ul style="list-style-type: none"> • Battelino 2012 (multicentre RCT – see Diabetologia (2012) 55:3155–3162 DOI 10.1007/s00125-012-2708-9)
Status	Published articles indexed since the searches for the 2004 guideline were completed	This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles), although it is unlikely that many of them will be relevant because technology has moved on. Short-term use and loan of monitoring devices is, however, still relevant
Population	Children and young people with type 1 diabetes	
Intervention or index test	<p>Any form of continuous subcutaneous glucose monitoring, including</p> <ul style="list-style-type: none"> • sustained use of continuous subcutaneous glucose monitoring (providing real-time, ongoing output) • continuous subcutaneous glucose monitoring performed intermittently and analysed retrospectively without the child or young person seeing the measurements 	<p>In all instances, finger-prick testing needs to be used alongside continuous subcutaneous glucose monitoring for the purposes of calibrating the continuous monitoring device</p> <p>Note to NCC-WCH: all monitoring methods that involve a subcutaneous cannula are of interest in this question, but evidence relating to any version of glucoWatch (which is now obsolete) should be excluded</p>
Comparator or reference standard	<p>Any form of capillary blood glucose testing, including:</p> <ul style="list-style-type: none"> • finger-prick testing • testing at another anatomical site • any frequency of testing 	<p>Self-monitoring of blood glucose (SMBG) is standard term in clinical practice and research articles</p> <p>The GDG agreed that all frequencies of SMBG will be included</p>
Clinical outcomes	<p>Physical outcomes</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ○ HbA1c (minimum follow-up 6 months – if not available then use 3-month follow-up) ○ mean blood glucose levels ○ severe hypoglycaemic episodes ○ nocturnal hypoglycaemic episodes • Adherence to diabetes management (including self-management) <p>Psycho-social outcomes</p> <ul style="list-style-type: none"> • Health-related quality of life 	<p>The GDG selected 7 outcomes and agreed to use these across the three questions relating to blood glucose monitoring (with the exception of mean blood glucose levels which would be excluded from the frequency question and replaced with DKA):</p> <ul style="list-style-type: none"> • frequency of finger-prick (capillary) testing, • sustained use of continuous subcutaneous glucose monitoring with real-time

Type 1 diabetes – blood glucose monitoring – finger prick testing versus continuous glucose monitoring	
<ul style="list-style-type: none"> • Children and young people's and families' satisfaction with intervention (impact of pain to be reflected here) 	<p>adjustment of insulin treatment versus intermittent use of continuous subcutaneous glucose monitoring with retrospective adjustment of insulin treatment, and</p> <ul style="list-style-type: none"> • finger-prick (capillary) testing versus continuous subcutaneous glucose monitoring <p>Continuous subcutaneous glucose monitoring may be associated with very good control (low HbA1c) yet may also occur as part of the management of type 1 diabetes in children and young people with poor long-term control</p> <p>The GDG considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes</p> <p>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</p> <p>Severe hypoglycaemic episodes defined according to either of the following criteria.</p> <ul style="list-style-type: none"> • International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose) • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with

Type 1 diabetes – blood glucose monitoring – finger prick testing versus continuous glucose monitoring		
		or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)
Health economics outcomes	This question was prioritised for health economic analysis Health-related quality of life (measured using quality adjusted life years (QALYs)) In particular, risk of complications or accidents resulting from mild or severe hypoglycaemic episodes	
Other criteria for inclusion/exclusion of studies	None	Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this Subgroup analysis for insulin pump therapy versus multiple daily injections would be of interest Subgroup analysis based on how continuous subcutaneous glucose monitoring is used (sustained versus intermittent) would be of interest
Search strategies	See separate document	A single search for evidence will be undertaken across the three questions relating to blood glucose monitoring
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The possibility of providing spare pens, meters, strips and continuous subcutaneous glucose monitoring devices to keep in school was raised by the GDG

Type 1 diabetes – blood glucose monitoring – intermittent versus real-time continuous glucose monitoring		
Existing recommendation(s) in 2004 guideline	<p>Children and young people with type 1 diabetes who have persistent problems with hypoglycaemia unawareness or repeated hypoglycaemia or hyperglycaemia should be offered continuous glucose monitoring systems.</p> <p>Children and young people with type 1 diabetes should be offered blood glucose monitors with memories (as opposed to monitors without memories) because these are associated with improved patient satisfaction.</p>	Update needs to be clear about which children and young people would benefit from using continuous glucose monitoring systems
Review question for update	What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?	<p>Continuous glucose monitoring can be used daily or just at night. Monitoring devices are often supplied by the diabetes care team for short-term use (4-5 days) for trouble-shooting multiple daily injection regimens, for example, to get an idea of when hypoglycaemia occurs (often at night). More recently, they have been made available to the child or young person for long-term use</p> <p>The child or young person may not see the results that are recorded – the results may be transmitted to the diabetes care team and analysed retrospectively</p>
Objectives	<p>To identify the optimal use of continuous subcutaneous glucose monitoring (sustained use with real-time adjustment versus intermittent use with retrospective adjustment) in children and young people with type 1 diabetes. The question focuses on the comparative effectiveness in children and young people with type 1 diabetes of:</p> <ul style="list-style-type: none"> • sustained continuous subcutaneous glucose monitoring (providing real-time, ongoing output and adjustment to insulin treatment where appropriate), and • continuous subcutaneous glucose monitoring performed intermittently with retrospective adjustment of insulin treatment. • In all instances, finger-prick testing needs to be used alongside continuous subcutaneous glucose monitoring for the purposes of calibrating the continuous monitoring device 	<p>NICE has confirmed that evidence relating to insulin pumps that perform a continuous glucose monitoring function can be considered in this review (alongside evidence relating to standalone continuous glucose monitoring devices). The guideline will not be able to make any specific recommendations in relation to insulin pumps and the review should avoid commenting on individual insulin pumps. The guideline will be able to cross-refer to the NICE technology appraisal (TA) 151 on insulin pump therapy for diabetes where appropriate (see http://publications.nice.org.uk/continuous-subcutaneous-insulin-infusion-for-the-treatment-of-diabetes-mellitus-ta151)</p>
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) only	A 2012 Cochrane review 'Continuous glucose monitoring systems for type 1 diabetes mellitus' contains seven RCTs

Type 1 diabetes – blood glucose monitoring – intermittent versus real-time continuous glucose monitoring		
		published since 2004
Status	Published articles indexed since the searches for the 2004 guideline were completed	This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles), although it is unlikely that many of them will be relevant because technology has moved on. Short-term use and loan of monitoring devices is, however, still relevant
Population	Children and young people with type 1 diabetes	
Intervention or index test	Sustained use of continuous subcutaneous glucose monitoring (providing real-time, ongoing output)	
Comparator or reference standard	Continuous subcutaneous glucose monitoring performed intermittently and analysed retrospectively without the child or young person seeing the measurements	Note to NCC-WCH: all monitoring methods that involve a subcutaneous cannula are of interest in this question, but evidence relating to any version of gluowatch (which is now obsolete) should be excluded
Clinical outcomes	<p>Physical outcomes</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ○ HbA1c (minimum follow-up 6 months) ○ Mean blood glucose levels ○ Severe hypoglycaemic episodes ○ Nocturnal hypoglycaemic episodes • Adherence to diabetes management (including self-management) <p>Psycho-social outcomes</p> <ul style="list-style-type: none"> • Health-related quality of life • Children and young people's and families' satisfaction with intervention (impact of pain to be reflected here) 	<p>The GDG selected 7 outcomes and agreed to use these across the three questions relating to blood glucose monitoring (with the exception of mean blood glucose levels which would be excluded from the frequency question and replaced with DKA):</p> <ul style="list-style-type: none"> • frequency of finger-prick (capillary) testing, • sustained use of continuous subcutaneous glucose monitoring with real-time adjustment of insulin treatment versus intermittent use of continuous subcutaneous glucose monitoring with retrospective adjustment of insulin treatment, and • finger-prick (capillary) testing versus continuous subcutaneous glucose monitoring <p>Continuous subcutaneous glucose monitoring may be associated with very good control (low HbA1c) yet may also occur as part of the management of type 1 diabetes in children and young people with poor long-term</p>

Type 1 diabetes – blood glucose monitoring – intermittent versus real-time continuous glucose monitoring		
		<p>control</p> <p>The GDG considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes</p> <p>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</p> <p>Severe hypoglycaemic episodes defined according to either of the following criteria.</p> <ul style="list-style-type: none"> • International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose) • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)
Health economics outcomes	<p>This question was prioritised for health economic analysis</p> <p>Health-related quality of life (measured using quality adjusted life years (QALYs))</p> <p>In particular, risk of complications or accidents resulting from mild or severe hypoglycaemic episodes</p>	
Other criteria for inclusion/exclusion of studies	None	<p>Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this</p>

Type 1 diabetes – blood glucose monitoring – intermittent versus real-time continuous glucose monitoring		
		Subgroup analysis for insulin pump therapy versus multiple daily injections would be of interest
Search strategies	See separate document	A single search for evidence will be undertaken across the three questions relating to blood glucose monitoring
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	The possibility of providing spare devices to keep in school was raised by the GDG

E.8 Type 1 diabetes – blood ketone monitoring

Review question: What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis?

Type 1 diabetes – blood ketone monitoring		
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes should have short-acting insulin or rapid-acting insulin analogues and blood and/or urine ketone testing strips available for use during intercurrent illness.	The 2004 guideline also includes a recommendation for further research to evaluate the role of blood ketone monitoring in preventing diabetic ketoacidosis (DKA) in children and young people with type 1 diabetes
Review question for update	What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of DKA?	
Objectives	To compare the clinical and cost effectiveness of blood ketone monitoring and urine ketone monitoring in the prevention or early detection of DKA in children and young people with type 1 diabetes. The question relates to home monitoring of ketones (rather than monitoring in hospital during treatment for DKA). It should include consideration of the frequency of monitoring, and the potential use of ketone monitoring will be interpreted more broadly than in relation to intercurrent illness. Comparisons between monitoring during intercurrent illness and at other times, depending on the insulin regimen being used (and especially when using insulin pump therapy), will be considered if the evidence allows	
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) Comparative observational studies (including cohort and case-control studies)	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion RCT by Laffel LM, Diabetes Medicine, 2006, pp 278-84 might provide useful evidence on relevant outcomes
Status	Published articles indexed since the searches for the 2004 guideline were completed	This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles)
Population	Children and young people with type 1 diabetes	The guideline scope

Type 1 diabetes – blood ketone monitoring		
		defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	Blood ketone monitoring	Beta-hydroxybutyrate, ketosis, and acetoacetate might be useful search terms
Comparator or reference standard	Urine ketone monitoring	Historically urine ketone monitoring would have been usual practice
Clinical outcomes	<p>Physical outcomes</p> <ul style="list-style-type: none"> • Development of DKA (number of episodes) • Severity of DKA (measured by pH at admission) • Hospital admission rates • Mortality • Contact with the diabetes care team (for example, to interpret ketone measurements and determine appropriate action) as a measure of healthcare utilization • Adherence to diabetes management (including self-management) <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> • Health-related quality of life • Children and young people's and families' satisfaction with intervention 	<p>The GDG noted that use of out-of-date testing strips would constitute a lack of adherence and such practice should be discouraged. The group did not prioritise adherence to diabetes management (including self-management) as an outcome for extraction initially because it was unlikely to be reported in clinical studies. The group did, however, note that discouraging the use of out-of-date testing strips might be discussed in the evidence to recommendations section of the guideline</p> <p>Due to the sparsity of evidence identified for inclusion, the NCC-WCH technical team extracted data on adherence to diabetes management (percentage of time the test was used during sick days)</p>
Health economics outcomes	<p>This question was prioritised for health economic analysis</p> <p>Health-related quality of life (measured using quality adjusted life years (QALYs))</p> <p>Hospitalisation episodes</p>	Full recovery usually occurs with appropriate management, although a risk of long-term intellectual impairment may occur even in children and young people without cerebral oedema. DKA is the most common form of diabetic related death in children and young

Type 1 diabetes – blood ketone monitoring		
		<p>people with a 2-5% mortality from cases</p> <p>Most of the potential QALY gain from monitoring is, therefore, likely to arise from averted mortality, although there is additionally some long-term morbidity from neurological deficits in about 35% of children and young people who survive an episode of cerebral oedema</p> <p>In addition to the QALY gain, cost-effectiveness will be dependent on monitoring averting expensive episodes of hospitalisation</p>
Other criteria for inclusion/exclusion of studies	None	NCC-WCH to inform the team developing the type 1 diabetes in adults guideline whether studies involving home ketone monitoring report numbers of hospital admissions (this outcome was prioritised for consideration in this question). The team developing the type 1 diabetes in adults guideline would also like to know whether studies involving monitoring of ketones in hospital report severity or length of stay, but this relates to ketone monitoring during treatment for DKA, which will be covered in this guideline by the questions relating to management of DKA
Search strategies	See separate document	
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p> <p>Evidence tables and an evidence profile will be used to summarise the evidence</p>	
Equality	Equalities issues will be assessed according to	

Type 1 diabetes – blood ketone monitoring

	processes described in NICE guidelines manual (November 2012)	
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E.9 Type 1 diabetes – dietary advice

Review questions:

What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?

What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?

Type 1 diabetes – dietary advice – carbohydrate counting		
Existing recommendation(s) in 2004 guideline	<p>Children and young people with type 1 diabetes and their families should be informed that they have the same basic nutritional requirements as other children and young people. The food choices of children and young people should provide sufficient energy and nutrients for optimal growth and development, with total daily energy intake being distributed as follows:</p> <ul style="list-style-type: none"> • carbohydrates – more than 50% • protein – 10–15% • fat – 30–35%. <p>The consumption of five portions of fruit and vegetables per day is also recommended. Neonates, infants and pre-school children require individualised dietary assessment to determine their energy needs.</p> <p>Children and young people using multiple daily injection regimens should be offered education about insulin and dietary management as part of their diabetes care package, to enable them to adjust their insulin dose to reflect their carbohydrate intake.</p>	<p>The 2004 guideline does not make specific recommendations about carbohydrate counting, but it includes the recommendations listed which refer to carbohydrate intake as a percentage of the total diet and adjusting insulin doses to reflect carbohydrate intake</p>
Review question for update	<p>What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?</p>	
Objectives	<p>To determine whether dietetic advice using carbohydrate counting is effective in children and young people with type 1 diabetes. The term carbohydrate counting is taken here to mean the calculation of insulin:carbohydrate ratios, as used with multiple daily injection regimens or insulin pump therapy (that is, level 3 carbohydrate counting in the American Dietetic Association classification)</p> <p>The American Dietetic Association classifies approaches to carbohydrate counting using the following three levels (see Gillespie et al, 1998 and Rabasa-Lhoret et al, 1999)</p> <ul style="list-style-type: none"> • Level 1 – consistent carbohydrate intake. At this level the patient is introduced to the fundamental concept that carbohydrate is the food component that raises blood glucose. A consistent intake of carbohydrate is encouraged based on predefined quantities of food 	<p>Note that dietary management using glycaemic index, which can be used with or without carbohydrate counting, is considered in a separate review question</p> <p>References for the American Dietetic Association classification are as follows:</p> <ul style="list-style-type: none"> • Gillespie SJ, Kulkarni KD, Daly AE. Using carbohydrate counting in diabetes clinical practice. J Am Diet Assoc 1998; 98: 897–905. • Rabasha-Lhoret R, Garon J, Langelier H et al. Effects of meal carbohydrate content on insulin requirements in Type 1 diabetic patients treated with Ultralente-Regular) insulin regimen. Diabetes Care 1999:

Type 1 diabetes – dietary advice – carbohydrate counting		
	<ul style="list-style-type: none"> • Level 2 – pattern management principles. At this level, patients continue to eat regular carbohydrate, use a consistent baseline insulin dose and monitor blood glucose levels frequently. They recognise patterns of blood glucose response to carbohydrate (and other food) intake, and changes that occur with insulin and exercise. They learn to adjust their insulin dose, or change carbohydrate intake or timing of exercise, to meet blood glucose targets • Level 3 – insulin:carbohydrate ratios. At this level, which is appropriate for people on multiple daily injection regimens or insulin pump therapy, calculation of insulin:carbohydrate ratios are individualised according to age, sex, pubertal status, duration of diabetes, time of day, and activity. Adjustment of pre-meal insulin according to the estimated carbohydrate content of the meal or snack is then undertaken using the specified insulin:carbohydrate ratios 	<p>22: 667–673.</p> <p>The GDG clarified that level 3 carbohydrate counting is used only with multiple daily injection regimens and insulin pump therapy</p>
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) only	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	Dietetic advice involving carbohydrate counting (level 3 in the American Dietetic Association classification)	<p>Include studies only if dietetic advice includes direct contact and training with healthcare professionals (for example, providing an information leaflet is not enough)</p> <p>Exclude studies in which advice about carbohydrate counting is given, but insulin is not adjusted according to carbohydrate intake (level 3 carbohydrate counting implies participants will be using multiple daily injection regimens or insulin pump therapy)</p> <p>Evidence tables should document the insulin regimen in the intervention and comparison groups</p>

Type 1 diabetes – dietary advice – carbohydrate counting		
Comparator or reference standard	Usual care	<p>Usual care could include dietetic advice which does not incorporate specific advice about carbohydrate counting, including levels 1 and 2 in the American Dietetic Association classification</p> <p>NCC-WCH technical team to clarify with the GDG whether specific interventions and comparators are relevant to this question once the search has been completed and/or weeded; the appropriate focus may depend on the conclusions from the multiple daily injections review question</p>
Clinical outcomes	<p>Physical outcomes</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ○ HbA1c (minimum follow-up 6 months) ○ Severe hypoglycaemic episodes ○ Postprandial hyperglycaemia (for example, glucose excursions or larger area under the glucose concentration curve) • Adherence to diabetes management (including self-management) • Changes in body mass index (BMI) standard deviation score (SDS) <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> • Health-related quality of life • Children and young people's and families' satisfaction with intervention 	<p>The GDG selected the same priority outcomes for the questions on carbohydrate counting and glycaemic index, and the outcomes selected were the same as those for the question on multiple daily injection regimens except that postprandial hyperglycaemia was substituted for diabetic ketoacidosis (DKA)</p> <p>The GDG considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes</p> <p>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</p> <p>Severe hypoglycaemic episodes defined according to either of the following criteria.</p> <ul style="list-style-type: none"> • International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose)

Type 1 diabetes – dietary advice – carbohydrate counting		
		<ul style="list-style-type: none"> • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)
Health economic outcomes	<p>This question was prioritised for health economic analysis, but only in connection with the question on multiple daily injections</p> <p>Health-related quality of life and quality adjusted life years (QALYs)</p> <p>Adherence to diabetes management (including self-management)</p> <p>It may be possible attach a QALY to various long-term complications – long-term outcomes are not prioritised per se but might be affected through glycaemic control</p>	GDG to note that, although mortality is not prioritised as a clinical outcome, health economic modelling incorporating data on mortality might be relevant through the link between hypoglycaemia and mortality
Other criteria for inclusion/exclusion of studies		Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allow this (although the availability of such studies is not expected)
Search strategies	See separate document	
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p> <p>Evidence tables and an evidence profile will be used to summarise the evidence</p>	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	

Type 1 diabetes – dietary advice – glycaemic index		
Existing recommendation(s) in 2004 guideline	<p>Children and young people with type 1 diabetes and their families should be informed of the importance of healthy eating in reducing the risk of cardiovascular disease (including foods with a low glycaemic index, fruit and vegetables, and types and amounts of fats), and means of making appropriate nutritional changes in the period after diagnosis and according to need and interest at intervals thereafter.</p> <p>Children and young people using multiple daily</p>	The 2004 guideline does not make specific recommendations about glycaemic intake in children and young people, but it includes the recommendations listed which refer to the importance of foods with low glycaemic index as part of a healthy diet, and adjusting insulin doses to reflect carbohydrate intake

Type 1 diabetes – dietary advice – glycaemic index		
	injection regimens should be offered education about insulin and dietary management as part of their diabetes care package, to enable them to adjust their insulin dose to reflect their carbohydrate intake.	The type 1 diabetes in adults guideline update includes a parallel question for which the initial systematic review was undertaken by the NCC-WCH team; material differences between the two reviews are indicated here
Review question for update	What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?	
Objectives	To determine whether dietetic advice using glycaemic index is effective in children and young people with type 1 diabetes in terms of maintaining glycaemic control. The GDG noted that knowledge about foods with a low glycaemic index and those with a high glycaemic index could be relevant for the update	
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) only	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	Dietetic advice taking account of the glycaemic index of carbohydrates	
Comparator or reference standard	Dietetic advice that does not take account of glycaemic index Carbohydrate counting without taking account of glycaemic index	<p>The only difference between the intervention and comparator arms should be the use of glycaemic index</p> <p>Evidence tables should document the insulin regimen and whether or not carbohydrate counting was used</p> <p>Expect more evidence for this question than for carbohydrate counting</p> <p>Articles to consider include:</p> <ul style="list-style-type: none"> • Brand-Miller J, Hayne J, Petocz P, Colagiuri, C, Low-Glycemic Index Diets in the Management of Diabetes: A meta-analysis of randomized controlled trials, <i>Diabetes Care</i> 26:2261–2267,

Type 1 diabetes – dietary advice – glycaemic index		
		<p>2003</p> <ul style="list-style-type: none"> • Gilbertson HR, Brand-Miller JC, Thorburn AW, Evans S, Chondros P, Werther GA, The Effect of Flexible Low Glycemic Index Dietary Advice Versus Measured Carbohydrate Exchange Diets on Glycemic Control in Children With Type 1 Diabetes, <i>Diabetes Care</i> 24:1137–1143, 2001
Clinical outcomes	<p>Physical outcomes</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ○ HbA1c (minimum follow-up 6 months) ○ Severe hypoglycaemic episodes ○ Postprandial hyperglycaemia (for example, glucose excursions or larger area under the glucose concentration curve) • Adherence to diabetes management (including self-management) • Changes in body mass index (BMI) standard deviation score (SDS) <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> • Health-related quality of life • Children and young people's and families' satisfaction with intervention 	<p>The GDG for diabetes in children and young people selected the same priority outcomes for the review questions on carbohydrate counting and glycaemic index, and the outcomes selected were the same as those for the question on multiple daily injection (MDI) regimens except that postprandial hyperglycaemia was substituted for diabetic ketoacidosis (DKA)</p> <p>The GDG for type 1 diabetes in adults selected the same priority outcomes as for children and young people, except that nocturnal hypoglycaemia was substituted for changes in BMI SDS. The latter was considered to be more important in children and young people with type 1 diabetes across the questions about dietetic advice and MDI regimens because any dietetic intervention might affect weight gain, whereas daytime food intake is unlikely to result in nocturnal hypoglycaemia because food intake will be covered by administration of short-acting insulin that will generally have little effect during sleep</p> <p>The GDG for diabetes in children and young people considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes. The same approach was used in the question related to adults with type 1 diabetes</p>

Type 1 diabetes – dietary advice – glycaemic index		
		<p>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</p> <p>Severe hypoglycaemic episodes defined according to either of the following criteria.</p> <ul style="list-style-type: none"> • International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose) • ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)
Health economic outcomes	<p>This question was not prioritised for health economic analysis</p> <p>Health-related quality of life and quality adjusted life years (QALYs)</p> <p>Adherence to diabetes management (including self-management)</p> <p>It may be possible attach a QALY to various long-term complications – long-term outcomes are not prioritised per se but might be affected through glycaemic control</p>	<p>GDG to note that, although mortality is not prioritised as a clinical outcome, health economic modelling incorporating data on mortality might be relevant through the link between hypoglycaemia and mortality</p>
Other criteria for inclusion/exclusion of studies	None	<p>Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this (although the availability of such studies is not expected)</p>
Search strategies	See separate document	
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p>	

Type 1 diabetes – dietary advice – glycaemic index		
	Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	

E.10 Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

Review question: What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?

Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs		
Existing recommendation(s) in 2004 guideline	<p>Management from diagnosis</p> <p>Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document.</p> <p>Diabetic ketoacidosis</p> <p>Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes.</p> <p>Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward.</p> <p>Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit.</p> <p>Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit.</p> <p>Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.</p>	<p>All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness</p> <p>The guidelines published by the British Society for Paediatric Endocrinology and Diabetes (BSPED) were reproduced in an appendix of the 2004 guideline</p> <p>The 2004 guideline was specific to type 1 diabetes</p> <p>The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the GDG plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full GDG will ratify all conclusions and recommendations based on the DKA evidence</p>
Review question for update	What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of DKA in children and young people?	The review questions for type 1 and type 2 diabetes are identical
Objectives	To evaluate the predictive value of symptoms, signs and biochemical abnormalities as indicators of DKA in children and young people with type 1 or type 2 diabetes. These questions cover children and young people who have either type 1 or type 2 diabetes. The diagnosis of diabetes may have been made previously, or they may be presenting for the first time with DKA	
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) only Comparative observational studies (including	Study designs other than RCTs will be considered only if no RCT evidence is identified for

Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs		
	cohort and case-control studies)	<p>inclusion</p> <p>The GDG noted that for these questions RCTs are unlikely to be identified, and so the systematic search for evidence should encompass observational studies from the outset</p> <p>The GDG discussed the feasibility of identifying prospective observational studies for inclusion and concluded that it might be necessary to consider retrospective studies (for example, case-control studies, because of the rarity of DKA) despite their potential limitations</p>
Status	Published articles (no limitation on year of publication)	Although this is an update and expansion of a review question considered in the 2004 guideline, no date limit will be applied to searches for these specific review questions to ensure that all relevant articles are identified for both type 1 and 2 diabetes
Population	Children and young people (in whom type 1 or type 2 diabetes may or may not have been recognised previously)	<p>The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years</p> <p>The GDG noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services</p>
Intervention or index test	<p>Symptoms, signs and biochemical abnormalities that are suggestive of DKA and their predictive values individually or in combination</p> <p>Symptoms and signs</p> <ul style="list-style-type: none"> • polydypsia • polyuria (possibly manifesting as bedwetting, that is, secondary enuresis) • weight loss • dehydration • nausea or vomiting 	<p>The clinical problem is that DKA is not always recognised (rather than it being overdiagnosed)</p> <p>The GDG agreed to consider the symptoms, signs and biochemical abnormalities listed in terms of their value as predictive features</p> <p>The order in which the symptoms and signs are</p>

Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs		
	<ul style="list-style-type: none"> • abdominal pain • respiratory distress • altered level of consciousness <p>Biochemical abnormalities</p> <ul style="list-style-type: none"> • hyperglycaemia • acidosis • ketosis 	<p>currently listed reflects increasing severity of DKA; it might be useful to reflect this in the review</p> <p>GDG to consider tests (capillary blood glucose), recognition, prevention at diagnosis somewhere in the guideline (not directly this question)</p>
Comparator or reference standard	Hospital-based diagnosis of DKA (based on pH or bicarbonate, blood glucose and blood or urine ketones)	
Clinical outcomes	Diagnostic test (predictive) accuracy (sensitivity, specificity and positive and negative likelihood ratios) applied to symptoms, signs and biochemical abnormalities individually or in groups	
Health economics outcomes	These questions were not prioritised for health economic analysis	This will remain true provided the recommendations arising from these questions are restricted to giving a list of symptoms, signs and biochemical abnormalities to look out for, rather than interventions that should follow based on them
Other criteria for inclusion/exclusion of studies	Exclude studies with <10 participants in total	<p>Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation</p> <p>Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this</p>
Search strategies	See separate document	A single search for evidence will be undertaken across the two questions
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p> <p>Evidence tables and an evidence profile will be used to summarise the evidence</p>	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	The GDG's view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first

Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs		
		presentation with diabetes
		Communication problems (young children and neurodisabilities) might also be of relevance for this question

E.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions:

What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?

Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:

- general observations (for example, heart and respiratory rate and blood pressure)
- body weight
- hydration status
- fluid balance
- neurological observations
- electrocardiographic (ECG) monitoring?

Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:

- blood glucose
- blood or urine ketones
- serum urea or electrolytes
- acid/base status?

Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations		
Existing recommendation(s) in 2004 guideline	<p>Management from diagnosis</p> <p>Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document.</p> <p>Diabetic ketoacidosis</p> <p>Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes.</p> <p>Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward.</p> <p>Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit.</p> <p>Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit.</p> <p>Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than</p>	<p>All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness</p> <p>The guidelines published by the British Society for Paediatric Endocrinology and Diabetes (BSPED) were reproduced in an appendix of the 2004 guideline</p> <p>The 2004 guideline was specific to type 1 diabetes</p> <p>The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the GDG plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full GDG will ratify all conclusions and</p>

Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations		
	<p>50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.</p>	<p>recommendations based on the DKA evidence</p>
<p>Review question for update</p>	<p>What routine assessments and investigations should be used to inform management in children and young people who present with DKA? Which of the following should be performed as clinical monitoring during treatment of DKA in children and young people:</p> <ul style="list-style-type: none"> • general observations (for example, heart and respiratory rate and blood pressure) • body weight • hydration status • fluid balance • neurological observations • electrocardiographic (ECG) monitoring? <p>Which of the following laboratory investigations should be performed to monitor children and young people during treatment for DKA:</p> <ul style="list-style-type: none"> • blood glucose • blood or urine ketones • serum urea or electrolytes • acid/base status? 	<p>The review questions for type 1 and type 2 diabetes are identical</p> <p>The GDG needs to address assessment of, and typical degree of, dehydration somewhere, and volume of fluids for rehydration, and this protocol is intended to be broad enough to accommodate this</p> <p>The GDG might want to consider recommending the use of early warning scores</p>
<p>Objectives</p>	<p>To identify the appropriate clinical assessments and laboratory investigations that should be performed in order to guide treatment for children and young people with DKA, and to monitor the response during treatment. The guideline scope requires the GDG to consider all of the following.</p> <ul style="list-style-type: none"> • Immediate management at presentation (for example, maintenance of airway, breathing and circulation or the potential need for a nasogastric tube to prevent pulmonary aspiration) • Clinical assessment and investigations at presentation to guide management • Fluid management, including: <ul style="list-style-type: none"> ○ assessment of dehydration ○ volume of administration • Clinical monitoring (to assess the response to treatment and to look for evidence of cerebral oedema), including: <ul style="list-style-type: none"> ○ general observations (for example, heart and respiratory rate and blood pressure) ○ body weight ○ hydration status ○ fluid balance ○ neurological observations ○ ECG monitoring • Laboratory monitoring (to assess the response to treatment and to look for evidence of 	<p>Other aspects of fluid management (route and rate of administration, choice of fluid, and additives) are addressed through separate questions and a different protocol</p>

Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations		
	hypokalaemia), including: <ul style="list-style-type: none"> ○ blood glucose ○ blood or urine ketones ○ serum urea and electrolytes ○ acid/base status 	
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) Comparative observational studies (including cohort and case-control studies)	There are unlikely to be any RCTs for this question and so the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies
Status	Published articles (no limitation on year of publication)	No date limit will be applied to searches for these specific review questions to ensure that all relevant articles are identified for both type 1 and 2 diabetes
Population	Children and young people with type 1 or type 2 diabetes (although the diabetes may not yet have been recognised, for example, if the child or young person is presenting for the first time with DKA)	<p>The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years</p> <p>The GDG noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services</p>
Intervention or index test	Any approach to clinical assessment and/or laboratory investigations for children and young people presenting with DKA or during treatment	<p>Although the intervention and comparison are specified very broadly, the guideline scope requires the GDG to address all of the following, whether or not relevant evidence is identified through the systematic search</p> <p>Immediate management at presentation (for example, maintenance of airway, breathing and circulation or the potential need for a nasogastric tube to prevent pulmonary aspiration)</p> <p>Clinical assessment and investigations at presentation to guide management</p>

Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

		<p>Fluid management, including:</p> <ul style="list-style-type: none">• assessment of dehydration• volume of administration• (other aspects of fluid management will be addressed through separate questions and a different protocol) <p>Clinical monitoring (to assess the response to treatment and to look for evidence of cerebral oedema), including:</p> <ul style="list-style-type: none">• general observations (for example, heart and respiratory rate and blood pressure)• body weight• hydration status• fluid balance• neurological observations• ECG monitoring <p>Laboratory monitoring (to assess the response to treatment and to look for evidence of hypokalaemia), including:</p> <ul style="list-style-type: none">• blood glucose• blood or urine ketones• serum urea and electrolytes• acid/base status <p>The GDG noted that the following terminology might be helpful when selecting search terms</p> <p>Clinical assessment</p> <ul style="list-style-type: none">• General observations (vital signs):<ul style="list-style-type: none">○ temperature○ level of consciousness• Clinical signs of dehydration:<ul style="list-style-type: none">○ altered skin colour○ sunken eyes○ cold extremities○ prolonged capillary refill time○ dry mucous membranes○ reduced skin turgor○ reduced urine output
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Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations		
		<ul style="list-style-type: none"> • Signs of deep vein thrombosis (including leg pain or swelling) <p>Laboratory investigations</p> <ul style="list-style-type: none"> • Blood ketones to include near-patient testing • Plasma osmolality (tonicity) <p>The evidence identified for inclusion could provide guidance on the frequency and duration with which to perform laboratory investigations</p>
Comparator or reference standard	Any other approach to clinical assessment and/or laboratory investigations for children and young people presenting with DKA or during treatment	<p>There may be few comparative studies identified for inclusion, but where necessary the GDG will be able to use informal consensus based on knowledge and experience to formulate recommendations addressing all areas required by the scope</p> <p>There may be comparative studies relating to blood ketone testing</p>
Clinical outcomes	<p>Physical outcomes</p> <ul style="list-style-type: none"> • Mortality • Degree of dehydration confirmed by post-recovery weight • Detection of hypovolaemia • Detection of laboratory abnormalities: <ul style="list-style-type: none"> ○ hypoglycaemia ○ hypokalaemia ○ hyponatraemia ○ persistent acidosis ○ persistent ketosis • Detection of complications: <ul style="list-style-type: none"> ○ cerebral oedema ○ venous thrombosis ○ aspiration • Healthcare utilisation (for example, duration of admission, requirement for ventilation (as a proxy for severity of DKA or presence of cerebral oedema)) 	<p>Note for NCC-WCH: Consider splitting outcomes by question but check first how much evidence is available for inclusion (that is, screen search results)</p> <p>Include consideration of frequency of monitoring and intervals</p> <p>GDG to consider changing terminology from 'hypokalaemia' to 'serum potassium concentration', etc in review questions related to DKA</p>
Health economics outcomes	These questions were not selected as priorities for health economic analysis	
Other criteria for inclusion/exclusion of studies	Exclude studies with <10 participants in total	Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation

Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations		
		Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this
Search strategies	See separate document	A single search for evidence will be undertaken across the six questions to cover all the aspects of interest in this protocol
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	The GDG's view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first presentation with diabetes

E.12 Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

Review questions:

What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?

At what rate should children and young people with diabetic ketoacidosis be rehydrated?

What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids		
Existing recommendation(s) in 2004 guideline	<p>Management from diagnosis</p> <p>Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document.</p> <p>Diabetic ketoacidosis</p> <p>Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes.</p> <p>Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward.</p> <p>Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit.</p> <p>Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit.</p> <p>Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.</p>	<p>All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness</p> <p>The guidelines published by the British Society for Paediatric Endocrinology and Diabetes (BSPED) were reproduced in an appendix of the 2004 guideline</p> <p>The 2004 guideline was specific to type 1 diabetes</p> <p>The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the GDG plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full GDG will ratify all conclusions and recommendations based on the DKA evidence</p>

Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids		
Review question for update	<p>What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?</p> <p>At what rate should children and young people with diabetic ketoacidosis be rehydrated?</p> <p>What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?</p>	<p>The review questions for type 1 and type 2 diabetes are identical</p> <p>All six questions will be covered by a single protocol. The available evidence will be presented in such a way as to emphasise the difference between the questions</p>
Objectives	<p>To determine the optimal fluid management regimen for children and young people with DKA. The review will address the following aspects of fluid management:</p> <ul style="list-style-type: none"> • route of administration ('route' in the table of outcomes below) • rate of administration ('rate' in the table of outcomes below) • choice of fluid (including sodium chloride content; 'fluid/sodium' in the table of outcomes below) • other additives (for example, <ul style="list-style-type: none"> ○ glucose ('glucose' in the table of outcomes below) ○ potassium ('potassium' in the table of outcomes below) ○ bicarbonate ('bicarbonate' in the table of outcomes below) ○ phosphate ('phosphate' in the table of outcomes below)) 	<p>The scope also requires consideration of assessment of dehydration and the volume of fluid administration; these will be covered by separate review questions linked to the questions about clinical assessment and investigations at presentation and during management of DKA</p> <p>The questions relating to route of administration should include consideration of the effectiveness of intraosseous administration</p>
Language	English	
Study design	<p>Systematic reviews and randomised controlled trials (RCTs)</p> <p>Comparative observational studies (including cohort and case-control studies)</p>	<p>There are unlikely to be RCTs that fully address all of these question and so the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies</p>
Status	Published articles (no limitation on year of publication)	<p>Although this is an update and expansion of a review question considered in the 2004 guideline, no date limit will be applied to searches for these specific review questions to ensure that all</p>

Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids									
								relevant articles are identified for both type 1 and 2 diabetes	
Population	Children and young people with type 1 or type 2 diabetes (although the diabetes may not yet have been recognised, for example, if the child or young person is presenting for the first time with DKA)								<p>The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years</p> <p>The GDG noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services</p>
Intervention or index test	Any fluid management regimen for children and young people presenting with DKA								
Comparator or reference standard	Any other fluid management regimen for children and young people presenting with DKA								
Clinical outcomes	Physical outcomes								<p>The GDG prioritised different outcomes for the different aspects of the review questions covered by this protocol ('route', 'rate', 'fluid/sodium', 'glucose', 'potassium', 'bicarbonate' and 'phosphate'); 'Y' in the cells of the table indicates that an outcome was prioritised for the corresponding aspect of the questions covered by the protocol. Some outcomes (for example, mortality) are common to all aspects of the questions</p> <p>The GDG discussed whether serum urea</p>
		Route	Rate	Fluid/sodium	Glucose	Potassium	Bicarbonate	Phosphate	
	Mortality	Y	Y	Y	Y	Y	Y	Y	
	Time to resolution of dehydration	Y	Y	Y					
	Rate of change of blood glucose concentration (this is likely to be reported in research studies, whereas resolution of hyperglycaemia (which would otherwise be of interest) might not be)		Y		Y				
Incidence of hypoglycaemia				Y					

Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids									
Resolution of acidosis (this is likely to be reported, especially in older studies that do not report resolution of blood ketosis, but it is likely to be of lower priority in formulating recommendations)	Y	Y	Y	Y	Y	Y	Y	Y	<p>concentration was an important outcome to consider for these questions and concluded that it was not because it is a marker of severity of DKA but it will not have an impact on management</p> <p>For some aspects, the GDG prioritised 8 outcomes initially and this remained acceptable because of the sparsity of the evidence identified for inclusion</p> <p>GDG to consider changing terminology from 'hypokalaemia' to 'serum potassium concentration', etc in review questions related to DKA</p>
Resolution of blood ketosis	Y			Y		Y			
Serum chloride concentration (a raised concentration is linked to acidosis)		Y	Y		Y		Y		
Incidence of cerebral oedema (this could cause morbidity or mortality), to include participants with symptoms or signs suggestive of cerebral oedema (for example, development of unconsciousness) provided these are reported as being related to cerebral oedema	Y	Y	Y	Y	Y	Y	Y	Y	
Hypokalaemia (this is important because people with DKA die of this)					Y	Y			
Serum sodium concentration	Y	Y	Y			Y			
Serum calcium concentration								Y	
Carbon dioxide (CO ₂)			Y			Y			

Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids								
	concentration							
	Healthcare utilisation (for example, duration of admission, requirement for ventilation (as a proxy for severity of DKA or presence of cerebral oedema))	Y	Y	Y	Y	Y	Y	Y
Health economics outcomes	These questions were not prioritised for health economic analysis							
Other criteria for inclusion/exclusion of studies	Exclude studies with <10 participants in total							
								<p>Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation</p> <p>Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this</p>
Search strategies	See separate document							
								<p>A single search for evidence will be undertaken across the questions relating to fluid management in children and young people presenting with DKA</p> <p>Possible search terms to include the following</p> <p>For fluid composition:</p> <ul style="list-style-type: none"> • sodium chloride or sodium lactate concentration • pH • specific fluids such as Ringer's solution, Hartmann's solution, isolyte, and plasmalyte

Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids		
		<p>For route of administration:</p> <ul style="list-style-type: none"> • intravenous • intraosseus • oral • not intramuscular
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p> <p>Evidence tables and an evidence profile will be used to summarise the evidence</p>	
Equality	<p>Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)</p>	<p>The GDG's view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first presentation with diabetes</p>

E.13 Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents

Review question: What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?

Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents		
Existing recommendation(s) in 2004 guideline	<p>Management from diagnosis Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document.</p> <p>Diabetic ketoacidosis Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes.</p> <p>Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward.</p> <p>Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit.</p> <p>Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit.</p> <p>Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.</p>	<p>All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness</p> <p>The guidelines published by the British Society for Paediatric Endocrinology and Diabetes (BSPED) were reproduced in an appendix of the 2004 guideline</p> <p>The 2004 guideline was specific to type 1 diabetes</p> <p>The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the GDG plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full GDG will ratify all conclusions and recommendations based on the DKA evidence</p>
Review question for update	What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?	The review questions for type 1 and type 2 diabetes are identical
Objectives	To assess the effectiveness of intravenous osmotic agents in the treatment of cerebral oedema associated with DKA in children and young people	<p>The main intervention of interest from the GDG is the urgent administration of mannitol whilst the child is still on a general paediatric ward</p> <p>Note the setting in which agents are administered and the duration of treatment in the evidence tables</p>

Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents		
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) Comparative observational studies (including cohort and case-control studies)	Although there may be some RCTs for this question the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies
Status	Published articles (no limitation on year of publication)	
Population	Children and young people with DKA and cerebral oedema	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years The GDG noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services
Intervention or index test	Any treatment based on administration of intravenous osmotic agents	For example, mannitol, hypertonic saline or a combination of the two May also be referred to as osmotic therapy or osmotherapy
Comparator or reference standard	Any other treatment based on administration of intravenous osmotic agents No treatment with osmotic agents	
Clinical outcomes	Physical outcomes <ul style="list-style-type: none"> • Mortality • Persistent neurological deficit • Healthcare utilisation (for example, duration of admission, requirement for ventilation (as a proxy for severity of DKA or presence of cerebral oedema)) 	
Health economics outcomes	This question was not prioritised for health economic analysis	
Other criteria for inclusion/exclusion of studies	Exclude studies with <10 participants in total	Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this

Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents		
Search strategies	See separate document	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	The GDG's view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first presentation with diabetes

E.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

Review questions:

When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?

How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – timing		
Existing recommendation(s) in 2004 guideline	<p>Management from diagnosis</p> <p>Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document.</p> <p>Diabetic ketoacidosis</p> <p>Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes.</p> <p>Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward.</p> <p>Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit.</p> <p>Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit.</p> <p>Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.</p>	<p>All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness</p> <p>The guidelines published by the British Society for Paediatric Endocrinology and Diabetes (BSPED) were reproduced in an appendix of the 2004 guideline</p> <p>The 2004 guideline was specific to type 1 diabetes</p> <p>The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the GDG plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full GDG will ratify all conclusions and recommendations based on the DKA evidence</p>
Review question for update	When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?	The review questions for type 1 and type 2 diabetes are identical
Objectives	To determine when intravenous insulin therapy should be started and stopped in children and young people with DKA. The two aspects of the review question will be addressed separately. Cerebral oedema is a potential	

Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – timing		
	<p>adverse consequence of starting intravenous insulin therapy too early (during intravenous infusion of fluids without glucose), whereas the optimal time to stop intravenous insulin therapy is likely to be determined by the timescale for continuing intravenous glucose infusion once ketoacidosis has been resolved. In some children and young people with DKA or ketonaemia who are not very ill it may not be necessary to use intravenous insulin therapy at all, and the question also covers this scenario. The GDG may also wish to make recommendations for the insulin regimen to be used immediately after stopping intravenous insulin therapy (taking into account the fact that the child or young person may or may not have been recognised as having type 1 or type 2 diabetes before presenting with DKA). Overall the GDG noted that the part of the question that deals with when to start intravenous insulin therapy was of greater clinical importance (as it could be associated with a risk of mortality)</p>	
Language	English	
Study design	<p>Systematic reviews and randomised controlled trials (RCTs)</p> <p>Comparative observational studies (including cohort and case-control studies)</p>	<p>For the part of the question about when to start intravenous insulin infusion: there may be no RCTs but some comparative observational studies</p> <p>For the part of the question about when to stop intravenous insulin infusion: it is very unlikely that there will be any RCTs and evidence from observational studies will be considered</p> <p>The GDG noted, therefore, that for these questions the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies</p>
Status	Published articles (no limitation on year of publication)	<p>Although this is an update and expansion of a review question considered in the 2004 guideline, no date limit will be applied to searches for these specific review questions to ensure that all relevant articles are identified for</p>

Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – timing		
		both type 1 and 2 diabetes
Population	Children and young people with type 1 or type 2 diabetes (although the diabetes may not yet have been recognised, for example, if the child or young person is presenting for the first time with DKA)	<p>The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years</p> <p>The GDG noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services</p>
Intervention or index test	<p>For the part of the question about when to start intravenous insulin infusion: delayed insulin (delaying the start of intravenous insulin therapy until intravenous fluid therapy is established)</p> <p>For the part of the question about when to stop intravenous insulin infusion: outcomes should be compared according to the blood ketone concentration at which intravenous insulin is stopped</p>	<p>For the part of the question about when to start intravenous insulin infusion: the important consideration is the timing of intravenous insulin in relation to the timing of intravenous fluids</p> <p>For the part of the question about when to stop intravenous insulin infusion: there may be evidence in terms of retrospective comparison of outcomes before and after resolution of ketosis</p>
Comparator or reference standard	<p>For the part of the question about when to start intravenous insulin infusion: immediate insulin (starting intravenous insulin therapy before or at the same time as starting intravenous fluids)</p> <p>For the part of the question about when to stop intravenous insulin infusion: outcomes should be compared according to the blood ketone concentration at which intravenous insulin is stopped</p>	
Clinical outcomes	<p>For the part of the question about when to start intravenous insulin infusion</p> <p>Physical outcomes</p> <p>Mortality</p> <p>Rate of change of blood glucose concentration (this is likely to be reported in research studies, whereas resolution of hyperglycaemia (which would otherwise be of interest) might not be)</p>	

Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – timing		
	<p>Incidence of hypoglycaemia</p> <p>Resolution of acidosis (this is likely to be reported, especially in older studies that do not report resolution of blood ketosis, but it is likely to be of lower priority in formulating recommendations)</p> <p>Incidence of cerebral oedema (this could cause morbidity or mortality), to include participants with symptoms or signs suggestive of cerebral oedema (for example, development of unconsciousness) provided these are reported as being related to cerebral oedema</p> <p>Hypokalaemia (this is important because people with DKA die of this)</p> <p>Healthcare utilisation (for example, duration of admission, requirement for ventilation (as a proxy for severity of DKA or presence of cerebral oedema))</p> <p>For the part of the question about when to stop intravenous insulin infusion</p> <p>Physical outcomes</p> <p>Resolution of blood ketosis</p> <p>Healthcare utilisation (for example, duration of admission, requirement for ventilation (as a proxy for severity of DKA or presence of cerebral oedema))</p>	<p>Terminology:</p> <p>diabetic coma might be relevant to cerebral oedema but is too general a term to use in the extraction/description of evidence</p> <p>consider using 'serum potassium concentration' rather than 'hypokalaemia' etc</p>
Health economics outcomes	These questions were not prioritised for health economic analysis	
Other criteria for inclusion/exclusion of studies	Exclude studies with <10 participants in total	<p>Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation</p> <p>Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this</p>
Search strategies	See separate document	A single search for evidence will be undertaken across the questions relating to timing of intravenous insulin therapy and calculation of the insulin dosage
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p> <p>Evidence tables and an evidence profile will be used to</p>	

Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – timing		
	summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	The GDG's view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first presentation with diabetes

Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – dosage		
Existing recommendation(s) in 2004 guideline	<p>Management from diagnosis</p> <p>Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document.</p> <p>Diabetic ketoacidosis</p> <p>Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes.</p> <p>Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward.</p> <p>Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit.</p> <p>Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit.</p> <p>Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.</p>	<p>All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness</p> <p>The guidelines published by the British Society for Paediatric Endocrinology and Diabetes (BSPED) were reproduced in an appendix of the 2004 guideline</p> <p>The 2004 guideline was specific to type 1 diabetes</p> <p>The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the GDG plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full GDG will ratify all conclusions and recommendations based on the DKA evidence</p>
Review	How should the dosage of insulin be calculated for	The review questions for

Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – dosage		
question for update	children and young people with diabetic ketoacidosis?	type 1 and type 2 diabetes are identical
Objectives	To determine the optimal insulin dosage for children and young people with DKA. A smoother recovery from ketoacidosis and a lower risk of cerebral oedema might be achieved with a 'small' dosage of intravenous insulin (for example, a low-dose intravenous insulin infusion with no initial bolus (higher dose)). Current practice is typically to use a dosage of 0.1 units/kg/hour and the review for this question will focus on comparison of outcomes for this conventional dosage with those for alternative dosages, such as 0.05 units/kg/hour or 0.025 units/kg/hour	
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) Comparative observational studies (including cohort and case-control studies)	Although there may be some RCTs for this question the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies
Status	Published articles (no limitation on year of publication)	Although this is an update and expansion of a review question considered in the 2004 guideline, no date limit will be applied to searches for these specific review questions to ensure that all relevant articles are identified for both type 1 and 2 diabetes
Population	Children and young people with type 1 or type 2 diabetes (although the diabetes may not yet have been recognised, for example, if the child or young person is presenting for the first time with DKA)	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years The GDG noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services
Intervention or index	Insulin dosage of 0.05 units/kg/hour or lower	There may be some small studies to answer

Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – dosage		
test		this question. Most studies are likely to compare 0.05 units/kg/hour with 0.1 units/kg/hour; a few might compare 0.025 units/kg/hour with 0.05 units/kg/hour or 0.1 units/kg/hour
Comparator or reference standard	Insulin dosage of 0.1 units/kg/hour	0.1 units/kg/hour, 0.05 units/kg/hour, and 0.025 units/kg/hour are the dosages likely to be used; the intended starting dosage will be important and evidence tables and GRADE profiles should reflect this
Clinical outcomes	<p>Physical outcomes</p> <p>Mortality</p> <ul style="list-style-type: none"> • Rate of change of blood glucose concentration (this is likely to be reported in research studies, whereas resolution of hyperglycaemia (which would otherwise be of interest) might not be) • Incidence of hypoglycaemia • Resolution of acidosis (this is likely to be reported, especially in older studies that do not report resolution of blood ketosis, but it is likely to be of lower priority in formulating recommendations) • Resolution of blood ketosis • Incidence of cerebral oedema (this could cause morbidity or mortality), to include participants with symptoms or signs suggestive of cerebral oedema (for example, development of unconsciousness) provided these are reported as being related to cerebral oedema • Hypokalaemia (this is important because people with DKA die of this) • Healthcare utilisation (for example, duration of admission, requirement for ventilation (as a proxy for severity of DKA or presence of cerebral oedema)) 	<p>The GDG prioritised 8 outcomes initially (based on those selected for the question on when to start and stop intravenous insulin infusion in children and young people with DKA); this was found to be acceptable based on the sparsity of evidence identified for inclusion</p> <p>GDG to consider using the terminology 'serum potassium concentration' rather than 'hypokalaemia' etc</p>
Health economics outcomes	These questions were not prioritised for health economic analysis	
Other criteria for inclusion/exclusion of studies	Exclude studies with <10 participants in total	<p>Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation</p> <p>Additionally, subgroup analysis by age group (for example, pre-school versus primary school or</p>

Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – dosage		
		secondary school) would be useful if the evidence from the included studies allows this
Search strategies	See separate document	A single search for evidence will be undertaken across the questions relating to timing of intravenous insulin therapy and calculation of the insulin dosage
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	The GDG's view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first presentation with diabetes

E.15 Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis

Review question: What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?

Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis		
Existing recommendation(s) in 2004 guideline	<p>Management from diagnosis</p> <p>Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document.</p> <p>Diabetic ketoacidosis</p> <p>Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes.</p> <p>Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward.</p> <p>Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit.</p> <p>Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit.</p> <p>Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.</p>	<p>All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness</p> <p>The guidelines published by the British Society for Paediatric Endocrinology and Diabetes (BSPED) were reproduced in an appendix of the 2004 guideline</p> <p>The 2004 guideline was specific to type 1 diabetes</p> <p>The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the GDG plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full GDG will ratify all conclusions and recommendations based on the DKA evidence</p>
Review question for update	What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with DKA?	The review questions for type 1 and type 2 diabetes are identical
Objectives	To determine whether anticoagulant prophylaxis is effective in preventing venous thrombosis in children and young people with DKA. The GDG noted that deep vein thrombosis, visceral thrombosis, and cerebral thrombosis would all be relevant in this review question	Children and young people with DKA who have central venous lines inserted are at greater risk of developing central venous thrombosis. Current practice is typically to provide prophylactic anticoagulation to these children and young people. The review for this question will focus on comparison of outcomes for some

Type 1 and type 2 diabetes – diabetic ketoacidosis –anticoagulant prophylaxis		
		form of prophylactic anticoagulation compared with no anticoagulation
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) Comparative observational studies (including cohort and case-control studies)	Although there may be some RCTs for this question the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies
Status	Published articles (no limitation on year of publication)	As this is a new question which was not considered in the original 2004 guideline, no date limit will be applied to searches for these review questions to ensure that all relevant articles are identified for both type 1 and 2 diabetes
Population	Children and young people with type 1 or type 2 diabetes (although the diabetes may not yet have been recognised, for example, if the child or young person is presenting for the first time with DKA)	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years The GDG noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services
Intervention or index test	Any anticoagulation prophylaxis regimen	The following terminology may be useful in relation to specifying search terms relevant to anticoagulation regimens: <ul style="list-style-type: none"> • aspirin • dalterparin • dicoumarol • fragmin • heparin • low-dose heparin • synthetic warfarins (these newer products are not licensed for use in children and young people but any relevant evidence can still be considered as part of the review) • warfarin
Comparator or reference standard	No anticoagulation prophylaxis regimen	The review will not compare different anticoagulation regimens with one another
Clinical outcomes	Physical outcomes <ul style="list-style-type: none"> • Mortality • Incidence of venous thrombosis (of any type, including deep vein thrombosis, visceral 	

Type 1 and type 2 diabetes – diabetic ketoacidosis –anticoagulant prophylaxis		
	<p>thrombosis, and cerebral thrombosis)</p> <ul style="list-style-type: none"> • Incidence of pulmonary embolism • Healthcare utilisation (for example, duration of admission, admission to intensive care) • Adverse events, including bleeding and thrombocytopenia <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> • Children and young people's and families' satisfaction with intervention 	
Health economics outcomes	These questions were not prioritised for health economic analysis	If any evidence is identified in relation to healthcare utilisation the decision not to prioritise this question for health economic analysis might be revisited (but the GDG does not expect there to be much evidence at all)
Other criteria for inclusion/exclusion of studies	Exclude studies with <10 participants in total	<p>Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation</p> <p>Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this</p>
Search strategies	See separate document	A single search for evidence will be undertaken for both type 1 and type 2 diabetes
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p> <p>Evidence tables and an evidence profile will be used to summarise the evidence</p>	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	The GDG's view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first presentation with diabetes

E.16 Type 1 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?

Type 1 diabetes – retinopathy		
Existing recommendation(s) in 2004 guideline	Children and young people with type 1 diabetes should be offered screening for: <ul style="list-style-type: none"> • coeliac disease at diagnosis • thyroid disease at diagnosis and annually thereafter until transfer to adult services • retinopathy annually from the age of 12 years • microalbuminuria annually from the age of 12 years • blood pressure annually from the age of 12 years. 	Only those aspects relating to retinopathy and nephropathy in the 2004 recommendation about screening for complications in children and young people with type 1 diabetes are being updated The reason for updating this recommendation is to reconsider the time at which to test (age/duration of diabetes), not how to test
Review question for update	What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?	Useful background reading in http://www.guidelines.gov/content.aspx?id=13502
Objectives	To determine when retinopathy screening should start following diagnosis of type 1 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter, and taking account of the severity (grade) of retinopathy, including the clinical importance of any background retinopathy	Note that background retinopathy can revert to normal, giving rise to intermittent retinopathy The GDG's recommendations should take into account the practicalities of starting screening based on duration of diabetes rather than age (because screening for retinopathy requires referral to an ophthalmologist and ophthalmology services may not have access to information about duration of diabetes)
Language	English	
Study design	Cohort studies or consecutive case series	Cross-sectional studies which report prevalence and longitudinal studies which report incidence will be considered
Status	Published articles (no limitation on year of publication)	This is different to the review questions considered in the 2004 guideline and so no date limitations will be applied during the search for evidence
Population	Children and young people with type 1 diabetes	The guideline scope defines children and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are presented on an age group which extends into people aged >18 years, these will be included only if the mean age in the group is ≤ 18 years

Type 1 diabetes – retinopathy		
		<p>or if more than 50% of group participants are aged \leq 18 years</p> <p>Studies will be included only if they provide data on prevalence for specific groups of children or young people (stratified by age or duration of diabetes)</p> <p>Only include data on incidence if exact figures (for example, incidence per hundred person years) are described in the text, and not if data are solely presented as survival curve analysis</p>
Intervention or index test	Universal retinopathy screening using digital retinal photography	<p>Digital retinal photography is the method currently recommended in the NHS Diabetic Eye Screening Programme</p> <p>Exclude studies which consider only fluorescein angiography or ophthalmoscopy</p>
Comparator or reference standard	Prevalence or incidence at different time intervals after diagnosis and/or at different ages	
Clinical outcomes	<p>Prevalence of retinopathy at different timepoints after diagnosis (this might include data obtained via 'survival analysis' methods)</p> <p>Incidence of retinopathy over time</p> <p>When available, severity (grade) of retinopathy will be reported based on the NHS Diabetic Eye Screening Programme (see, for example, http://medweb.bham.ac.uk/easdec/gradingretinopathy.htm)</p>	<ul style="list-style-type: none"> • Look at finding the earliest time at which retinopathy becomes sufficiently common/severe to warrant screening • The GDG may need to consider not just the existence of retinopathy but also the severity (grade) of retinopathy • Current practice is to refer children and young people with diabetes to an ophthalmologist only if they have sight-threatening diabetic retinopathy, and this is unlikely in people younger than 12 years; as noted above, background retinopathy can revert to normal • It might be worth identifying retinopathy that will not lead to referral to an ophthalmologist if this would support provision of education about risks associated with retinopathy • Subgroup analysis based on age may be relevant
Health economic outcomes	This question was not identified as a priority for health economic analysis	
Other criteria for	<p>Exclude studies that do not:</p> <ul style="list-style-type: none"> • report prevalence of retinopathy at a 	

Type 1 diabetes – retinopathy		
inclusion/ exclusion of studies	<p>particular timepoint after diagnosis</p> <ul style="list-style-type: none"> • have a systematic approach to screening, as opposed to selective patient screening based on individual concerns 	
Search strategies	See separate document	NCC-WCH to consider using a single search to cover both review questions relating to monitoring for retinopathy (type 1 diabetes and type 2 diabetes)
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p> <p>Evidence tables and an evidence profile will be used to summarise the evidence</p>	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	The practicalities of offering screening for retinopathy will vary according to the child or young person's age and whether or not they have learning difficulties (because digital retinal photography requires the person to sit still and stare at a fixed point)

E.17 Type 1 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?

Type 1 diabetes – nephropathy		
Existing recommendation(s) in 2004 guideline	<p>Children and young people with type 1 diabetes should be offered screening for:</p> <ul style="list-style-type: none"> • coeliac disease at diagnosis • thyroid disease at diagnosis and annually thereafter until transfer to adult services • retinopathy annually from the age of 12 years • microalbuminuria annually from the age of 12 years • blood pressure annually from the age of 12 years. 	<p>Only those aspects relating to retinopathy and nephropathy in the 2004 recommendation about screening for complications in children and young people with type 1 diabetes are being updated</p> <p>The existing recommendation about screening for microalbuminuria relates to testing based on urine albumin:creatinine ratio. The reason for updating this recommendation is to reconsider the time at which to test (age/duration of diabetes) not how to test</p> <p>If the GDG intends to recommend screening for microalbuminuria (as a marker of nephropathy) from an age lower than 12 years then the possibility of revising the recommendation about when to start monitoring blood pressure should be raised with NICE (because hypertension is also associated with nephropathy)</p>
Review question for update	What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?	Background information: http://www.kidney.org/professionals/kdoqi/pdf/Diabetes_AJKD_FebSuppl_07.pdf recommends starting screening 5 years after diagnosis of type 1 diabetes
Objectives	To determine when nephropathy screening should start following diagnosis of type 1 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter, and taking account of issues such as the clinical importance of intermittent microalbuminuria	
Language	English	
Study design	Cohort studies or consecutive case series	Cross-sectional studies which report prevalence and longitudinal studies which report incidence will be considered
Status	Published articles (no limitation on year of publication)	This is different to the review questions considered in the 2004 guideline and so no date limitations will be applied during the search for evidence
Population	Children and young people with type 1	The guideline scope defines children

Type 1 diabetes – nephropathy		
	diabetes	<p>and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are presented on an age group which extends into people aged >18 years, these will be included only if the mean age in the group is ≤ 18 years or if more than 50% of group participants are aged ≤ 18 years</p> <p>Studies will be included only if they provide data on prevalence for specific groups of children or young people (stratified by age or duration of diabetes)</p> <p>Only include data on incidence if exact figures (for example, incidence per hundred person years) are described in the text, and not if data are solely presented as survival curve analysis</p>
Intervention or index test	Screening for microalbuminuria (however measured, and including using measurement through urine albumin:creatinine ratio (ACR))	<p>The guidelines relating to type 1 diabetes in adults and type 2 diabetes in adults include specific recommendations on:</p> <ul style="list-style-type: none"> • repeated measurement of ACR over a 4-month period to establish a diagnosis of microalbuminuria • measuring serum creatinine at the same time, and • in type 2 diabetes, estimating the glomerular filtration rate (GFR) at the same time (using the method-abbreviated modification of diet in renal disease four-variable equation) <p>Usual practice is to measure only microalbuminuria in children and young people with type 1 diabetes (serum creatinine concentration is measured only if the microalbuminuria measurement is abnormal because this provides evidence of renal damage from microalbuminuria or hypertension); an abnormal urine ACR is the first feature of nephropathy, whereas abnormal serum creatinine concentration is a later feature that is not relevant in children and young people with type 1 diabetes because</p>

Type 1 diabetes – nephropathy		
		<p>they are unlikely to have nephropathy at diagnosis</p> <p>Urine ACR is the practice for screening of microalbuminuria in the UK. For studies which report on albumin excretion rate (AER) rather than ACR for the confirmation of microalbuminuria, convert to ACR measurements using separate conversion equations for males and females (Schultz et al. 1999)</p> <p>Reference is: Schultz, C.J., et al. 1999. Microalbuminuria prevalence varies with age, sex, and puberty in children with type 1 diabetes followed from diagnosis in a longitudinal study. <i>Diabetes Care</i>, 22 (3): 495-502)</p> <p>Using ACR > 2.5mg/mmol for males and ACR > 3.5 mg/mmol for females (at least 2 of 3 consecutive collections over a period of 3-4 months) which are the standards for confirming microalbuminuria in UK adults, exclude studies where the ACR measurement falls below 2.5 mg/mmol or 3.5mg/mmol for males and females, respectively</p>
Comparator or reference standard	Prevalence or incidence at different time intervals after diagnosis and/or at different ages	
Clinical outcomes	Prevalence of microalbuminuria (however measured, and including using measurement through urine albumin:creatinine ratio) Incidence of microalbuminuria over time	<p>Evidence tables should document cut-offs and definitions of microalbuminuria used in included studies</p> <p>NCC-WCH to discuss with GDG to determine which studies should be included if necessary</p> <p>Note that the 2004 guideline on type 1 diabetes in adults, and the 2008 guideline on type 2 diabetes in adults use repeated tests of ACR >2.5mg/mmol for men, and >3.5mg/mmol for women (in at least 2 of 3 consecutive collections over a period of 3-4 months) to confirm microalbuminuria</p> <p>It will be important to consider the severity of microalbuminuria and</p>

Type 1 diabetes – nephropathy		
		how should this be reported (for example, thresholds for 'severe microalbuminuria', etc)
Health economic outcomes	This question was not identified as a priority for health economic analysis	
Other criteria for inclusion/exclusion of studies	Exclude studies that do not: <ul style="list-style-type: none"> • report prevalence of microalbuminuria • have a systematic approach to screening, as opposed to selective patient screening based on individual concerns 	
Search strategies	See separate document	NCC-WCH to consider using a single search to cover both review questions relating to monitoring for nephropathy (type 1 diabetes and type 2 diabetes) The search terms microalbuminuria and diabetes should identify relevant studies
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	

E.18 Type 2 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?

Type 2 diabetes – education		
Existing recommendation(s) in 2004 guideline	None	<p>The 2004 guideline was specific to type 1 diabetes</p> <p>An external adviser has been appointed to advise the GDG on technical aspects of clinical research relating to behavioural interventions and the interface with education programmes</p>
Review question for update	What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?	
Objectives	To determine the effectiveness of structured education programmes in improving outcomes for children and young people with type 2 diabetes	
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) only	<p>Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion</p> <p>The next step might be to include systematic reviews of RCTs and nonrandomised comparative studies (but not individual nonrandomised studies)</p>
Status	Published papers (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	<p>The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years</p> <p>This review question will focus solely on 'patient' education (that is, education of healthcare professionals will be excluded)</p>
Intervention	Structured education programmes specific to type 2 diabetes (education aimed at children and young people or their families)	<p>Useful reference (systematic review) for educational and behavioural interventions is AHQR 2008 (Evidence report 166 http://www.ahrq.gov/clinic/tp/diabetesedtp.htm)</p> <p>Possible search terms (based on AHRQ 2008 systematic review plus GDG suggestions):</p>

Type 2 diabetes – education		
		<ul style="list-style-type: none"> • education • game • information • instruction • intervention • knowledge • management • multimedia • online • self-help • skills • teach • train • patient care • phone • video <p>The above terms were listed in the corresponding protocol for children and young people with type 1 diabetes; for type 2 diabetes the search also needs to be broad enough to encompass relevant education about:</p> <ul style="list-style-type: none"> • exercise • physical activity • lifestyle • weight loss or management programmes <p>This review should cover: all settings (diabetes clinics, schools, etc), while recognising that recommendations will be limited to the clinical practice context all forms of delivery of education (for example, one-to-one, brief, face-to-face, and remote (telemedicine, including text messaging))</p> <p>Names of studies that might be relevant (not to be used as search terms): DESMOND X-PERT</p>
Comparator or reference standard	Alternative models of education Usual care	Usual care in this context usually includes unstructured, informal education, provision of information leaflets or multimedia
Clinical Outcomes	Physical outcomes <ul style="list-style-type: none"> • Glycaemic control 	The priority outcomes selected by the GDG are different to those for

Type 2 diabetes – education		
	<ul style="list-style-type: none"> ○ HbA1c (minimum follow-up 6 months after completion of primary intervention) ● Adherence to education intervention ● Changes in body mass index (BMI) standard deviation score (SDS) ● Achievement and maintenance of weight loss during the programme ● Change in level of physical activity (for example, hours of exercise per week; minimum follow-up 6 months after completion of primary intervention) <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> ● Health-related quality of life ● Children and young people’s and families’ satisfaction with intervention (education intervention) 	<p>the review questions on behavioural interventions because psychosocial outcomes are more relevant there</p> <p>The GDG identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and change in level of physical activity, and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required</p> <p>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</p> <p>BMI SDS MID is 0.5 for weight-loss interventions and 0 for all other interventions</p> <p>Note that incidence of severe hypoglycaemic episodes is not a relevant outcome in children and young people with type 2 diabetes because their diabetes is not likely to be treated with insulin or any other pharmaceutical agent that would cause hypoglycaemia. Also diabetic ketoacidosis (DKA) may be a problem at initial presentation but it is unlikely to occur subsequently</p> <p>Adherence to diabetes management, including self-management was not prioritised as an outcome for this question. The GDG agreed that this was a lower priority than adherence to the educational intervention itself because insulin is not always used in the treatment of type 2 diabetes</p> <p>No long-term complications needed to be prioritised as outcomes because HbA1c will determine these</p>
Health economic outcomes	This question was not prioritised for health economic analysis	
Other criteria for	None	Studies that evaluate education programmes for healthcare

Type 2 diabetes – education		
inclusion/ exclusion of studies		<p>professionals will be excluded (see above)</p> <p>Subgroup analysis according to the presence of associated conditions such as autism spectrum disorder or learning difficulties, and according to language and culture-specific interventions would be useful if the evidence allows this</p> <p>Subgroup analysis by ethnicity may be of interest</p>
Search strategies	See separate document	NCC-WCH technical team to search the PsycINFO bibliographic database for this review question (in addition to the standard bibliographic databases)
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p> <p>Evidence tables and an evidence profile will be used to summarise the evidence</p>	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	Ethnicity, languages other than English, and literacy may all be important considerations for this question. These issues are specific to children and young people with type 2 diabetes (because of the increased risk of this type of diabetes according to ethnicity and socioeconomic status)

E.19 Type 2 diabetes – behavioural interventions

Review questions:

What is the effectiveness of behavioural interventions to promote engagement with clinical services in children and young people with type 2 diabetes?

What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 2 diabetes?

Type 2 diabetes – behavioural interventions		
Existing recommendation(s) in 2004 guideline	None	<p>The 2004 guideline was specific to type 1 diabetes</p> <p>An expert adviser has been appointed to advise the GDG on technical aspects of clinical research relating to behavioural interventions and the interface with education programmes</p>
Review question for update	<p>What is the effectiveness of behavioural interventions to promote engagement with clinical services in children and young people with type 2 diabetes?</p> <p>What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 2 diabetes?</p>	Both questions will be covered by a single protocol. The available evidence will be presented in such a way as to emphasise the difference between the two questions
Objectives	<p>To determine the effectiveness of behavioural interventions in promoting engagement with clinical services in children and young people with type 2 diabetes and improving outcomes of care. The question is sufficiently broad to cover interventions aimed at families and healthcare professionals as well as those aimed at the child or young person. The GDG prioritised behavioural interventions that should be addressed in this question as follows.</p> <ul style="list-style-type: none"> • Family therapy (including behavioural family systems therapy (BFST)): this is always delivered to one family unit but it can include separate sessions with different members (individuals/groups) within the unit • Cognitive behavioural therapy (CBT): this can be delivered one-to-one or in groups. The intervention focuses on recognising specific triggers for maladaptive behaviour and bringing about changes to behaviour • Motivational interviewing: this can be delivered one-to-one or in groups. The intervention focuses on general exploration of ambivalence around maladaptive behaviours and what the person wants to do or should do. The intervention develops insight into maladaptive behaviour • Counselling: this is delivered one-to-one but the content of interventions termed counselling may vary • Mentoring: this can be delivered one-to-one or in groups. The mentor is typically older 	

Type 2 diabetes – behavioural interventions		
	<p>than the person receiving mentoring or is influential in the community</p> <ul style="list-style-type: none"> Peer support (and peer-led interventions): these can be delivered one-to-one or in groups. The intervention typically involves people of similar age to the person receiving peer support 	
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) only	<p>Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion</p> <p>The next step might be to include systematic reviews of RCTs and nonrandomised comparative studies (but not individual nonrandomised studies)</p>
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	<p>Behavioural interventions specific to the management of type 2 diabetes in children and young people (this could involve interventions aimed at families and healthcare professionals as well as those aimed at the child or young person)</p> <ul style="list-style-type: none"> Family therapy (include only validated therapies such as BFST – expert adviser to advise in relation to search results) CBT motivational interviewing counseling mentoring peer support (and peer-led interventions) 	<p>Use the terms specific to the prioritised behavioural interventions when conducting the searches for this question</p> <p>Useful reference (systematic review) for educational and behavioural interventions is AHQR 2008 (Evidence report 166 http://www.ahrq.gov/clinic/tp/diabetdp.htm)</p> <p>The following search terms from the AHRQ 2008 systematic review were considered by the GDG and expert adviser as part of the prioritisation of behavioural interventions for this question but they were not selected for the reasons given and they should not be used as search terms for this question:</p> <ul style="list-style-type: none"> adherence (an outcome not an intervention) behavioural therapy (poorly defined so not a priority) biofeedback (more relevant to the question relating to education programmes) cognitive therapy (not a priority because it focuses on awareness)

Type 2 diabetes – behavioural interventions		
		<p>of behaviour but not changing behaviour)</p> <ul style="list-style-type: none"> • conjoint therapy (refers to any two therapies joined together) • educational therapy (will be addresses in the education question) • psychological interventions (not specific) • psychological therapy (not specific) • solution-focused therapy (not specific – refers to any therapy that focuses on solutions rather than problems; several of the prioritised interventions are solution-focused) • therapy (not specific) <p>This review should cover:</p> <ul style="list-style-type: none"> • all settings (diabetes clinics, schools, etc), while recognising that recommendations will be limited to the clinical practice context • all forms of delivery of the prioritised behavioural interventions (for example, one-to-one, brief, face-to-face, and remote (telemedicine)) <p>Names of studies that might be relevant (not to be used as search terms):</p> <ul style="list-style-type: none"> • DESMOND • X-PERT
Comparator or reference standard	<p>An alternative behavioural intervention listed above</p> <p>An alternative and well defined behavioural intervention not listed above (expert adviser to advise on what is well defined in relation to search results)</p> <p>Any other intervention aimed at changing a specific behaviour, a range of behaviours, or psychosocial adjustment to diabetes self-management</p> <p>Usual care (this will be the most common comparator)</p>	<p>Usual care in this context usually includes education, no therapy, provision of information leaflets or multimedia (DVDs, CDs, websites, apps)</p>
Clinical outcomes	<p>For the question about engagement with clinical services</p> <p>Physical outcomes</p> <ul style="list-style-type: none"> • Adherence to diabetes management (the scope requires this; to include self-management) <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> • Children and young people's and families' 	<p>The GDG identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and change in level of physical activity, and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required</p>

Type 2 diabetes – behavioural interventions		
	<p>satisfaction with intervention</p> <ul style="list-style-type: none"> • Risk-taking behaviours (such as smoking) • Engagement with clinical services (for example, attendance at clinic appointments) <p>For the general question about improving outcomes</p> <p>Physical outcomes</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ○ HbA1c (minimum follow-up 6 months after completion of primary intervention) ○ Adverse events (for example, diabetes-related hospital admission or self-harm) • Changes in body mass index (BMI) standard deviation score (SDS) • Achievement and maintenance of weight loss during the programme (NCC-WCH to seek clarification from GDG about whether weight-loss outcomes are relevant after searches have been completed) • Change in level of physical activity (for example, hours of exercise per week; minimum follow-up 6 months after completion of primary intervention) <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> • Health-related quality of life (this outcome might capture bullying about weight) • Depression or anxiety 	<p>The GDG agreed that change in body mass index (BMI) standard deviation score (SDS) would be more important than DKA than in the corresponding question for type 1 diabetes</p> <p>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</p> <p>BMI SDS MID is 0.5 for weight-loss interventions and 0 for all other interventions</p> <p>No long-term complications needed to be prioritised as outcomes because HbA1c will determine these</p>
Health economic outcomes	This question was not prioritised for health economic analysis	The GDG might wish to evaluate the cost effectiveness of behavioural interventions for type 2 diabetes – see notes on protocol for weight loss in type 2 diabetes
Other criteria for inclusion/exclusion of studies	None	Evidence tables should document who delivered the intervention(s) and the frequency of contact with healthcare or other relevant professionals to deliver the intervention(s)
Search strategies	See separate document	A single search will be used to cover both questions NCC-WCH technical team to search the PsycINFO bibliographic database for this review question (in addition to the standard bibliographic databases)
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	

Type 2 diabetes – behavioural interventions		
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	Ethnicity, languages other than English, and literacy may all be important considerations for this question. These issues are specific to children and young people with type 2 diabetes (because of the increased risk of this type of diabetes according to ethnicity and socioeconomic status)

E.20 Type 2 diabetes – dietary advice

Review question: What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?

Type 2 diabetes – dietary advice		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?	
Objectives	To identify the dietetic advice to be given to children and young people with type 2 diabetes to optimise glycaemic control. The question includes evaluation of the effectiveness of different forms of dietetic advice in terms of achieving outcomes relating to glycaemic control	Dietetic advice for type 2 diabetes will usually focus on dietary advice to achieve weight loss; weight loss will improve glycaemic control The GDG agreed that the objectives of the question should remain open to allow consideration of evidence relating to any form of dietetic advice relevant to type 2 diabetes, although the intention was to look for evidence relating to improving glycaemic control
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) only	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	Dietetic advice intended to optimise glycaemic control	Include studies only if dietetic advice includes direct contact and training with healthcare professionals (for example, providing an information leaflet is not enough) Evidence tables should document any pharmacological treatment (for example, metformin or insulin) in the intervention and comparison groups
Comparator or reference standard	Usual care	Usual care could include dietetic advice which does not incorporate specific advice about optimising glycaemic control, or dietary advice that does not involve direct contact and/or training with healthcare

Type 2 diabetes – dietary advice		
		professionals (for example, providing an information leaflet only)
Clinical outcomes	<p>Physical outcomes</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ○ HbA1c (minimum follow-up 6 months) ○ Postprandial hyperglycaemia (for example, glucose excursions or larger area under the glucose concentration curve) • Adherence to dietary advice • Adverse events (for example, changes in body mass index (BMI) standard deviation score (SDS) or changes in weight) <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> • Health-related quality of life • Children and young people's and families' satisfaction with intervention 	<p>The GDG considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes</p> <p>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</p> <p>BMI SDS minimally important difference is 0.5 for weight-loss interventions and 0 for all other interventions</p> <p>Note that incidence of severe hypoglycaemic episodes is not a relevant outcome in children and young people with type 2 diabetes because their diabetes is not likely to be treated with insulin or any other pharmaceutical agent that would cause hypoglycaemia. Also diabetic ketoacidosis (DKA) may be a problem at initial presentation but it is unlikely to occur subsequently</p>
Health economic outcomes	This question was not prioritised for health economic analysis	
Other criteria for inclusion/exclusion of studies	None	
Search strategies	See separate document	
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p> <p>Evidence tables and an evidence profile will be used to summarise the evidence</p>	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	Ethnicity, languages other than English, and literacy may all be important considerations for this question. These issues are specific to children and young people with type 2 diabetes (because of the

Type 2 diabetes – dietary advice		
		increased risk of this type of diabetes according to ethnicity and socioeconomic status)

E.21 Type 2 diabetes – weight loss

Review question: Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?

Type 2 diabetes – weight loss		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by haemoglobin A1c (HbA1c)?	
Objectives	To evaluate the effectiveness of weight loss (by whatever means) in children and young people with type 2 diabetes who are overweight or obese in improving glycaemic control. The primary measure of glycaemic control to be considered in this question is HbA1c. The purpose of including this topic in the guideline update is to form the basis for advising weight loss to improve glycaemic control. The means for achieving weight loss will not be addressed in this guideline (except to document in the evidence tables the method of weight management used in the included studies) but through a cross-reference to the NICE clinical guideline on obesity (http://guidance.nice.org.uk/CG43). This guideline is currently being updated	<p>The NICE clinical guideline on obesity (http://guidance.nice.org.uk/CG43) includes the following recommendations</p> <p>Bariatric surgery is recommended as a treatment option for people with obesity if all of the following criteria are fulfilled:</p> <ul style="list-style-type: none"> • they have a body mass index (BMI) of 40 kg/m² or more, or between 35 kg/m² and 40 kg/m² and other significant disease (for example, type 2 diabetes or high blood pressure) that could be improved if they lost weight [other bullets in this recommendation omitted for brevity] <p>Surgical intervention is not generally recommended in children or young people.</p> <p>Bariatric surgery may be considered for young people only in exceptional circumstances, and if they have achieved or nearly achieved physiological maturity.</p>
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) Observational studies	It is not expected that there will be RCTs that fully answer this question (in terms of the association between weight loss and glycaemic control) and so no restriction in study design will be applied to this question
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2	The guideline scope defines children

Type 2 diabetes – weight loss		
	diabetes who are overweight or obese	and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	<p>RCTs: Weight loss interventions specific to the management of type 2 diabetes in children and young people. Note that the guideline scope relates specifically to children and young people with diabetes, and so studies that focus on prevention of type 2 diabetes should be excluded</p> <p>Observational studies: Any study that reports weight change in children and young people with type 2 diabetes</p>	<p>The specified interventions assume that RCTs are available but as noted above the review will include consideration of observational studies from the outset so that any association between weight loss and glycaemic control can be evaluated</p> <p>Evidence tables should document any pharmacological treatment (for example, metformin or insulin) in the intervention and comparison groups</p>
Comparator or reference standard	<p>RCTs: An alternative weight loss intervention or usual care</p> <p>Observational studies: Weight change in relation to glycaemic control</p>	<p>Usual care could include informal, general advice or programmes relating to weight loss</p> <p>Weight change or a comparable measure such as change in body mass index (BMI) standard deviation score (SDS)</p>
Clinical outcomes	<p>Physical outcomes</p> <ul style="list-style-type: none"> • Glycaemic control <ul style="list-style-type: none"> ◦ HbA1c (minimum follow-up 6 months) • Adherence to diabetes management, including self-management • Changes in body mass index (BMI) standard deviation score (SDS) • Remission of diabetes (normal HbA1c and no treatment for diabetes, for example at 1 year after starting the weight loss intervention) • Time to treatment failure (when insulin is required to manage diabetes; the physiological basis for this is that initial management should postpone the need for insulin, but insulin will be needed eventually as insulin resistance changes and secretion of insulin by the pancreas stops) <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> • Health-related quality of life • Children and young people's and families' satisfaction with intervention 	<p>The GDG considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes</p> <p>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</p> <p>BMI SDS MID is 0.5 for weight-loss interventions and 0 for all other interventions</p> <p>Note that incidence of severe hypoglycaemic episodes is not a relevant outcome in children and young people with type 2 diabetes because their diabetes is not likely to be treated with insulin or any other pharmaceutical agent that would cause hypoglycaemia. Also diabetic ketoacidosis (DKA) may be a problem at initial presentation but it is unlikely to occur subsequently</p>
Health economic outcomes	This question was not prioritised for health economic analysis	This question was proposed as the top priority for health economic analysis among the questions relating to type 2 diabetes, but the

Type 2 diabetes – weight loss		
		NCC-WCH will refer to the guidelines on obesity (update) and type 2 diabetes in adults rather than undertaking any modelling for this guideline
Other criteria for inclusion/exclusion of studies	None	
Search strategies	See separate document	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	Ethnicity, languages other than English, and literacy may all be important considerations for this question. These issues are specific to children and young people with type 2 diabetes (because of the increased risk of this type of diabetes according to ethnicity and socioeconomic status)

E.22 Type 2 diabetes – metformin

Review question: What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?

Type 2 diabetes – metformin		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?	
Objectives	To determine the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes	
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) only	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years
Intervention or index test	Metformin	
Comparator or reference standard	<ul style="list-style-type: none"> • Usual care • Placebo 	Usual care in this instance includes lifestyle advice, education, etc
Clinical outcomes	<ul style="list-style-type: none"> • Haemoglobin A1c (HbA1c) • Number needing rescue medication • Number of dropouts • Number with any adverse events, including diabetic ketoacidosis (DKA) • Changes in fasting plasma glucose (FPG) • Changes in body mass index (BMI) standard deviation score (SDS) • Patient satisfaction with the intervention 	
Health economic outcomes	<p>This question was not prioritised for health economic analysis</p> <p>Most of the outcomes above, but should not necessarily be limited to seven and could be extended to include generic measures of health-related quality of life</p>	
Other criteria for inclusion/exclusion of studies	None	

Type 2 diabetes – metformin		
Search strategies	See separate document	
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	Ethnicity, languages other than English, and literacy may all be important considerations for this question. These issues are specific to children and young people with type 2 diabetes (because of the increased risk of this type of diabetes according to ethnicity and socioeconomic status)

E.23 Type 2 diabetes – HbA1c targets

Review question: what is the optimal HbA1c target for children and young people with type 2 diabetes?

Type 2 diabetes – HbA1c targets		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	What is the optimal HbA1c target for children and young people with type 2 diabetes?	
Objectives	To determine the optimal HbA1c target value in terms of minimising the risk of long-term complications without incurring an increased risk of hypoglycaemic episodes as an adverse effect	
Language	English	
Study design	Systematic reviews and randomised controlled trials (RCTs) Comparative observational studies (including cohort and case-control studies)	Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion No RCTs that report results specific to children and young people are expected. A large RCT (involving adults) by Turner R, UKPDS Intervention Group, Lancet, 1998, and a meta-analysis by Hemmingsen B, BMJ, 2011 may be relevant. NCC-WCH to check whether these report any evidence specific to children and young people. Only consider studies involving adults if no RCTs or observational studies report data for children and young, and then only by cross-referring to the type 2 diabetes in adults guideline in which HbA1c targets are being updated
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years Note, however, that inclusion/exclusion of studies will be based on time at diagnosis and application of HbA1c targets, whereas long-term follow-up into adulthood will be relevant for this question
Intervention	Specified target value for HbA1c or HbA1c values achieved (recorded)	

Type 2 diabetes – HbA1c targets		
Comparator or reference standard	Comparisons to be made between outcomes according to target values for HbA1c and/or HbA1c values achieved (recorded)	
Clinical outcomes	<p>Physical outcomes</p> <p>Development or worsening of long-term complications</p> <ul style="list-style-type: none"> ○ hypertension (important in children and young people with type 2 diabetes because they often have it at diagnosis and/or are obese) ○ retinopathy ○ nephropathy (important in children and young people with type 2 diabetes because they often have it at diagnosis and/or are obese) ● Glycaemic control <ul style="list-style-type: none"> ○ Severe hypoglycaemic episodes (including nocturnal hypoglycaemia, although neither is very important in type 2 diabetes treated using metformin) ● Changes in body mass index (BMI) standard deviation score (SDS) <p>Psychosocial outcomes</p> <ul style="list-style-type: none"> ● Health-related quality of life ● Children and young people's and families' satisfaction with intervention (the impact of blood sampling would be reflected here) 	<p>Development or worsening of long-term complications are the most important outcomes for this question</p> <p>The GDG identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required</p> <p>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</p> <p>Severe hypoglycaemic episodes defined according to either of the following criteria.</p> <ul style="list-style-type: none"> ● International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose) ● ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3) <p>BMI SDS minimally important difference is 0.5 for weight-loss interventions and 0 for all other interventions</p>
Health economic outcomes	This question was not prioritised for health economic analysis	
Other criteria for inclusion/exclusion of studies	None	
Search strategies	See separate document	

Type 2 diabetes – HbA1c targets		
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	

E.24 Type 2 diabetes – hypertension

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Type 2 diabetes – hypertension		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?	
Objectives	To determine when monitoring for hypertension should start following diagnosis of type 2 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter	<p>This review will need to consider how to identify hypertension, in terms of:</p> <ul style="list-style-type: none"> • which parameters to measure (systolic and/or diastolic blood pressure) • which thresholds to use for parameters of interest (for example, \geq 95th or \geq 98th centile for sex, age and height), and • how many measurements to use (for example, measure once and if above the chosen threshold measure again at same clinic visit; if still elevated measure a third time at same visit; and accept the lowest value recorded). <p>GDG to note that in children and young people in whom clinic blood pressure measurements suggest hypertension, confirmation will be necessary using ambulatory 24-hour monitoring or home blood pressure monitoring, for example, as described in the NICE guideline on hypertension in adults (CG127). The guideline comments on the choice and maintenance of devices used to measure blood pressure. The GDG may wish to consider cuff size to be used when measuring blood pressure in children and young people with type 2 diabetes</p> <p>The National Screening Committee 2010 review may provide useful information for reference</p>
Language	English	
Study design	Cohort studies or consecutive case series	Cross-sectional studies which report prevalence and longitudinal studies which report incidence will be considered
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied

Type 2 diabetes – hypertension		
		to searches
Population	Children and young people with type 2 diabetes	<p>The guideline scope defines children and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are presented on an age group which extends into people aged >18 years, these will be included only if the mean age in the group is \leq 18 years or if more than 50% of group participants are aged \leq 18 years</p> <p>Studies will be included only if they provide data on prevalence for specific groups of children or young people (stratified by age or duration of diabetes)</p> <p>Only include data on incidence if exact figures (for example, incidence per hundred person years) are described in the text, and not if data are solely presented as survival curve analysis</p>
Intervention or index test	Screening for hypertension	Inclusion of studies will not be restricted by the approach to defining hypertension, but the GDG can consider whether the thresholds used in included studies are appropriate for children and young people in the UK
Comparator or reference standard	Prevalence or incidence at different time intervals after diagnosis and/or at different ages	
Clinical outcomes	Prevalence of hypertension at different timepoints after diagnosis Incidence of hypertension over time	<ul style="list-style-type: none"> • Look at finding the earliest time at which hypertension becomes sufficiently common/severe to warrant screening • Subgroup analysis based on age may be relevant
Health economic outcomes	This question was not identified as a priority for health economic analysis	
Other criteria for inclusion/exclusion of studies	Exclude studies that do not: <ul style="list-style-type: none"> • report prevalence of hypertension at a particular timepoint after diagnosis • have a systematic approach to screening, as opposed to selective patient screening based on individual concerns 	
Search strategies	See separate document	
Review	Evidence will be assessed for quality	

Type 2 diabetes – hypertension		
strategies	<p>according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p> <p>Evidence tables and an evidence profile will be used to summarise the evidence</p>	
Equality	<p>Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)</p>	<p>Type 2 diabetes is associated with obesity and so the GDG may wish to consider the appropriate cuff size to use when measuring blood pressure in children and young people with type 2 diabetes</p>

E.25 Type 2 diabetes – dyslipidaemia

Review question: What is the optimal monitoring strategy for identifying dyslipidaemia in children and young people with type 2 diabetes?

Type 2 diabetes – dyslipidaemia		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	What is the optimal monitoring strategy for identifying dyslipidaemia in children and young people with type 2 diabetes?	The NICE guideline on lipid modification (adults; CG67) is being updated and a cross-reference may be relevant; the draft for consultation of the guideline on lipid modification (update) was published in February 2014
Objectives	To determine when monitoring for dyslipidaemia should start following diagnosis of type 2 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter	<p>This review will need to consider how to identify dyslipidaemia, in terms of which serum lipids to measure, for example:</p> <ul style="list-style-type: none"> • total cholesterol • high-density lipoprotein (HDL) cholesterol • low-density lipoprotein (LDL) cholesterol • triglycerides <p>The ratio of HDL:total cholesterol is also of interest</p>
Language	English	
Study design	Cohort studies or consecutive case series	Cross-sectional studies which report prevalence and longitudinal studies which report incidence will be considered
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	<p>The guideline scope defines children and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are presented on an age group which extends into people aged >18 years, these will be included only if the mean age in the group is ≤ 18 years or if more than 50% of group participants are aged ≤ 18 years</p> <p>Studies will be included only if they provide data on prevalence for</p>

Type 2 diabetes – dyslipidaemia		
		<p>specific groups of children or young people (stratified by age or duration of diabetes)</p> <p>Only include data on incidence if exact figures (for example, incidence per hundred person years) are described in the text, and not if data are solely presented as survival curve analysis</p>
Intervention or index test	<p>Measurement of any of the following serum lipids:</p> <ul style="list-style-type: none"> • total cholesterol • HDL cholesterol • LDL cholesterol • triglycerides <p>The ratio of HDL:total cholesterol is also of interest</p>	<p>The terms in the bullet list to the left, plus lipoprotein (US synonym for cholesterol) should be used as search terms</p> <p>Evidence tables should document whether the evidence identified for inclusion relates to fasting or non-fasting measurements (both are of interest)</p>
Comparator or reference standard	Prevalence or incidence at different time intervals after diagnosis and/or at different ages	
Clinical outcomes	<p>Prevalence of dyslipidaemia at different timepoints after diagnosis</p> <p>Incidence of dyslipidaemia over time</p>	<ul style="list-style-type: none"> • Look at finding the earliest time at which dyslipidaemia becomes sufficiently common to warrant screening • Subgroup analysis based on age may be relevant
Health economic outcomes	This question was not identified as a priority for health economic analysis	
Other criteria for inclusion/exclusion of studies	<p>Exclude studies that do not:</p> <ul style="list-style-type: none"> • report prevalence of dyslipidaemia at a particular timepoint after diagnosis <p>have a systematic approach to screening, as opposed to selective patient screening based on individual concerns</p>	
Search strategies	See separate document	
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p> <p>Evidence tables and an evidence profile will be used to summarise the evidence</p>	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	

E.26 Type 2 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?

Type 2 diabetes – retinopathy		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?	Useful background reading in http://www.guidelines.gov/content.aspx?id=13502
Objectives	To determine when retinopathy screening should start following diagnosis of type 2 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter, and taking account of the severity (grade) of retinopathy, including the clinical importance of any background retinopathy	Note that background retinopathy can revert to normal, giving rise to intermittent retinopathy The GDG's recommendations should take into account the practicalities of starting screening based on duration of diabetes rather than age (because screening for retinopathy requires referral to an ophthalmologist and ophthalmology services may not have access to information about duration of diabetes)
Language	English	
Study design	Cohort studies or consecutive case series	Cross-sectional studies which report prevalence and longitudinal studies which report incidence will be considered
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are

Type 2 diabetes – retinopathy		
		<p>presented on an age group which extends into people aged >18 years, these will be included only if the mean age in the group is ≤ 18 years or if more than 50% of group participants are aged ≤ 18 years</p> <p>Studies will be included only if they provide data on prevalence for specific groups of children or young people (stratified by age or duration of diabetes)</p> <p>Only include data on incidence if exact figures (for example, incidence per hundred person years) are described in the text, and not if data are solely presented as survival curve analysis</p>
Intervention or index test	Universal retinopathy screening using digital retinal photography	Digital retinal photography is the method currently recommended in the NHS Diabetic Eye Screening Programme
Comparator or reference standard	Prevalence or incidence at different time intervals after diagnosis and/or at different ages	
Clinical outcomes	<p>Prevalence of retinopathy at different timepoints after diagnosis (this might include data obtained via ‘survival analysis’ methods)</p> <p>Incidence of retinopathy over time</p> <p>When available, severity (grade) of retinopathy will be reported based on the NHS Diabetic Eye Screening Programme (see, for example, http://medweb.bham.ac.uk/easdec/gradingretinopathy.htm)</p>	<ul style="list-style-type: none"> • Look at finding the earliest time at which retinopathy becomes sufficiently common/severe to warrant screening • The GDG may need to consider not just the existence of retinopathy but also the severity (grade) of retinopathy • Current practice is to refer children and young people with diabetes to an ophthalmologist only if they have sight-threatening diabetic retinopathy, and this is unlikely in people younger than 12 years;

Type 2 diabetes – retinopathy		
		<p>as noted above, background retinopathy can revert to normal</p> <ul style="list-style-type: none"> • It might be worth identifying retinopathy that will not lead to referral to an ophthalmologist if this would support provision of education about risks associated with retinopathy • Subgroup analysis based on age may be relevant
Health economic outcomes	This question was not identified as a priority for health economic analysis	
Other criteria for inclusion/exclusion of studies	<p>Exclude studies that do not:</p> <ul style="list-style-type: none"> • report prevalence of retinopathy at a particular timepoint after diagnosis • have a systematic approach to screening, as opposed to selective patient screening based on individual concerns 	
Search strategies	See separate document	NCC-WCH to consider using a single search to cover both review questions relating to monitoring for retinopathy (type 1 diabetes and type 2 diabetes)
Review strategies	<p>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</p> <p>A list of excluded studies will be provided following weeding</p> <p>Evidence tables and an evidence profile will be used to summarise the evidence</p>	
Equality	Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)	<p>The practicalities of offering screening for retinopathy will vary according to the child or young person's age and whether or not they have learning difficulties (because digital retinal photography requires the person to sit still and stare at a fixed point); learning difficulties are more often associated with type 2 diabetes than with type 1 diabetes</p>

E.27 Type 2 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

Type 2 diabetes – nephropathy		
Existing recommendation(s) in 2004 guideline	None	The 2004 guideline was specific to type 1 diabetes
Review question for update	What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?	Background information: http://www.kidney.org/professionals/kdoqi/pdf/Diabetes_AJKD_Feb_Suppl_07.pdf recommends starting screening at diagnosis of type 2 diabetes
Objectives	To determine when nephropathy screening should start following diagnosis of type 2 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter, and taking account of issues such as the clinical importance of intermittent microalbuminuria	
Language	English	
Study design	Cohort studies or consecutive case series	Cross-sectional studies which report prevalence and longitudinal studies which report incidence will be considered
Status	Published articles (no limitation on year of publication)	This is a completely new topic for the update so no date limit will be applied to searches
Population	Children and young people with type 2 diabetes	The guideline scope defines children and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are presented on an age group which extends into people aged >18 years, these will be included only if the mean age in the group is ≤ 18 years or if more than 50% of group participants are aged ≤ 18 years Studies will be included only if they provide data on prevalence for specific groups of children or young people (stratified by age or duration of diabetes) Only include data on incidence if

Type 2 diabetes – nephropathy		
		<p>exact figures (for example, incidence per hundred person years) are described in the text, and not if data are solely presented as survival curve analysis</p>
Intervention or index test	<ul style="list-style-type: none"> • Screening for microalbuminuria (however measured, and including using measurement through urine albumin:creatinine ratio (ACR)) • Screening using serum creatinine concentration 	<p>The guidelines relating to type 1 diabetes in adults and type 2 diabetes in adults include specific recommendations on:</p> <ul style="list-style-type: none"> • repeated measurement of ACR over a 4-month period to establish a diagnosis of microalbuminuria • measuring serum creatinine at the same time, and • in type 2 diabetes, estimating the glomerular filtration rate (GFR) at the same time (using the method-abbreviated modification of diet in renal disease four-variable equation) <p>An abnormal urine ACR is the first feature of nephropathy, whereas abnormal serum creatinine concentration is a later feature; both may be relevant in children and young people with type 2 diabetes because they may have nephropathy at diagnosis (because the diabetes can go undetected for longer in the case of type 2 diabetes); children and young people with type 2 diabetes are also likely to have hypertension at diagnosis and/or to be obese, and both of these are independent risk factors for impaired renal function</p> <p>Urine ACR is the practice for screening of microalbuminuria in the UK. For studies which report on albumin excretion rate (AER) rather than ACR for the confirmation of microalbuminuria, convert to ACR measurements using separate conversion equations for males and females (Schultz et al. 1999)</p> <p>Reference is: Schultz, C.J., et al. 1999. Microalbuminuria prevalence varies with age, sex, and puberty in children with type 1 diabetes followed from diagnosis in a</p>

Type 2 diabetes – nephropathy		
		<p>longitudinal study. Diabetes Care, 22 (3): 495-502)</p> <p>Using ACR > 2.5mg/mmol for males and ACR > 3.5 mg/mmol for females (at least 2 of 3 consecutive collections over a period of 3-4 months) which are the standards for confirming microalbuminuria in UK adults, exclude studies where the ACR measurement falls below 2.5 mg/mmol or 3.5mg/mmol for males and females, respectively</p>
Comparator or reference standard	Prevalence or incidence at different time intervals after diagnosis and/or at different ages	
Clinical outcomes	<p>Prevalence of microalbuminuria (however measured, and including using measurement through urine albumin:creatinine ratio (ACR))</p> <p>Incidence of microalbuminuria over time</p> <p>Prevalence of elevated serum creatinine (and/or reduced estimated GFR) using serum creatinine concentration</p>	<p>Evidence tables should document cut-offs and definitions of microalbuminuria used in included studies</p> <p>NCC-WCH to discuss with GDG to determine which studies should be included if necessary</p> <p>Note that the 2004 guideline on type 1 diabetes in adults, and the 2008 guideline on type 2 diabetes in adults use repeated tests of ACR >2.5mg/mmol for men, and >3.5mg/mmol for women (in at least 2 of 3 consecutive collections over a period of 3-4 months) to confirm microalbuminuria</p> <p>It will be important to consider the severity of microalbuminuria and how should this be reported (for example, thresholds for 'severe microalbuminuria', etc)</p>
Health economic outcomes	This question was not identified as a priority for health economic analysis	
Other criteria for inclusion/exclusion of studies	<p>Exclude studies that do not</p> <ul style="list-style-type: none"> • report either prevalence of microalbuminuria or prevalence of elevated serum creatinine at a particular time-point after diagnosis • have a systematic approach to screening as opposed to selective patient screening based on individual concerns 	
Search strategies	See separate document	NCC-WCH to consider using a single search to cover both review questions relating to monitoring for nephropathy (type

Type 2 diabetes – nephropathy		
		1 diabetes and type 2 diabetes) The search terms microalbuminuria and diabetes should identify relevant studies
Review strategies	Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence	
Equality	Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)	

Appendix F: Search strategies

F.1 Diagnosis

Review question: What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?

The systematic review for this question was conducted by the guidance-producing centre for the guideline 'Type 1 diabetes in adults'.

Database(s): Ovid MEDLINE(R), Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily Update

- # Searches
- 1 Diabetes mellitus, type 1/
 - 2 Diabetic ketoacidosis/
 - 3 ((diabet* or DM) adj4 (type 1 or type1 or type I or type one)).ti,ab.
 - 4 (diabet* adj2 (autoimmun* or auto immun*)).ti,ab.
 - 5 (LADA or MODY).ti,ab.
 - 6 (diabet* adj2 (brittle or labile)).ti,ab.
 - 7 (diabet* adj2 (sudden onset or maturity onset or juvenile or childhood)).ti,ab.
 - 8 (diabet* adj3 (keto* or acido* or gastropare*)).ti,ab.
 - 9 (dm1 or iddm or t1d* or dka).ti,ab.
 - 10 ((diabet* adj2 (insulin depend* or insulin deficien*)) not non insulin depend*).ti,ab.
 - 11 diabetes mellitus.ti.
 - 12 or/1-11
 - 13 (pregnan* or gestation*).ti.
 - 14 12 not 13
 - 15 letter/
 - 16 editorial/
 - 17 news/
 - 18 exp historical article/
 - 19 Anecdotes as Topic/
 - 20 comment/
 - 21 case report/
 - 22 (letter or comment*).ti.

- 23 or/15-22
- 24 23 not (randomized controlled trial/ or random*.ti,ab.)
- 25 animals/ not humans/
- 26 exp Animals, Laboratory/
- 27 exp Animal Experimentation/
- 28 exp Models, Animal/
- 29 exp Rodentia/
- 30 (rat or rats or mouse or mice).ti.
- 31 or/24-30
- 32 14 not 31
- 33 limit 32 to english language
- 34 C-peptide/
- 35 *Autoantibodies/
- 36 Glutamate decarboxylase/
- 37 Insulinoma/
- 38 Glucose-6-phosphatase/
- 39 C peptide*.ti,ab.
- 40 ((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod*or autoantibod*)).ti,ab.
- 41 zinc transporter 8.ti,ab.
- 42 (islet adj5 (phosphatase or catalytic)).ti,ab.
- 43 (IGRP* or ICA* or IA-2* or IA2* or ZnT8* or GAD*).ti,ab.
- 44 or/34-43
- 45 33 and 44
- 46 (diagnos* or screen* or test*).ti,ab,hw.
- 47 exp "sensitivity and specificity"/
- 48 ROC Curve/
- 49 Area Under Curve/
- 50 Proportional Hazards Models/
- 51 (ROC or AUC or (area and curve)).ti,ab.
- 52 (sensitivity or specificity).ti,ab.
- 53 gold standard.ab.
- 54 (predictive value* or PPV or NPV).ti,ab.
- 55 likelihood ratio*.ti,ab.
- 56 or/46-55
- 57 45 and 56
- 58 randomized controlled trial.pt.
- 59 controlled clinical trial.pt.
- 60 randomi#ed.ab.
- 61 placebo.ab.
- 62 randomly.ab.
- 63 Clinical Trials as topic.sh.
- 64 trial*.ti.
- 65 or/58-64
- 66 Meta-Analysis/
- 67 Meta-Analysis as Topic/
- 68 (meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
- 69 ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
- 70 (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
- 71 (search strategy or search criteria or systematic search or study selection or data extraction).ab.
- 72 (search* adj4 literature).ab.

- 73 (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
74 cochrane.jw.
75 ((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
76 or/66-75
77 Epidemiologic studies/
78 exp case control studies/
79 exp cohort studies/
80 Cross-sectional studies/
81 case control.ti,ab.
82 ((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
83 ((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys*)).ti,ab.
84 (study and (participant* or patient* or subject* or group*)).ti,ab.
85 cohort*.ti,ab.
86 or/77-85
87 57 and (65 or 76 or 86)
88 (2003\$ or 2004\$ or 2005\$ or 2006\$ or 2007\$ or 2008\$ or 2009\$ or 2010\$ or 2011\$ or 2012\$ or 2013\$).ed,dc.
89 87 and 88

Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

- # Searches
1 Diabetes mellitus, type 1/
2 Diabetic ketoacidosis/
3 ((diabet* or DM) adj4 (type 1 or type1 or type I or type one)).ti,ab.
4 (diabet* adj2 (autoimmun* or auto immun*)).ti,ab.
5 (LADA or MODY).ti,ab.
6 (diabet* adj2 (brittle or labile)).ti,ab.
7 (diabet* adj2 (sudden onset or maturity onset or juvenile or childhood)).ti,ab.
8 (diabet* adj3 (keto* or acido* or gastropare*)).ti,ab.
9 (dm1 or iddm or t1d* or dka).ti,ab.
10 ((diabet* adj2 (insulin depend* or insulin deficien*)) not non insulin depend*).ti,ab.
11 diabetes mellitus.ti.
12 or/1-11
13 (pregnan* or gestation*).ti.
14 12 not 13
15 letter/
16 editorial/
17 news/
18 exp historical article/
19 Anecdotes as Topic/
20 comment/
21 case report/
22 (letter or comment*).ti.
23 or/15-22
24 23 not (randomized controlled trial/ or random*.ti,ab.)
25 animals/ not humans/
26 exp Animals, Laboratory/
27 exp Animal Experimentation/
28 exp Models, Animal/

29 exp Rodentia/
30 (rat or rats or mouse or mice).ti.
31 or/24-30
32 14 not 31
33 limit 32 to english language
34 C-peptide/
35 *Autoantibodies/
36 Glutamate decarboxylase/
37 Insulinoma/
38 Glucose-6-phosphatase/
39 C peptide*.ti,ab.
40 ((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod* or autoantibod*)).ti,ab.
41 zinc transporter 8.ti,ab.
42 (islet adj5 (phosphatase or catalytic)).ti,ab.
43 [or/34-43]
44 [or/46-55]
45 [or/58-64]
46 [or/66-75]
47 [or/77-85]
48 Diabetes mellitus, type 1/
49 Diabetic ketoacidosis/
50 ((diabet* or DM) adj4 (type 1 or type1 or type I or type one)).ti,ab.
51 (diabet* adj2 (autoimmun* or auto immun*)).ti,ab.
52 (LADA or MODY).ti,ab.
53 (diabet* adj2 (brittle or labile)).ti,ab.
54 (diabet* adj2 (sudden onset or maturity onset or juvenile or childhood)).ti,ab.
55 (diabet* adj3 (keto* or acido* or gastropare*)).ti,ab.
56 (dm1 or iddm or t1d* or dka).ti,ab.
57 ((diabet* adj2 (insulin depend* or insulin deficien*)) not non insulin depend*).ti,ab.
58 diabetes mellitus.ti.
59 or/48-58
60 (pregnan* or gestation*).ti.
61 59 not 60
62 letter/
63 editorial/
64 news/
65 exp historical article/
66 Anecdotes as Topic/
67 comment/
68 case report/
69 (letter or comment*).ti.
70 or/62-69
71 70 not (randomized controlled trial/ or random*.ti,ab.)
72 animals/ not humans/
73 exp Animals, Laboratory/
74 exp Animal Experimentation/
75 exp Models, Animal/
76 exp Rodentia/
77 (rat or rats or mouse or mice).ti.
78 or/71-77
79 61 not 78
80 limit 79 to english language

- 81 C-peptide/
- 82 *Autoantibodies/
- 83 Glutamate decarboxylase/
- 84 Insulinoma/
- 85 Glucose-6-phosphatase/
- 86 C peptide*.ti,ab.
- 87 ((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod* or autoantibod*)).ti,ab.
- 88 zinc transporter 8.ti,ab.
- 89 (islet adj5 (phosphatase or catalytic)).ti,ab.
- 90 (IGRP* or ICA* or IA-2* or IA2* or ZnT8* or GAD*).ti,ab.
- 91 or/81-90
- 92 80 and 91
- 93 (diagnos* or screen* or test*).ti,ab,hw.
- 94 exp "sensitivity and specificity"/
- 95 ROC Curve/
- 96 Area Under Curve/
- 97 Proportional Hazards Models/
- 98 (ROC or AUC or (area and curve)).ti,ab.
- 99 (sensitivity or specificity).ti,ab.
- 100 gold standard.ab.
- 101 (predictive value* or PPV or NPV).ti,ab.
- 102 likelihood ratio*.ti,ab.
- 103 or/93-102
- 104 92 and 103
- 105 randomized controlled trial.pt.
- 106 controlled clinical trial.pt.
- 107 randomi#ed.ab.
- 108 placebo.ab.
- 109 randomly.ab.
- 110 Clinical Trials as topic.sh.
- 111 trial*.ti.
- 112 or/105-111
- 113 Meta-Analysis/
- 114 Meta-Analysis as Topic/
- 115 (meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
- 116 ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
- 117 (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
- 118 (search strategy or search criteria or systematic search or study selection or data extraction).ab.
- 119 (search* adj4 literature).ab.
- 120 (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
- 121 cochrane.jw.
- 122 ((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
- 123 or/113-122
- 124 Epidemiologic studies/
- 125 exp case control studies/
- 126 exp cohort studies/
- 127 Cross-sectional studies/
- 128 case control.ti,ab.
- 129 ((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.

- 130 ((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys*)).ti,ab.
131 (study and (participant* or patient* or subject* or group*)).ti,ab.
132 cohort*.ti,ab.
133 or/124-132
134 104 and (112 or 123 or 133)
135 (201402* or 201403* or 201404* or 201405* or 201406* or 201407* or 201408*).ed,dc.
136 134 and 135

Database(s): Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Health Technology Assessment, Database of Abstracts of Reviews of Effects, NHS Economic Evaluation Database

- No. Search terms
- #1 MeSH descriptor: [Diabetes Mellitus, Type 1] explode all trees
#2 MeSH descriptor: [Diabetic Ketoacidosis] this term only
#3 ((diabet* or DM) near/4 ("type 1" or type1 or "type I" or "type one")):ti,ab
#4 (diabet* near/2 (autoimmun* or "auto immun*")):ti,ab
#5 (diabet* near/2 (brittle or labile)):ti,ab
#6 (diabet* near/2 ("sudden onset" or "maturity onset" or juvenile or child*)):ti,ab
#7 (diabet* near/3 (keto* or acido* or gastropare*)):ti,ab
#8 (dm1 or iddm or t1d* or dka or LADA or MODY):ti,ab
#9 (diabet* near/2 (insulin next depend*)):ti,ab
#10 #9 and not "non insulin dependent"
#11 diabetes mellitus:ti
#12 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11
#13 (pregnan* or gestation*):ti
#14 #12 not #13
#15 #14 from 2003 to 2012
#16 MeSH descriptor: [C-Peptide] this term only
#17 MeSH descriptor: [Autoantibodies] this term only
#18 MeSH descriptor: [Glutamate Decarboxylase] this term only
#19 MeSH descriptor: [Insulinoma] this term only
#20 MeSH descriptor: [Glucose-6-Phosphatase] this term only
#21 (C next (peptide or peptides)):ti,ab
#22 (("islet cell" or decarboxylase or glutamic or insulinoma) and (antibody or antibodies or "anti body" or "anti bodies" or autoantibody or autoantibodies)):ti,ab
#23 ("zinc transporter 8"):ti,ab
#24 (islet* and (phosphatase or catalytic)):ti,ab
#25 (IGRP* or ICA* or "IA-2" or IA2* or ZnT8* or GAD*):ti,ab
#26 #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25
#27 #15 and #26
#28 MeSH descriptor: [Diagnosis] explode all trees
#29 (diagnos* or screen* or test*):ti,ab
#30 MeSH descriptor: [Sensitivity and Specificity] explode all trees
#31 MeSH descriptor: [Area Under Curve] this term only
#32 MeSH descriptor: [Proportional Hazards Models] this term only
#33 ((ROC or AUC) or (area and curve)):ti,ab
#34 (sensitivity or specificity):ti,ab
#35 "gold standard":ab
#36 ("predictive value" or PPV or NPV):ti,ab
#37 "likelihood ratio":ti,ab
#38 #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37
#39 #38 and #27

Database(s): Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Health Technology Assessment, Database of Abstracts of Reviews of Effects, NHS Economic Evaluation Database

- No. Search terms
- #1 MeSH descriptor: [Diabetes Mellitus, Type 1] explode all trees
 - #2 MeSH descriptor: [Diabetic Ketoacidosis] this term only
 - #3 ((diabet* or DM) near/4 ("type 1" or type1 or "type I" or "type one")):ti,ab
 - #4 (diabet* near/2 (autoimmun* or "auto immun*")):ti,ab
 - #5 (diabet* near/2 (brittle or labile)):ti,ab
 - #6 (diabet* near/2 ("sudden onset" or juvenile or child*)):ti,ab
 - #7 (diabet* near/3 (keto* or acido* or gastropare*)):ti,ab
 - #8 (dm1 or iddm or t1d* or dka or LADA):ti,ab
 - #9 (diabet* near/2 (insulin next depend*)):ti,ab
 - #10 #9 and not "non insulin dependent"
 - #11 diabetes mellitus:ti
 - #12 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #10 or #11)
 - #13 (pregnan* or gestation*):ti
 - #14 #12 not #13
 - #15 MeSH descriptor: [C-Peptide] this term only
 - #16 MeSH descriptor: [Autoantibodies] this term only
 - #17 MeSH descriptor: [Glutamate Decarboxylase] this term only
 - #18 MeSH descriptor: [Insulinoma] this term only
 - #19 MeSH descriptor: [Glucose-6-Phosphatase] this term only
 - #20 (C next (peptide or peptides)):ti,ab
 - #21 ("islet cell" or decarboxylase or glutamic or insulinoma) and (antibody or antibodies or "anti body" or "anti bodies" or autoantibody or autoantibodies):ti,ab
 - #22 ("zinc transporter 8"):ti,ab
 - #23 (islet* and (phosphatase or catalytic)):ti,ab
 - #24 (IGRP* or ICA* or "IA-2" or IA2* or ZnT8* or GAD*):ti,ab
 - #25 #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24
 - #26 #14 and #25
 - #27 MeSH descriptor: [Diagnosis] explode all trees
 - #28 (diagnos* or screen* or test*):ti,ab
 - #29 MeSH descriptor: [Sensitivity and Specificity] explode all trees
 - #30 MeSH descriptor: [Area Under Curve] this term only
 - #31 MeSH descriptor: [Proportional Hazards Models] this term only
 - #32 ((ROC or AUC) or (area and curve)):ti,ab
 - #33 (sensitivity or specificity):ti,ab
 - #34 gold standard:ab
 - #35 ("predictive value" or PPV or NPV):ti,ab
 - #36 likelihood ratio:ti,ab
 - #37 #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36
 - #38 #26 and #37

Database(s): Embase

- No. Search terms
- 1 Insulin dependent diabetes mellitus/
 - 2 Juvenile diabetes mellitus/
 - 3 Diabetic ketoacidosis/
 - 4 ((diabet* or DM) adj4 (type 1 or type1 or type I or type one)).ti,ab.
 - 5 (diabet* adj2 (autoimmun* or auto immun*)).ti,ab.
 - 6 (LADA or MODY).ti,ab.
 - 7 (diabet* adj2 (brittle or labile)).ti,ab.

- 8 (diabet* adj2 (sudden onset or maturity onset or juvenile or childhood)).ti,ab.
- 9 (diabet* adj3 (keto* or acido* or gastropare*)).ti,ab.
- 10 (dm1 or iddm or t1d* or dka).ti,ab.
- 11 ((diabet* adj2 (insulin depend* or insulin deficient*)) not non insulin depend*).ti,ab.
- 12 diabetes mellitus.ti.
- 13 or/1-12
- 14 (pregnan* or gestation*).ti.
- 15 13 not 14
- 16 letter.pt. or letter/
- 17 note.pt.
- 18 editorial.pt.
- 19 case report/ or case study/
- 20 (letter or comment*).ti.
- 21 or/16-20
- 22 21 not (randomized controlled trial/ or random*.ti,ab.)
- 23 animal/ not human/
- 24 nonhuman/
- 25 exp Animal Experiment/
- 26 exp Experimental Animal/
- 27 animal model/
- 28 exp Rodent/
- 29 (rat or rats or mouse or mice).ti.
- 30 or/22-29
- 31 15 not 30
- 32 (2003\$ or 2004\$ or 2005\$ or 2006\$ or 2007\$ or 2008\$ or 2009\$ or 2010\$ or 2011\$ or 2012\$ or 2013\$).em.
- 33 31 and 32
- 34 C peptide/
- 35 Glutamate decarboxylase 65 antibody/
- 36 Insulinoma/
- 37 *Autoantibody/
- 38 Glucose 6 phosphatase/
- 39 ((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod* or autoantibod*)).ti,ab.
- 40 zinc transporter 8.ti,ab.
- 41 (islet adj5 (phosphatase or catalytic)).ti,ab.
- 42 (IGRP* or ICA* or IA-2* or IA2* or ZnT8* or GAD*).ti,ab.
- 43 or/34-42
- 44 33 and 43
- 45 (diagnos* or screen* or test*).ti,ab,hw.
- 46 exp "sensitivity and specificity"/
- 47 Receiver operating characteristic/
- 48 Area under the curve/
- 49 Proportional hazards model/
- 50 (ROC or AUC or (area and curve)).ti,ab.
- 51 (sensitivity or specificity).ti,ab.
- 52 gold standard.ab.
- 53 (predictive value* or PPV or NPV).ti,ab.
- 54 likelihood ratio*.ti,ab.
- 55 or/45-54
- 56 44 and 55
- 57 random*.ti,ab.
- 58 factorial*.ti,ab.

- 59 (crossover* or cross over*).ti,ab.
- 60 ((doubl* or singl*) adj blind*).ti,ab.
- 61 (assign* or allocat* or volunteer* or placebo*).ti,ab.
- 62 crossover procedure/
- 63 single blind procedure/
- 64 randomized controlled trial/
- 65 double blind procedure/
- 66 or/57-65
- 67 Meta-Analysis/
- 68 Meta-Analysis as Topic/
- 69 (meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
- 70 ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
- 71 (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
- 72 (search strategy or search criteria or systematic search or study selection or data extraction).ab.
- 73 (search* adj4 literature).ab.
- 74 (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
- 75 cochrane.jw.
- 76 ((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
- 77 or/67-76
- 78 Clinical study/
- 79 exp case control study/
- 80 family study/
- 81 longitudinal study/
- 82 retrospective study/
- 83 prospective study/
- 84 cross-sectional study/
- 85 cohort analysis/
- 86 case control.ti,ab.
- 87 ((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
- 88 ((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys*)).ti,ab.
- 89 (study and (participant* or patient* or subject* or group*)).ti,ab.
- 90 cohort*.ti,ab.
- 91 or/78-90
- 92 56 and (66 or 77 or 91)
- 93 limit 92 to english language

Database(s): Embase

- # Searches
- 1 Insulin dependent diabetes mellitus/
- 2 Juvenile diabetes mellitus/
- 3 Diabetic ketoacidosis/
- 4 ((diabet* or DM) adj4 (type 1 or type1 or type I or type one)).ti,ab.
- 5 (diabet* adj2 (autoimmun* or auto immun*)).ti,ab.
- 6 (LADA or MODY).ti,ab.
- 7 (diabet* adj2 (brittle or labile)).ti,ab.
- 8 (diabet* adj2 (sudden onset or maturity onset or juvenile or childhood)).ti,ab.
- 9 (diabet* adj3 (keto* or acido* or gastropare*)).ti,ab.
- 10 (dm1 or iddm or t1d* or dka).ti,ab.
- 11 ((diabet* adj2 (insulin depend* or insulin deficien*)) not non insulin depend*).ti,ab.

12 diabetes mellitus.ti.
13 or/1-12
14 (pregnan* or gestation*).ti.
15 13 not 14
16 letter.pt. or letter/
17 note.pt.
18 editorial.pt.
19 case report/ or case study/
20 (letter or comment*).ti.
21 or/16-20
22 21 not (randomized controlled trial/ or random*.ti,ab.)
23 animal/ not human/
24 nonhuman/
25 exp Animal Experiment/
26 exp Experimental Animal/
27 animal model/
28 exp Rodent/
29 (rat or rats or mouse or mice).ti.
30 or/22-29
31 15 not 30
32 ("201406" or "201407" or "201408" or "201409" or 20141* or 20142* or 20143*).em.
33 31 and 32
34 C peptide/
35 Glutamate decarboxylase 65 antibody/
36 Insulinoma/
37 *Autoantibody/
38 Glucose 6 phosphatase/
39 ((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod* or autoantibod*)).ti,ab.
40 zinc transporter 8.ti,ab.
41 (islet adj5 (phosphatase or catalytic)).ti,ab.
42 [or/34-42]
43 [or/45-54]
44 [or/57-65]
45 [or/67-76]
46 [or/78-90]
47 [limit 92 to english language]
48 Insulin dependent diabetes mellitus/
49 Juvenile diabetes mellitus/
50 Diabetic ketoacidosis/
51 ((diabet* or DM) adj4 (type 1 or type1 or type I or type one)).ti,ab.
52 (diabet* adj2 (autoimmun* or auto immun*)).ti,ab.
53 (LADA or MODY).ti,ab.
54 (diabet* adj2 (brittle or labile)).ti,ab.
55 (diabet* adj2 (sudden onset or maturity onset or juvenile or childhood)).ti,ab.
56 (diabet* adj3 (keto* or acido* or gastropare*)).ti,ab.
57 (dm1 or iddm or t1d* or dka).ti,ab.
58 ((diabet* adj2 (insulin depend* or insulin deficien*)) not non insulin depend*).ti,ab.
59 diabetes mellitus.ti.
60 or/48-59
61 (pregnan* or gestation*).ti.
62 60 not 61
63 letter.pt. or letter/

64 note.pt.
65 editorial.pt.
66 case report/ or case study/
67 (letter or comment*).ti.
68 or/63-67
69 68 not (randomized controlled trial/ or random*.ti,ab.)
70 animal/ not human/
71 nonhuman/
72 exp Animal Experiment/
73 exp Experimental Animal/
74 animal model/
75 exp Rodent/
76 (rat or rats or mouse or mice).ti.
77 or/69-76
78 62 not 77
79 ("201406" or "201407" or "201408" or "201409" or 20141* or 20142* or 20143*).em.
80 78 and 79
81 C peptide/
82 Glutamate decarboxylase 65 antibody/
83 Insulinoma/
84 *Autoantibody/
85 Glucose 6 phosphatase/
86 ((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod* or autoantibod*)).ti,ab.
87 zinc transporter 8.ti,ab.
88 (islet adj5 (phosphatase or catalytic)).ti,ab.
89 (IGRP* or ICA* or IA-2* or IA2* or ZnT8* or GAD*).ti,ab.
90 or/81-89
91 80 and 90
92 (diagnos* or screen* or test*).ti,ab,hw.
93 exp "sensitivity and specificity"/
94 Receiver operating characteristic/
95 Area under the curve/
96 Proportional hazards model/
97 (ROC or AUC or (area and curve)).ti,ab.
98 (sensitivity or specificity).ti,ab.
99 gold standard.ab.
100 (predictive value* or PPV or NPV).ti,ab.
101 likelihood ratio*.ti,ab.
102 or/92-101
103 91 and 102
104 random*.ti,ab.
105 factorial*.ti,ab.
106 (crossover* or cross over*).ti,ab.
107 ((doubl* or singl*) adj blind*).ti,ab.
108 (assign* or allocat* or volunteer* or placebo*).ti,ab.
109 crossover procedure/
110 single blind procedure/
111 randomized controlled trial/
112 double blind procedure/
113 or/104-112
114 Meta-Analysis/
115 Meta-Analysis as Topic/

- 116 (meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
- 117 ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
- 118 (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
- 119 (search strategy or search criteria or systematic search or study selection or data extraction).ab.
- 120 (search* adj4 literature).ab.
- 121 (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
- 122 cochrane.jw.
- 123 ((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
- 124 or/114-123
- 125 Clinical study/
- 126 exp case control study/
- 127 family study/
- 128 longitudinal study/
- 129 retrospective study/
- 130 prospective study/
- 131 cross-sectional study/
- 132 cohort analysis/
- 133 case control.ti,ab.
- 134 ((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
- 135 ((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys*)).ti,ab.
- 136 (study and (participant* or patient* or subject* or group*)).ti,ab.
- 137 cohort*.ti,ab.
- 138 or/125-137
- 139 103 and (113 or 124 or 138)
- 140 limit 139 to english language

F.2 Type 1 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

Ovid MEDLINE(R)

- # Searches
- 1 randomized controlled trial.pt.
- 2 controlled clinical trial.pt.
- 3 DOUBLE BLIND METHOD/
- 4 SINGLE BLIND METHOD/
- 5 RANDOM ALLOCATION/
- 6 RANDOMIZED CONTROLLED TRIALS AS TOPIC/
- 7 or/1-6
- 8 ((single or double or triple or treble) adj5 (blind\$ or mask\$)).tw,sh.
- 9 clinical trial.pt.
- 10 exp CLINICAL TRIAL/
- 11 exp CLINICAL TRIALS AS TOPIC/
- 12 (clinic\$ adj5 trial\$).tw,sh.
- 13 PLACEBOS/
- 14 placebo\$.tw,sh.
- 15 random\$.tw,sh.

- 16 or/8-15
17 or/7,16
18 META ANALYSIS/
19 META ANALYSIS AS TOPIC/
20 meta analysis.pt.
21 (metaanaly\$ or meta-analy\$ or (meta adj analy\$)).tw,sh.
22 (systematic\$ adj5 (review\$ or overview\$)).tw,sh.
23 (methodologic\$ adj5 (review\$ or overview\$)).tw,sh.
24 or/18-23
25 review\$.pt.
26 (medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or
psyclit or "web of science" or "science citation" or scisearch).tw.
27 ((hand or manual\$) adj2 search\$).tw.
28 (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online
database\$).tw,sh.
29 (pooling or pooled or mantel haenszel).tw,sh.
30 (peto or dersimonian or der simonian or fixed effect).tw,sh.
31 or/26-30
32 and/25,31
33 or/24,32
34 letter.pt.
35 case report.tw.
36 comment.pt.
37 editorial.pt.
38 historical article.pt.
39 or/34-38
40 17 not 39
41 33 not 39
42 or/40-41
43 ADOLESCENT/ or MINORS/
44 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
45 exp CHILD/
46 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or
kindergar\$ or boy? or girl?).ti,ab,jw.
47 exp INFANT/
48 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
49 exp PEDIATRICS/ or exp PUBERTY/
50 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
51 or/43-50
52 exp DIABETES MELLITUS, TYPE 1/
53 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or Tl or insulin depend\$ or juvenile or
child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
54 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
55 or/52-54
56 and/51,55
57 PATIENT EDUCATION AS TOPIC/
58 PROBLEM SOLVING/
59 ed.fs.
60 ((educat\$ or training) adj6 (intervention\$ or program? or programme or programmes)).ti,ab.
61 (problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
62 ((patient? or parent? or parental or child\$ or adolescenc\$ or young or youth? or family\$ or
families) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or
instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.

- 63 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj3 information).ti,ab.
- 64 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
- 65 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
- 66 ((diabet\$ or insulin\$ or glyco?emi\$ or hypoglyco?emi\$ or "blood glucose" or "blood sugar") adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
- 67 ((diabet\$ or insulin\$ or glyco?emi\$ or hypoglyco?emi\$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
- 68 or/57-67
- 69 and/56,68
- 70 and/42,69
- 71 limit 70 to english language
- 72 LETTER/
73 EDITORIAL/
74 NEWS/
75 exp HISTORICAL ARTICLE/
76 ANECDOTES AS TOPIC/
77 COMMENT/
78 CASE REPORT/
79 (letter or comment* or abstracts).ti.
- 80 or/72-79
- 81 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 82 80 not 81
- 83 ANIMALS/ not HUMANS/
84 exp ANIMALS, LABORATORY/
85 exp ANIMAL EXPERIMENTATION/
86 exp MODELS, ANIMAL/
87 exp RODENTIA/
88 (rat or rats or mouse or mice).ti.
- 89 or/82-88
- 90 71 not 89

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 7 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 8 or/6-7
- 9 and/5,8
- 10 ((educat\$ or training) adj6 (intervention\$ or program? or programme or programmes)).ti,ab.
- 11 (problem-solving or "problem solving" or problem-based or "problem based").ti,ab.

- 12 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
- 13 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj3 information).ti,ab.
- 14 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
- 15 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
- 16 ((diabet\$ or insulin\$ or glyco?emi\$ or hypoglyco?emi\$ or "blood glucose" or "blood sugar") adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
- 17 ((diabet\$ or insulin\$ or glyco?emi\$ or hypoglyco?emi\$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
- 18 or/10-17
- 19 and/9,18
- 20 limit 19 to english language

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 1/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 13 or/10-12
- 14 and/9,13
- 15 PATIENT EDUCATION AS TOPIC/
- 16 PROBLEM SOLVING/
- 17 ed.fs.
- 18 ((educat\$ or training) adj6 (intervention\$ or program? or programme or programmes)).ti,ab.
- 19 (problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
- 20 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
- 21 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj3 information).ti,ab.
- 22 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
- 23 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.

- 24 ((diabet\$ or insulin\$ or glyco?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
- 25 ((diabet\$ or insulin\$ or glyco?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
- 26 or/15-25
- 27 and/14,26

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).kw,ti,ab,jw,rw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).kw,ti,ab,jw,rw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).kw,ti,ab,jw,rw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).kw,ti,ab,jw,rw.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).kw,ti,ab.
- 7 (IDDM or T1D or T1D or DM1 or DMI).kw,ti,ab.
- 8 or/6-7
- 9 and/5,8
- 10 "PATIENT EDUCATION AS TOPIC".kw.
- 11 "PROBLEM SOLVING".kw.
- 12 ((educat\$ or training) adj6 (intervention\$ or program? or programme or programmes)).tw,tx.
- 13 (problem-solving or "problem solving" or problem-based or "problem based").tw,tx.
- 14 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).tw,tx.
- 15 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj3 information).tw,tx.
- 16 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).tw,tx.
- 17 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).tw,tx.
- 18 ((diabet\$ or insulin\$ or glyco?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).tw,tx.
- 19 ((diabet\$ or insulin\$ or glyco?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj3 information).tw,tx.
- 20 or/10-19
- 21 and/9,20

Health Technology Assessment

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx,rw.
- 3 exp CHILD/

- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jx,rw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/
11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw.
12 (IDDM or T1D or T1D or DM1 or DMI).tw.
13 or/10-12
14 and/9,13
15 PATIENT EDUCATION AS TOPIC/
16 PROBLEM SOLVING/
17 ed.fs.
18 ((educat\$ or training) adj6 (intervention\$ or program? or programme or programmes)).tw.
19 (problem-solving or "problem solving" or problem-based or "problem based").tw.
20 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).tw.
21 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj3 information).tw.
22 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).tw.
23 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).tw.
24 ((diabet\$ or insulin\$ or glyc?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).tw.
25 ((diabet\$ or insulin\$ or glyc?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj3 information).tw.
26 or/15-25
27 and/14,26
28 limit 27 to english language

Embase

- # Searches
1 CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
2 (clinic\$ adj5 trial\$).ti,ab,sh.
3 SINGLE BLIND PROCEDURE/
4 DOUBLE BLIND PROCEDURE/
5 RANDOM ALLOCATION/
6 CROSSOVER PROCEDURE/
7 PLACEBO/
8 placebo\$.ti,ab,sh.
9 random\$.ti,ab,sh.
10 RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
11 ((single or double or triple or treble) adj (blind\$ or mask\$)).ti,ab,sh.
12 randomi?ed control\$ trial\$.tw.
13 or/1-12

14 META ANALYSIS/
15 ((meta adj analy\$) or metaanalys\$ or meta-analy\$).ti,ab,sh.
16 (systematic\$ adj5 (review\$ or overview\$)).ti,sh,ab.
17 (methodologic\$ adj5 (review\$ or overview\$)).ti,ab,sh.
18 or/14-17
19 review.pt.
20 (medline or medlars or embase).ab.
21 (scisearch or science citation index).ab.
22 (psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
23 ((hand or manual\$) adj2 search\$).tw.
24 (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online
database\$).tw.
25 (pooling or pooled or mantel haenszel).tw.
26 (peto or dersimonian or "der simonian" or fixed effect).tw.
27 or/20-26
28 and/19,27
29 or/18,28
30 (book or conference paper or editorial or letter or note or proceeding or short survey).pt.
31 13 not 30
32 29 not 30
33 or/31-32
34 exp ADOLESCENT/
35 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
36 exp CHILD/
37 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or
kindergar\$ or boy? or girl?).ti,ab,jx.
38 exp INFANT/
39 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
40 exp PEDIATRICS/ or exp PUBERTY/
41 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescens\$ or prepubescens\$).ti,ab,jx,ec.
42 or/34-41
43 INSULIN DEPENDENT DIABETES MELLITUS/
44 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or
child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
45 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
46 or/43-45
47 JUVENILE DIABETES MELLITUS/
48 and/42,46
49 or/47-48
50 PATIENT EDUCATION/
51 DIABETES EDUCATION/
52 DIABETES EDUCATOR/
53 EDUCATION PROGRAM/
54 PROBLEM SOLVING/
55 ((educat\$ or training) adj6 (intervention\$ or program? or programme or programmes)).ti,ab.
56 (problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
57 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or
families) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or
instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
58 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or
families) adj3 information).ti,ab.
59 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-
monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or

- cope or coping) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
- 60 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
- 61 ((diabet\$ or insulin\$ or glyc?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
- 62 ((diabet\$ or insulin\$ or glyc?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
- 63 or/50-62
- 64 and/49,63
- 65 and/33,64
- 66 conference abstract.pt.
- 67 letter.pt. or LETTER/
- 68 note.pt.
- 69 editorial.pt.
- 70 CASE REPORT/ or CASE STUDY/
- 71 (letter or comment* or abstracts).ti.
- 72 or/66-71
- 73 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 74 72 not 73
- 75 ANIMAL/ not HUMAN/
- 76 NONHUMAN/
- 77 exp ANIMAL EXPERIMENT/
- 78 exp EXPERIMENTAL ANIMAL/
- 79 ANIMAL MODEL/
- 80 exp RODENT/
- 81 (rat or rats or mouse or mice).ti.
- 82 or/74-81
- 83 65 not 82
- 84 limit 83 to english language

PsycINFO

- # Searches
- 1 LITERATURE REVIEW/
- 2 EXPERIMENTAL DESIGN/
- 3 RANDOM SAMPLING/
- 4 META-ANALYSIS/
- 5 exp TREATMENT/
- 6 (random\$ or search\$ or control\$ or risk\$).tw.
- 7 (meta-analys#s or metaanalys#s).ti.
- 8 (systematic\$ adj (review\$ or overview\$)).ti.
- 9 ((single or double or triple) adj (blind\$ or mask\$)).ti.
- 10 rct.tw.
- 11 or/1-10
- 12 adolescen\$.ag.
- 13 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,id,jw.
- 14 (child\$ or school\$ or preschool\$).ag.
- 15 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,id,jw.
- 16 (infan\$ or neonat\$).ag.
- 17 (infan\$ or neonat\$ or newborn\$ or baby or babies or p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,id,jw.

- 18 or/12-17
 19 DIABETES MELLITUS/
 20 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or Tl or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab,id.
 21 (IDDM or T1D or TID or DM1 or DMI).ti,ab,id.
 22 or/19-21
 23 and/18,22
 24 CLIENT EDUCATION/
 25 EDUCATIONAL PROGRAMS/ or EDUCATIONAL THERAPY/
 26 PROBLEM SOLVING/
 27 ((educat\$ or training) adj6 (intervention\$ or program? or programme or programmes)).ti,ab,id.
 28 (problem-solving or "problem solving" or problem-based or "problem based").ti,ab,id.
 29 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab,id.
 30 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj3 information).ti,ab,id.
 31 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab,id.
 32 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab,id.
 33 ((diabet\$ or insulin\$ or glyc?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab,id.
 34 ((diabet\$ or insulin\$ or glyc?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj3 information).ti,ab,id.
 35 or/24-34
 36 and/23,35
 37 and/11,36
 38 limit 37 to english language

CINAHL with Full Text

- | # | Query | Limiters/Expanders |
|-----|--|---|
| S31 | S6 AND S29 | Limiters - English Language; Exclude MEDLINE records
Search modes - Boolean/Phrase |
| S30 | S6 AND S29 | Search modes - Boolean/Phrase |
| S29 | S16 AND S28 | Search modes - Boolean/Phrase |
| S28 | S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 | Search modes - Boolean/Phrase |
| S27 | T1 ((diabet* or insulin* or glyc#emi* or hypoglyc#emi* or "blood glucose" or "blood sugar") N3 information) OR AB ((diabet* or insulin* or glyc#emi* or hypoglyc#emi* or "blood glucose" or "blood sugar") N3 information) | Search modes - Boolean/Phrase |
| S26 | T1 ((diabet* or insulin* or glyc#emi* or hypoglyc#emi* or "blood glucose" or "blood sugar") N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) OR AB ((diabet* or insulin* or glyc#emi* or hypoglyc#emi* or "blood glucose" or "blood sugar") N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) | Search modes - Boolean/Phrase |
| S25 | T1 ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N3 information) OR AB ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self | |

- manag*" or self-efficacy or "self efficacy" or cope or coping) N3 information) Search modes - Boolean/Phrase
- S24 TI ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) OR AB ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) Search modes - Boolean/Phrase
- S23 TI ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N3 information) OR AB ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N3 information) Search modes - Boolean/Phrase
- S22 TI ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) OR AB ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) Search modes - Boolean/Phrase
- S21 TI (problem-solving or "problem solving" or problem-based or "problem based") OR AB (problem-solving or "problem solving" or problem-based or "problem based") Search modes - Boolean/Phrase
- S20 TI ((educat* or training) N6 (intervention* or program# or programme or programmes)) OR AB ((educat* or training) N6 (intervention* or program# or programme or programmes)) Search modes - Boolean/Phrase
- S19 MW "ED" Search modes - Boolean/Phrase
- S18 (MH "Problem Solving+") Search modes - Boolean/Phrase
- S17 (MH "Patient Education") OR (MH "Diabetes Education") Search modes - Boolean/Phrase
- S16 S12 AND S15 Search modes - Boolean/Phrase
- S15 S13 OR S14 Search modes - Boolean/Phrase
- S14 TI (diabet* N5 ("type one" or "type 1" or "type I" or "insulin depend*" or juvenile or child* or earl* or labile or brittle or "sudden onset" or "auto immun*" or autoimmun* or "auto-immun*")) OR AB (diabet* N5 ("type one" or "type 1" or "type I" or "insulin depend*" or juvenile or child* or earl* or labile or brittle or "sudden onset" or "auto immun*" or autoimmun* or "auto-immun*")) Search modes - Boolean/Phrase
- S13 (MH "Diabetes Mellitus, Type 1+") Search modes - Boolean/Phrase
- S12 S7 OR S8 OR S9 OR S10 OR S11 Search modes - Boolean/Phrase
- S11 TI (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) OR AB (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) or SO (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) Search modes - Boolean/Phrase
- S10 TI (infan* or neonat* or newborn* or baby or babies) OR AB (infan* or neonat* or newborn* or baby or babies) OR SO (infan* or neonat* or newborn* or baby or babies) Search modes - Boolean/Phrase
- S9 TI (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR AB (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR SO (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) Search modes - Boolean/Phrase
- S8 TI (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR AB (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR SO (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) Search modes - Boolean/Phrase
- S7 (MH "Infant, Newborn+") OR (MH "Infant+") OR (MH "Child, Preschool") OR (MH "Child+") OR (MH "Adolescence+") Search modes - Boolean/Phrase
- S6 S1 OR S2 OR S3 OR S4 OR S5 Search modes - Boolean/Phrase

- S5 PT systematic review Search modes - Boolean/Phrase
S4 PT review Search modes - Boolean/Phrase
S3 TX meta-analysis OR "meta analysis" Search modes - Boolean/Phrase
S2 TX random* Search modes - Boolean/Phrase
S1 (MH "Treatment Outcomes+") OR (MH "Experimental Studies+") Search modes - Boolean/Phrase

F.3 Type 1 diabetes – behavioural interventions

Review question: What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 1 diabetes?

Ovid MEDLINE(R)

- # Searches
1 randomized controlled trial.pt.
2 controlled clinical trial.pt.
3 DOUBLE BLIND METHOD/
4 SINGLE BLIND METHOD/
5 RANDOM ALLOCATION/
6 RANDOMIZED CONTROLLED TRIALS AS TOPIC/
7 or/1-6
8 ((single or double or triple or treble) adj5 (blind\$ or mask\$)).tw,sh.
9 clinical trial.pt.
10 exp CLINICAL TRIAL/
11 exp CLINICAL TRIALS AS TOPIC/
12 (clinic\$ adj5 trial\$).tw,sh.
13 PLACEBOS/
14 placebo\$.tw,sh.
15 random\$.tw,sh.
16 or/8-15
17 or/7,16
18 META ANALYSIS/
19 META ANALYSIS AS TOPIC/
20 meta analysis.pt.
21 (metaanaly\$ or meta-analy\$ or (meta adj analy\$)).tw,sh.
22 (systematic\$ adj5 (review\$ or overview\$)).tw,sh.
23 (methodologic\$ adj5 (review\$ or overview\$)).tw,sh.
24 or/18-23
25 review\$.pt.
26 (medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or
psyclit or "web of science" or "science citation" or scisearch).tw.
27 ((hand or manual\$) adj2 search\$).tw.
28 (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online
database\$).tw,sh.
29 (pooling or pooled or mantel haenszel).tw,sh.
30 (peto or dersimonian or der simonian or fixed effect).tw,sh.
31 or/26-30
32 and/25,31
33 or/24,32
34 letter.pt.
35 case report.tw.
36 comment.pt.

- 37 editorial.pt.
- 38 historical article.pt.
- 39 or/34-38
- 40 17 not 39
- 41 33 not 39
- 42 or/40-41
- 43 ADOLESCENT/ or MINORS/
44 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
45 exp CHILD/
46 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or
kindergar\$ or boy? or girl?).ti,ab,jw.
- 47 exp INFANT/
48 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
49 exp PEDIATRICS/ or exp PUBERTY/
50 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
51 or/43-50
- 52 exp DIABETES MELLITUS, TYPE 1/
53 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or
child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
54 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
55 or/52-54
56 and/51,55
- 57 BEHAVIOR THERAPY/
58 COGNITIVE THERAPY/
59 PSYCHOTHERAPY/
60 PSYCHOTHERAPY, GROUP/
61 FAMILY THERAPY/
62 (psychotherap\$ or BFST or CBT).ti,ab.
63 ((cogniti\$ or psycho\$) adj5 (intervention\$ or treatment\$ or therap\$)).ti,ab.
64 ((behavio?r\$ or motivation\$) adj5 (intervention\$ or treatment\$ or therap\$ or chang\$ or
modif\$)).ti,ab.
65 ((family\$ or families or parent?) adj5 (intervention\$ or treatment\$ or therap\$ or team? or
teamwork\$ or team-work\$)).ti,ab.
- 66 COUNSELING/
67 MOTIVATIONAL INTERVIEWING/
68 MENTORS/
69 SOCIAL SUPPORT/
70 SELF-HELP GROUPS/
71 (motivation\$ or counsel?ing or mentor\$).ti,ab.
72 ((peer or social\$ or self help or self-help) adj3 (group? or support?)).ti,ab.
73 or/57-72
74 and/42,56,73
75 limit 74 to english language
- 76 LETTER/
77 EDITORIAL/
78 NEWS/
79 exp HISTORICAL ARTICLE/
80 ANECDOTES AS TOPIC/
81 COMMENT/
82 CASE REPORT/
83 (letter or comment* or abstracts).ti.
84 or/76-83
85 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.

- 86 84 not 85
- 87 ANIMALS/ not HUMANS/
- 88 exp ANIMALS, LABORATORY/
- 89 exp ANIMAL EXPERIMENTATION/
- 90 exp MODELS, ANIMAL/
- 91 exp RODENTIA/
- 92 (rat or rats or mouse or mice).ti.
- 93 or/86-92
- 94 75 not 93

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 7 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 8 or/6-7
- 9 and/5,8
- 10 (psychotherap\$ or BFST or CBT).ti,ab.
- 11 ((cogniti\$ or psycho\$) adj5 (intervention\$ or treatment\$ or therap\$)).ti,ab.
- 12 ((behavio?\$ or motivation\$) adj5 (intervention\$ or treatment\$ or therap\$ or chang\$ or modif\$)).ti,ab.
- 13 ((family\$ or families or parent?) adj5 (intervention\$ or treatment\$ or therap\$ or team? or teamwork\$ or team-work\$)).ti,ab.
- 14 (motivation\$ or counsel?ing or mentor\$).ti,ab.
- 15 ((peer or social\$ or self help or self-help) adj3 (group? or support?)).ti,ab.
- 16 or/10-15
- 17 and/9,16
- 18 limit 17 to english language

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 1/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 13 or/10-12
- 14 and/9,13

- 15 BEHAVIOR THERAPY/
- 16 COGNITIVE THERAPY/
- 17 PSYCHOTHERAPY/
- 18 PSYCHOTHERAPY, GROUP/
- 19 FAMILY THERAPY/
- 20 (psychotherap\$ or BFST or CBT).ti,ab.
- 21 ((cogniti\$ or psycho\$) adj5 (intervention\$ or treatment\$ or therap\$)).ti,ab.
- 22 ((behavio?r\$ or motivation\$) adj5 (intervention\$ or treatment\$ or therap\$ or chang\$ or modif\$)).ti,ab.
- 23 ((family\$ or families or parent?) adj5 (intervention\$ or treatment\$ or therap\$ or team? or teamwork\$ or team-work\$)).ti,ab.
- 24 COUNSELING/
- 25 MOTIVATIONAL INTERVIEWING/
- 26 MENTORS/
- 27 SOCIAL SUPPORT/
- 28 SELF-HELP GROUPS/
- 29 (motivation\$ or counsel?ing or mentor\$).ti,ab.
- 30 ((peer or social\$ or self help or self-help) adj3 (group? or support?)).ti,ab.
- 31 or/15-30
- 32 and/14,31

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
- 1 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).kw,ti,ab,jw,rw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).kw,ti,ab,jw,rw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).kw,ti,ab,jw,rw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).kw,ti,ab,jw,rw.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or Tl or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).kw,ti,ab.
- 7 (IDDM or T1D or TID or DM1 or DMI).kw,ti,ab.
- 8 or/6-7
- 9 and/5,8
- 10 BEHAVIOR THERAPY.kw.
- 11 COGNITIVE THERAPY.kw.
- 12 PSYCHOTHERAPY.kw.
- 13 PSYCHOTHERAPY, GROUP.kw.
- 14 FAMILY THERAPY.kw.
- 15 (psychotherap\$ or BFST or CBT).tw,tx.
- 16 ((cogniti\$ or psycho\$) adj5 (intervention\$ or treatment\$ or therap\$)).tw,tx.
- 17 ((behavio?r\$ or motivation\$) adj5 (intervention\$ or treatment\$ or therap\$ or chang\$ or modif\$)).tw,tx.
- 18 ((family\$ or families or parent?) adj5 (intervention\$ or treatment\$ or therap\$ or team? or teamwork\$ or team-work\$)).tw,tx.
- 19 COUNSELING.kw.
- 20 MOTIVATIONAL INTERVIEWING.kw.
- 21 MENTORS.kw.
- 22 SOCIAL SUPPORT.kw.
- 23 SELF-HELP GROUPS.kw.
- 24 (motivation\$ or counsel?ing or mentor\$).tw,tx.
- 25 ((peer or social\$ or self help or self-help) adj3 (group? or support?)).tw,tx.

- 26 or/10-25
27 and/9,26

Health Technology Assessment

- # Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx,rw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jx,rw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/
11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw.
12 (IDDM or T1D or T1D or DM1 or DMI).tw.
13 or/10-12
14 and/9,13
15 BEHAVIOR THERAPY/
16 COGNITIVE THERAPY/
17 PSYCHOTHERAPY/
18 PSYCHOTHERAPY, GROUP/
19 FAMILY THERAPY/
20 (psychotherap\$ or BFST or CBT).tw.
21 ((cogniti\$ or psycho\$) adj5 (intervention\$ or treatment\$ or therap\$)).tw.
22 ((behavio?r\$ or motivation\$) adj5 (intervention\$ or treatment\$ or therap\$ or chang\$ or modif\$)).tw.
23 ((family\$ or families or parent?) adj5 (intervention\$ or treatment\$ or therap\$ or team? or teamwork\$ or team-work\$)).tw.
24 COUNSELING/
25 MOTIVATIONAL INTERVIEWING/
26 MENTORS/
27 SOCIAL SUPPORT/
28 SELF-HELP GROUPS/
29 (motivation\$ or counsel?ing or mentor\$).tw.
30 ((peer or social\$ or self help or self-help) adj3 (group? or support?)).tw.
31 or/15-30
32 and/14,31
33 limit 32 to english language

Embase 1974 to 2014 Week 13

- # Searches
1 CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
2 (clinic\$ adj5 trial\$).ti,ab,sh.
3 SINGLE BLIND PROCEDURE/
4 DOUBLE BLIND PROCEDURE/
5 RANDOM ALLOCATION/
6 CROSSOVER PROCEDURE/
7 PLACEBO/
8 placebo\$.ti,ab,sh.

9 random\$.ti,ab,sh.
10 RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
11 ((single or double or triple or treble) adj (blind\$ or mask\$)).ti,ab,sh.
12 randomi?ed control\$ trial\$.tw.
13 or/1-12
14 META ANALYSIS/
15 ((meta adj analy\$) or metaanalys\$ or meta-analy\$).ti,ab,sh.
16 (systematic\$ adj5 (review\$ or overview\$)).ti,sh,ab.
17 (methodologic\$ adj5 (review\$ or overview\$)).ti,ab,sh.
18 or/14-17
19 review.pt.
20 (medline or medlars or embase).ab.
21 (scisearch or science citation index).ab.
22 (psyclit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
23 ((hand or manual\$) adj2 search\$).tw.
24 (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online
database\$).tw.
25 (pooling or pooled or mantel haenszel).tw.
26 (peto or dersimonian or "der simonian" or fixed effect).tw.
27 or/20-26
28 and/19,27
29 or/18,28
30 (book or conference paper or editorial or letter or note or proceeding or short survey).pt.
31 13 not 30
32 29 not 30
33 or/31-32
34 exp ADOLESCENT/
35 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
36 exp CHILD/
37 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or
kindergar\$ or boy? or girl?).ti,ab,jx.
38 exp INFANT/
39 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
40 exp PEDIATRICS/ or exp PUBERTY/
41 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescens\$ or prepubescens\$).ti,ab,jx,ec.
42 or/34-41
43 INSULIN DEPENDENT DIABETES MELLITUS/
44 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or
child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
45 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
46 or/43-45
47 JUVENILE DIABETES MELLITUS/
48 and/42,46
49 or/47-48
50 BEHAVIOR THERAPY/
51 BEHAVIOR MODIFICATION/
52 COGNITIVE THERAPY/
53 PSYCHOTHERAPY/
54 FAMILY THERAPY/
55 GROUP THERAPY/
56 MOTIVATIONAL INTERVIEWING/
57 (psychotherap\$ or BFST or CBT).ti,ab.
58 ((cogniti\$ or psycho\$) adj5 (intervention\$ or treatment\$ or therap\$)).ti,ab.

- 59 ((behavio?r\$ or motivation\$) adj5 (intervention\$ or treatment\$ or therap\$ or chang\$ or modif\$)).ti,ab.
60 ((family\$ or families or parent\$) adj5 (intervention\$ or treatment\$ or therap\$ or team? or teamwork\$ or team-work\$)).ti,ab.
61 COUNSELING/
62 FAMILY COUNSELING/
63 PARENT COUNSELING/
64 PATIENT COUNSELING/
65 PEER COUNSELING/
66 TEACHER/
67 SOCIAL SUPPORT/
68 SUPPORT GROUP/
69 SELF HELP/
70 (motivation\$ or counsel?ing or mentor\$).ti,ab.
71 ((peer or social\$ or self help or self-help) adj3 (group? or support?)).ti,ab.
72 or/50-71
73 and/33,49,72
74 limit 73 to english language
75 conference abstract.pt.
76 letter.pt. or LETTER/
77 note.pt.
78 editorial.pt.
79 CASE REPORT/ or CASE STUDY/
80 (letter or comment* or abstracts).ti.
81 or/75-80
82 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
83 81 not 82
84 ANIMAL/ not HUMAN/
85 NONHUMAN/
86 exp ANIMAL EXPERIMENT/
87 exp EXPERIMENTAL ANIMAL/
88 ANIMAL MODEL/
89 exp RODENT/
90 (rat or rats or mouse or mice).ti.
91 or/83-90
92 74 not 91

PsycINFO 1967 to March Week 4 2014

- # Searches
1 LITERATURE REVIEW/
2 EXPERIMENTAL DESIGN/
3 RANDOM SAMPLING/
4 META-ANALYSIS/
5 exp TREATMENT/
6 (random\$ or search\$ or control\$ or risk\$).tw.
7 (meta-analys#s or metaanalys#s).ti.
8 (systematic\$ adj (review\$ or overview\$)).ti.
9 ((single or double or triple) adj (blind\$ or mask\$)).ti.
10 rct.tw.
11 or/1-10
12 adolescen\$.ag.
13 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,id,jw.
14 (child\$ or school\$ or preschool\$).ag.

- 15 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,id,jw.
 16 (infan\$ or neonat\$).ag.
 17 (infan\$ or neonat\$ or newborn\$ or baby or babies or p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,id,jw.
 18 or/12-17
 19 DIABETES MELLITUS/
 20 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab,id.
 21 (IDDM or T1D or T1D or DM1 or DMI).ti,ab,id.
 22 or/19-21
 23 and/18,22
 24 BEHAVIOR THERAPY/
 25 COGNITIVE THERAPY/
 26 COGNITIVE BEHAVIOR THERAPY/
 27 PSYCHOTHERAPY/
 28 ADOLESCENT PSYCHOTHERAPY/
 29 CHILD PSYCHOTHERAPY/
 30 GROUP PSYCHOTHERAPY/
 31 FAMILY THERAPY/
 32 FAMILY INTERVENTION/
 33 MOTIVATIONAL INTERVIEWING/
 34 (psychotherap\$ or BFST or CBT).ti,ab.
 35 ((cogniti\$ or psycho\$) adj5 (intervention\$ or treatment\$ or therap\$)).ti,ab.
 36 ((behavio?r\$ or motivation\$) adj5 (intervention\$ or treatment\$ or therap\$ or chang\$ or modif\$)).ti,ab.
 37 ((family\$ or families or parent\$) adj5 (intervention\$ or treatment\$ or therap\$ or team? or teamwork\$ or team-work\$)).ti,ab.
 38 COUNSELING/
 39 GROUP COUNSELING/
 40 PEER COUNSELING/
 41 MENTOR/
 42 SOCIAL SUPPORT/
 43 SUPPORT GROUPS/
 44 SELF HELP TECHNIQUES/
 45 (motivation\$ or counsel?ing or mentor\$).ti,ab.
 46 ((peer or social\$ or self help or self-help) adj3 (group? or support?)).ti,ab.
 47 or/24-46
 48 and/23,47
 49 and/11,48
 50 limit 49 to english language

CINAHL with Full Text

- | # | Query | Limiters/Expanders |
|-----|--|---|
| S33 | S6 AND S31 | Limiters - English Language; Exclude MEDLINE records
Search modes - Boolean/Phrase |
| S32 | S6 AND S31 | Search modes - Boolean/Phrase |
| S31 | S16 AND S30 | Search modes - Boolean/Phrase |
| S30 | S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 | Search modes - Boolean/Phrase |
| S29 | T1 ((peer or social* or "self help" or self-help) N3 (group# or support#)) OR AB ((peer or social* or "self help" or self-help) N3 (group# or support#)) | Search modes - Boolean/Phrase |
| S28 | T1 (motivation* or counsel#ing or mentor*) OR AB (motivation* or counsel#ing or mentor*) | Search modes - Boolean/Phrase |

- S27 (MH "Support Groups") Search modes - Boolean/Phrase
- S26 (MH "Mentorship") Search modes - Boolean/Phrase
- S25 (MH "Counseling") OR (MH "Peer Counseling") Search modes - Boolean/Phrase
- S24 TI ((family* or families or parent#) N5 (intervention* or treatment* or therap* or team# or teamwork* or team-work*)) OR AB ((family* or families or parent#) N5 (intervention* or treatment* or therap* or team# or teamwork* or team-work*)) Search modes - Boolean/Phrase
- S23 TI ((behavi* or motivation*) N5 (intervention* or treatment* or therap* or chang* or modif*)) OR AB ((behavi* or motivation*) N5 (intervention* or treatment* or therap* or chang* or modif*)) Search modes - Boolean/Phrase
- S22 TI ((cogniti* or psycho*) N5 (intervention* or treatment* or therap*)) OR AB ((cogniti* or psycho*) N5 (intervention* or treatment* or therap*)) Search modes - Boolean/Phrase
- S21 TI (psychotherap* or BFST or CBT) OR AB (psychotherap* or BFST or CBT) Search modes - Boolean/Phrase
- S20 (MH "Motivational Interviewing") Search modes - Boolean/Phrase
- S19 (MH "Psychotherapy, Group") OR (MH "Family Therapy") Search modes - Boolean/Phrase
- S18 (MH "Psychotherapy") Search modes - Boolean/Phrase
- S17 (MH "Behavior Therapy+") OR (MH "Cognitive Therapy") Search modes - Boolean/Phrase
- S16 S12 AND S15 Search modes - Boolean/Phrase
- S15 S13 OR S14 Search modes - Boolean/Phrase
- S14 TI (diabet* N5 ("type one" or "type 1" or "type I" or "insulin depend*" or juvenile or child* or earl* or labile or brittle or "sudden onset" or "auto immun*" or autoimmun* or "auto-immun*)) OR AB (diabet* N5 ("type one" or "type 1" or "type I" or "insulin depend*" or juvenile or child* or earl* or labile or brittle or "sudden onset" or "auto immun*" or autoimmun* or "auto-immun*)) Search modes - Boolean/Phrase
- S13 (MH "Diabetes Mellitus, Type 1+") Search modes - Boolean/Phrase
- S12 S7 OR S8 OR S9 OR S10 OR S11 Search modes - Boolean/Phrase
- S11 TI (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) OR AB (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) or SO (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) Search modes - Boolean/Phrase
- S10 TI (infan* or neonat* or newborn* or baby or babies) OR AB (infan* or neonat* or newborn* or baby or babies) OR SO (infan* or neonat* or newborn* or baby or babies) Search modes - Boolean/Phrase
- S9 TI (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR AB (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR SO (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) Search modes - Boolean/Phrase
- S8 TI (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR AB (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR SO (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) Search modes - Boolean/Phrase
- S7 (MH "Infant, Newborn+") OR (MH "Infant+") OR (MH "Child, Preschool") OR (MH "Child+") OR (MH "Adolescence+") Search modes - Boolean/Phrase
- S6 S1 OR S2 OR S3 OR S4 OR S5 Search modes - Boolean/Phrase
- S5 PT systematic review Search modes - Boolean/Phrase
- S4 PT review Search modes - Boolean/Phrase
- S3 TX meta-analysis OR "meta analysis" Search modes - Boolean/Phrase
- S2 TX random* Search modes - Boolean/Phrase
- S1 (MH "Treatment Outcomes+") OR (MH "Experimental Studies+") Search modes - Boolean/Phrase

F.4 Type 1 diabetes – multiple daily injections

Review question: What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

Ovid MEDLINE(R)

Searches
1 ADOLESCENT/ or MINORS/
2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/
11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
13 or/10-12
14 and/9,13
15 exp INSULIN/ad, tu [Administration & Dosage, Therapeutic Use]
16 exp INSULINS/ad, tu [Administration & Dosage, Therapeutic Use]
17 (insulin\$ or Hagedorn).kw.
18 or/15-17
19 exp DRUG ADMINISTRATION SCHEDULE/
20 DOSE-RESPONSE RELATIONSHIP, DRUG/
21 exp INJECTIONS, SUBCUTANEOUS/
22 ((insulin\$ or inject\$) adj (regim\$ or schedul\$)).ti,ab.
23 ((intensiv\$ or conventional or flexib\$ or basal\$ or bolus\$) adj3 (treatment? or therap\$ or regime\$ or manag\$ or control\$ or program\$ or schedul\$)).ti,ab.
24 ((multiple or prandial\$ or preprandial\$ or postprandial\$ or meal\$ or premeal\$ or postmeal\$ or basal\$ or bolus\$) adj3 (inject\$ or insulin\$ or dose? or dosage?)).ti,ab.
25 ((mix\$ or premix\$ or freemix\$ or self titrat\$ or biphasic\$) adj5 insulin\$).ti,ab.
26 (MDI or FMDI).ti,ab.
27 or/19-26
28 and/14,18,27
29 limit 28 to english language
30 LETTER/
31 EDITORIAL/
32 NEWS/
33 exp HISTORICAL ARTICLE/
34 ANECDOTES AS TOPIC/
35 COMMENT/
36 CASE REPORT/
37 (letter or comment* or abstracts).ti.
38 or/30-37
39 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
40 38 not 39
41 ANIMALS/ not HUMANS/

- 42 exp ANIMALS, LABORATORY/
- 43 exp ANIMAL EXPERIMENTATION/
- 44 exp MODELS, ANIMAL/
- 45 exp RODENTIA/
- 46 (rat or rats or mouse or mice).ti.
- 47 or/40-46
- 48 29 not 47

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 7 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 8 or/6-7
- 9 ((insulin\$ or inject\$) adj (regim\$ or schedul\$)).ti,ab.
- 10 ((intensiv\$ or conventional or flexib\$ or basal\$ or bolus\$) adj3 (treatment? or therap\$ or regime\$ or manag\$ or control\$ or program\$ or schedul\$)).ti,ab.
- 11 ((multiple or prandial\$ or preprandial\$ or postprandial\$ or meal\$ or premeal\$ or postmeal\$ or basal\$ or bolus\$) adj3 (inject\$ or insulin\$ or dose? or dosage?)).ti,ab.
- 12 ((mix\$ or premix\$ or freemix\$ or self titrat\$ or biphasic\$) adj5 insulin\$).ti,ab.
- 13 (MDI or FMDI).ti,ab.
- 14 or/9-13
- 15 and/5,8,14

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 1/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 13 or/10-12
- 14 and/9,13
- 15 exp INSULIN/ad, tu [Administration & Dosage, Therapeutic Use]
- 16 exp INSULINS/ad, tu [Administration & Dosage, Therapeutic Use]
- 17 (insulin\$ or Hagedorn).kw.
- 18 or/15-17
- 19 exp DRUG ADMINISTRATION SCHEDULE/

- 20 DOSE-RESPONSE RELATIONSHIP, DRUG/
- 21 exp INJECTIONS, SUBCUTANEOUS/
- 22 ((insulin\$ or inject\$) adj (regim\$ or schedul\$)).ti,ab.
- 23 ((intensiv\$ or conventional or flexib\$ or basal\$ or bolus\$) adj3 (treatment? or therap\$ or regime\$ or manag\$ or control\$ or program\$ or schedul\$)).ti,ab.
- 24 ((multiple or prandial\$ or preprandial\$ or postprandial\$ or meal\$ or premeal\$ or postmeal\$ or basal\$ or bolus\$) adj3 (inject\$ or insulin\$ or dose? or dosage?)).ti,ab.
- 25 ((mix\$ or premix\$ or freemix\$ or self titrat\$ or biphasic\$) adj5 insulin\$).ti,ab.
- 26 (MDI or FMDI).ti,ab.
- 27 or/19-26
- 28 and/14,18,27

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
- 1 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).kw,ti,ab,jw,rw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).kw,ti,ab,jw,rw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).kw,ti,ab,jw,rw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).kw,ti,ab,jw,rw.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).kw,ti,ab.
- 7 (IDDM or T1D or TID or DM1 or DMI).kw,ti,ab.
- 8 or/6-7
- 9 and/5,8
- 10 INSULIN.kw.
- 11 INSULINS.kw.
- 12 (insulin\$ or Hagedorn).tw,tx.
- 13 or/10-12
- 14 DRUG ADMINISTRATION SCHEDULE.kw.
- 15 DOSE-RESPONSE RELATIONSHIP, DRUG.kw.
- 16 INJECTIONS, SUBCUTANEOUS.kw.
- 17 ((insulin\$ or inject\$) adj (regim\$ or schedul\$)).tw,tx.
- 18 ((intensiv\$ or conventional or flexib\$ or basal\$ or bolus\$) adj3 (treatment? or therap\$ or regime\$ or manag\$ or control\$ or program\$ or schedul\$)).tw,tx.
- 19 ((multiple or prandial\$ or preprandial\$ or postprandial\$ or meal\$ or premeal\$ or postmeal\$ or basal\$ or bolus\$) adj3 (inject\$ or insulin\$ or dose? or dosage?)).tw,tx.
- 20 ((mix\$ or premix\$ or freemix\$ or self titrat\$ or biphasic\$) adj5 insulin\$).tw,tx.
- 21 (MDI or FMDI).tw,tx.
- 22 or/14-21
- 23 and/9,13,22

Health Technology Assessment

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw.

- 9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/
11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or Tl or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw.
12 (IDDM or T1D or TID or DM1 or DMI).tw.
13 or/10-12
14 and/9,13
15 exp INSULIN/ad, tu [Administration & Dosage, Therapeutic Use]
16 exp INSULINS/ad, tu [Administration & Dosage, Therapeutic Use]
17 (insulin\$ or Hagedorn).tw.
18 or/15-17
19 exp DRUG ADMINISTRATION SCHEDULE/
20 DOSE-RESPONSE RELATIONSHIP, DRUG/
21 exp INJECTIONS, SUBCUTANEOUS/
22 ((insulin\$ or inject\$) adj (regim\$ or schedul\$)).tw.
23 ((intensiv\$ or conventional or flexib\$ or basal\$ or bolus\$) adj3 (treatment? or therap\$ or regime\$ or manag\$ or control\$ or program\$ or schedul\$)).tw.
24 ((multiple or prandial\$ or preprandial\$ or postprandial\$ or meal\$ or premeal\$ or postmeal\$ or basal\$ or bolus\$) adj3 (inject\$ or insulin\$ or dose? or dosage?)).tw.
25 ((mix\$ or premix\$ or freemix\$ or self titrat\$ or biphasic\$) adj5 insulin\$).tw.
26 (MDI or FMDI).tw.
27 or/19-26
28 and/14,18,27

Embase

- # Searches
1 exp ADOLESCENT/
2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescens\$ or prepubescens\$).ti,ab,jx,ec.
9 or/1-8
10 INSULIN DEPENDENT DIABETES MELLITUS/
11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or Tl or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
13 or/10-12
14 JUVENILE DIABETES MELLITUS/
15 and/9,13
16 or/14-15
17 exp INSULIN DERIVATIVE/co, do, dt [Drug Combination, Drug Dose, Drug Therapy]
18 (insulin\$ or Hagedorn).kw.
19 or/17-18
20 INSULIN TREATMENT/
21 NEUTRAL INSULIN INJECTION/
22 DRUG ADMINISTRATION/
23 DOSE CALCULATION/
24 DRUG DOSE REGIMEN/
25 DOSAGE SCHEDULE COMPARISON/

- 26 exp INJECTION/
- 27 SUBCUTANEOUS DRUG ADMINISTRATION/
- 28 ((insulin\$ or inject\$) adj (regim\$ or schedul\$)).ti,ab.
- 29 ((intensiv\$ or conventional or flexib\$ or basal\$ or bolus\$) adj3 (treatment? or therap\$ or regime\$ or manag\$ or control\$ or program\$ or schedul\$)).ti,ab.
- 30 ((multiple or prandial\$ or preprandial\$ or postprandial\$ or meal\$ or premeal\$ or postmeal\$ or basal\$ or bolus\$) adj3 (inject\$ or insulin\$ or dose? or dosage?)).ti,ab.
- 31 ((mix\$ or premix\$ or freemix\$ or self titrat\$ or biphasic\$) adj5 insulin\$).ti,ab.
- 32 (MDI or FMDI).ti,ab.
- 33 or/20-32
- 34 and/16,19,33
- 35 limit 34 to english language
- 36 conference abstract.pt.
- 37 letter.pt. or LETTER/
- 38 note.pt.
- 39 editorial.pt.
- 40 CASE REPORT/ or CASE STUDY/
- 41 (letter or comment* or abstracts).ti.
- 42 or/36-41
- 43 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 44 42 not 43
- 45 ANIMAL/ not HUMAN/
- 46 NONHUMAN/
- 47 exp ANIMAL EXPERIMENT/
- 48 exp EXPERIMENTAL ANIMAL/
- 49 ANIMAL MODEL/
- 50 exp RODENT/
- 51 (rat or rats or mouse or mice).ti.
- 52 or/44-51
- 53 35 not 52

F.5 Type 1 diabetes – HbA1c targets

Review question: What is the optimal haemoglobin A1c (HbA1c) target for children and young people with type 1 diabetes?

Ovid MEDLINE(R)

- # Searches
- 1 randomized controlled trial.pt.
- 2 controlled clinical trial.pt.
- 3 DOUBLE BLIND METHOD/
- 4 SINGLE BLIND METHOD/
- 5 RANDOM ALLOCATION/
- 6 or/1-5
- 7 ((single or double or triple or treble) adj5 (blind\$ or mask\$)).tw,sh.
- 8 clinical trial.pt.
- 9 exp CLINICAL TRIAL/
- 10 exp CLINICAL TRIALS AS TOPIC/
- 11 (clinic\$ adj5 trial\$).tw,sh.
- 12 PLACEBOS/
- 13 placebo\$.tw,sh.

14 random\$.tw,sh.
15 or/7-14
16 or/6-15
17 META ANALYSIS/
18 META ANALYSIS AS TOPIC/
19 meta analysis.pt.
20 (metaanaly\$ or meta-analy\$ or (meta adj analy\$)).tw,sh.
21 (systematic\$ adj5 (review\$ or overview\$)).tw,sh.
22 (methodologic\$ adj5 (review\$ or overview\$)).tw,sh.
23 or/17-22
24 review\$.pt.
25 (medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or
psyclit or "web of science" or "science citation" or scisearch).tw.
26 ((hand or manual\$) adj2 search\$).tw.
27 (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online
database\$).tw,sh.
28 (pooling or pooled or mantel haenszel).tw,sh.
29 (peto or dersimonian or der simonian or fixed effect).tw,sh.
30 or/25-29
31 and/24,30
32 exp CASE-CONTROL STUDIES/
33 (case\$ adj2 control\$).tw.
34 exp COHORT STUDIES/
35 cohort\$.tw.
36 or/32-35
37 letter.pt.
38 or/16,23,31,36
39 comparative study.pt.
40 or/38-39
41 ADOLESCENT/ or MINORS/
42 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
43 exp CHILD/
44 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or
kindergar\$ or boy? or girl?).ti,ab,jw.
45 exp INFANT/
46 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
47 exp PEDIATRICS/ or exp PUBERTY/
48 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescens\$ or prepubescens\$).ti,ab,jw.
49 or/41-48
50 exp DIABETES MELLITUS, TYPE 1/
51 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or
child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
52 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
53 or/50-52
54 HEMOGLOBIN A, GLYCOSYLATED/
55 (h?emoglobin? adj3 glycosylat\$).ti,ab.
56 (glycated adj3 h?emoglobin?).ti,ab.
57 (glycoh?emoglobin? or HbA1c or HbA1c or Hb A1c or Hb A1c).ti,ab.
58 "hemoglobin A1c protein, human".nm.
59 or/54-58
60 REFERENCE STANDARDS/ or REFERENCE VALUES/
61 ((reference? or normal\$ or standard?) adj3 (value? or target\$ or rang\$ or level\$ or
threshold?)).ti,ab.

- 62 ((F#G or BG) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold\$)).ti,ab.
63 ((normogly?emi\$ or euglyc?emi\$ or glyc?emi\$) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold?)).ti,ab.
64 or/60-63
65 and/49,53,59,64
66 and/40,65
67 LETTER/
68 EDITORIAL/
69 NEWS/
70 exp HISTORICAL ARTICLE/
71 ANECDOTES AS TOPIC/
72 COMMENT/
73 CASE REPORT/
74 (letter or comment* or abstracts).ti.
75 or/67-74
76 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
77 75 not 76
78 ANIMALS/ not HUMANS/
79 exp ANIMALS, LABORATORY/
80 exp ANIMAL EXPERIMENTATION/
81 exp MODELS, ANIMAL/
82 exp RODENTIA/
83 (rat or rats or mouse or mice).ti.
84 or/77-83
85 66 not 84
86 limit 85 to english language

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
5 or/1-4
6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or Tl or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
7 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
8 or/6-7
9 (h?emoglobin? adj3 glycosylat\$).ti,ab.
10 (glycated adj3 h?emoglobin?).ti,ab.
11 (glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).ti,ab.
12 or/9-11
13 ((reference? or normal\$ or standard?) adj3 (value? or target\$ or rang\$ or level\$ or threshold?)).ti,ab.
14 ((F#G or BG) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold\$)).ti,ab.
15 ((normogly?emi\$ or euglyc?emi\$ or glyc?emi\$) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold?)).ti,ab.
16 or/13-15
17 and/5,8,12,16

Cochrane Central Register of Controlled Trials

- # Searches

- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 1/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 13 or/10-12
- 14 HEMOGLOBIN A, GLYCOSYLATED/
- 15 (h?emoglobin? adj3 glycosylat\$).ti,ab.
- 16 (glycated adj3 h?emoglobin?).ti,ab.
- 17 (glycoh?emoglobin? or HbA1c or HbA1c or Hb A1c or Hb A1c).ti,ab.
- 18 or/14-17
- 19 REFERENCE STANDARDS/ or REFERENCE VALUES/
- 20 ((reference? or normal\$ or standard?) adj3 (value? or target\$ or rang\$ or level\$ or threshold?)).ti,ab.
- 21 ((F#G or BG) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold\$)).ti,ab.
- 22 ((normogly?emi\$ or euglyc?emi\$ or glyco?emi\$) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold?)).ti,ab.
- 23 or/19-22
- 24 and/9,13,18,23
- 25 limit 24 to yr="2013 -Current"

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
- 1 (ADOLESCENT or MINORS).kw.
 - 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,tx,jw,rw.
 - 3 CHILD.kw.
 - 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,tx,jw,rw.
 - 5 INFANT.kw.
 - 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx,jw,rw.
 - 7 (PEDIATRICS or PUBERTY).kw.
 - 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,tx,jw,rw.
 - 9 or/1-8
 - 10 DIABETES MELLITUS, TYPE 1.kw.
 - 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw,tx.
 - 12 (IDDM or T1D or T1D or DM1 or DMI).tw,tx.
 - 13 or/10-12
 - 14 HEMOGLOBIN A, GLYCOSYLATED.kw.
 - 15 (h?emoglobin? adj3 glycosylat\$).tw,tx.
 - 16 (glycated adj3 h?emoglobin?).tw,tx.
 - 17 (glycoh?emoglobin? or HbA1c or HbA1c or Hb A1c or Hb A1c).tw,tx.
 - 18 or/14-17

- 19 (REFERENCE STANDARDS or REFERENCE VALUES).kw.
- 20 ((reference? or normal\$ or standard?) adj3 (value? or target\$ or rang\$ or level\$ or threshold?)).tw,tx.
- 21 ((F#G or BG) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold\$)).tw,tx.
- 22 ((normogly?emi\$ or euglyc?emi\$ or glyc?emi\$) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold?)).tw,tx.
- 23 or/19-22
- 24 and/9,13,18,23

Health Technology Assessment

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx,rw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jx,rw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 1/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or Tl or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw.
- 12 (IDDM or T1D or TID or DM1 or DMI).tw.
- 13 or/10-12
- 14 HEMOGLOBIN A, GLYCOSYLATED/
- 15 (h?emoglobin? adj3 glycosylat\$).tw.
- 16 (glycated adj3 h?emoglobin?).tw.
- 17 (glycoh?emoglobin? or HbA1c or HbA1c or Hb A1c or Hb A1c).tw.
- 18 or/14-17
- 19 REFERENCE STANDARDS/ or REFERENCE VALUES/
- 20 ((reference? or normal\$ or standard?) adj3 (value? or target\$ or rang\$ or level\$ or threshold?)).tw.
- 21 ((F#G or BG) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold\$)).tw.
- 22 ((normogly?emi\$ or euglyc?emi\$ or glyc?emi\$) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold?)).tw.
- 23 or/19-22
- 24 and/9,13,18,23

Embase

- # Searches
- 1 CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
- 2 (clinic\$ adj5 trial\$).tw,sh.
- 3 SINGLE BLIND PROCEDURE/
- 4 DOUBLE BLIND PROCEDURE/
- 5 RANDOM ALLOCATION/
- 6 CROSSOVER PROCEDURE/
- 7 PLACEBO/
- 8 placebo\$.tw,sh.
- 9 random\$.tw,sh.
- 10 RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
- 11 ((single or double or triple or treble) adj (blind\$ or mask\$)).tw,sh.

12 randomi?ed control\$ trial\$.tw.
13 or/1-12
14 META ANALYSIS/
15 ((meta adj analy\$) or metaanalys\$ or meta-analy\$).tw,sh.
16 (systematic\$ adj5 (review\$ or overview\$)).tw,sh.
17 (methodologic\$ adj5 (review\$ or overview\$)).tw,sh.
18 or/14-17
19 review.pt.
20 (medline or medlars or embase).ab.
21 (scisearch or science citation index).ab.
22 (psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
23 ((hand or manual\$) adj2 search\$).tw.
24 (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online database\$).tw.
25 (pooling or pooled or mantel haenszel).tw.
26 (peto or dersimonian or "der simonian" or fixed effect).tw.
27 or/20-26
28 and/19,27
29 exp CASE CONTROL STUDY/
30 RETROSPECTIVE STUDY/
31 (case\$ adj2 control\$).tw.
32 COHORT ANALYSIS/
33 LONGITUDINAL STUDY/
34 FOLLOW UP/
35 PROSPECTIVE STUDY/
36 cohort\$.tw.
37 or/29-36
38 or/13,18,28,37
39 (book or conference paper or editorial or letter or note or proceeding or short survey).pt.
40 38 not 39
41 COMPARATIVE STUDY/
42 (compar\$ adj3 stud\$).tw.
43 or/41-42
44 or/40,43
45 exp ADOLESCENT/
46 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
47 exp CHILD/
48 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
49 exp INFANT/
50 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
51 exp PEDIATRICS/ or exp PUBERTY/
52 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescens\$ or prepubescens\$).ti,ab,jx,ec.
53 or/45-52
54 INSULIN DEPENDENT DIABETES MELLITUS/
55 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
56 (IDDM or T1D or T1DM or DM1 or DMI).ti,ab.
57 JUVENILE DIABETES MELLITUS/
58 or/54-57
59 HEMOGLOBIN A1c/
60 (glycoh?emoglobin? or HbA1c or HbA1c or Hb A1c or Hb A1c).ti,ab.
61 (h?emoglobin? adj3 glycosylat\$).ti,ab.

62 (glycated adj3 h?emoglobin?).ti,ab.
63 or/59-62
64 STANDARD/
65 REFERENCE VALUE/
66 ((reference? or normal\$ or standard?) adj3 (value? or target\$ or rang\$ or level\$ or threshold?)).ti,ab.
67 or/64-66
68 ((F#G or BG) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold\$)).ti,ab.
69 ((normogly?emi\$ or euglyc?emi\$ or glyco?emi\$) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold?)).ti,ab.
70 or/67-69
71 and/53,58,63,70
72 and/44,71
73 conference abstract.pt.
74 letter.pt. or LETTER/
75 note.pt.
76 editorial.pt.
77 CASE REPORT/ or CASE STUDY/
78 (letter or comment* or abstracts).ti.
79 or/73-78
80 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
81 79 not 80
82 ANIMAL/ not HUMAN/
83 NONHUMAN/
84 exp ANIMAL EXPERIMENT/
85 exp EXPERIMENTAL ANIMAL/
86 ANIMAL MODEL/
87 exp RODENT/
88 (rat or rats or mouse or mice).ti.
89 or/81-88
90 72 not 89
91 limit 90 to english language

F.6 Type 1 diabetes blood glucose targets

Review question: What are the optimal blood glucose targets for children and young people with type 1 diabetes?

Ovid MEDLINE(R)

Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/
11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.

12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
13 or/10-12
14 BLOOD GLUCOSE/
15 BLOOD GLUCOSE SELF-MONITORING/
16 ((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
17 (F#G or P#G or R#G or BG or HMBG or SMBG or BGM).ti,ab.
18 (normoglyc?emi\$ or euglyc?emi\$).ti,ab.
19 (glyc?emi\$ adj3 (norm\$ or near?norm\$)).ti,ab.
20 or/14-19
21 REFERENCE STANDARDS/ or REFERENCE VALUES/
22 GOALS/
23 ((reference? or normal\$ or standard?) adj3 (value\$ or rang\$ or level\$ or threshold?)).ti,ab.
24 target\$.ti.
25 target\$.ab. /freq=2
26 ((tight\$ or intens\$ or aggressive\$ or strict\$ or rigid\$ or liberal\$ or conventional\$ or regular or
usual or routin\$ or standard?) adj3 (control\$ or target\$ or goal\$ or rang\$ or therap\$ or
regime\$ or treatment? or interven\$ or manag\$ or monitor\$)).ti,ab.
27 or/21-26
28 and/20,27
29 (("American Diabetic Association" or ADA or "Australasian P?ediatric Endocrine Group" or
APEG or "International Society for P?ediatric and Adolescent Diabetes" or ISPAD) adj3
(value\$ or target\$ or goal\$ or rang\$ or level\$ or threshold?)).ti,ab.
30 (glyc?emi\$ adj3 control\$ adj3 (target\$ or goal\$)).ti,ab.
31 or/28-30
32 TIME FACTORS/
33 ((time or timing or prandial or preprandial or postprandial) adj3 (monitor\$ or test\$ or measur\$
or value\$ or target\$ or goal\$ or rang\$ or level\$ or threshold?)).ti,ab.
34 or/32-33
35 and/20,34
36 or/31,35
37 and/9,13,36
38 limit 37 to english language
39 LETTER/
40 EDITORIAL/
41 NEWS/
42 exp HISTORICAL ARTICLE/
43 ANECDOTES AS TOPIC/
44 COMMENT/
45 CASE REPORT/
46 (letter or comment* or abstracts).ti.
47 or/39-46
48 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
49 47 not 48
50 ANIMALS/ not HUMANS/
51 exp ANIMALS, LABORATORY/
52 exp ANIMAL EXPERIMENTATION/
53 exp MODELS, ANIMAL/
54 exp RODENTIA/
55 (rat or rats or mouse or mice).ti.
56 or/49-55
57 38 not 56

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab.
 - 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab.
 - 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
 - 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab.
 - 5 or/1-4
 - 6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
 - 7 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
 - 8 or/6-7
 - 9 ((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
 - 10 (F#G or P#G or R#G or BG or HMBG or SMBG or BGM).ti,ab.
 - 11 (normoglyc?emi\$ or euglyc?emi\$).ti,ab.
 - 12 (glyc?emi\$ adj3 (norm\$ or near?norm\$)).ti,ab.
 - 13 or/9-12
 - 14 ((reference? or normal\$ or standard?) adj3 (value\$ or rang\$ or level\$ or threshold?)).ti,ab.
 - 15 target\$.ti.
 - 16 target\$.ab. /freq=2
 - 17 ((tight\$ or intens\$ or aggressive\$ or strict\$ or rigid\$ or liberal\$ or conventional\$ or regular or usual or routin\$ or standard?) adj3 (control\$ or target\$ or goal\$ or rang\$ or therap\$ or regime\$ or treatment? or interven\$ or manag\$ or monitor\$)).ti,ab.
 - 18 or/14-17
 - 19 and/13,18
 - 20 (("American Diabetic Association" or ADA or "Australasian P?ediatric Endocrine Group" or APEG or "International Society for P?ediatric and Adolescent Diabetes" or ISPAD) adj3 (value\$ or target\$ or goal\$ or rang\$ or level\$ or threshold?)).ti,ab.
 - 21 (glyc?emi\$ adj3 control\$ adj3 (target\$ or goal\$)).ti,ab.
 - 22 or/19-21
 - 23 ((time or timing or prandial or preprandial or postprandial) adj3 (monitor\$ or test\$ or measur\$ or value\$ or target\$ or goal\$ or rang\$ or level\$ or threshold?)).ti,ab.
 - 24 and/13,23
 - 25 or/22,24
 - 26 and/5,8,25

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
 - 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab.
 - 3 exp CHILD/
 - 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab.
 - 5 exp INFANT/
 - 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
 - 7 exp PEDIATRICS/ or exp PUBERTY/
 - 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab.
 - 9 or/1-8
 - 10 exp DIABETES MELLITUS, TYPE 1/
 - 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
 - 12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
 - 13 or/10-12
 - 14 BLOOD GLUCOSE/

- 15 BLOOD GLUCOSE SELF-MONITORING/
16 ((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
17 (F#G or P#G or R#G or BG or HMBG or SMBG or BGM).ti,ab.
18 (normoglyc?emi\$ or euglyc?emi\$).ti,ab.
19 (glyc?emi\$ adj3 (norm\$ or near?norm\$)).ti,ab.
20 or/14-19
21 REFERENCE STANDARDS/ or REFERENCE VALUES/
22 GOALS/
23 ((reference? or normal\$ or standard?) adj3 (value\$ or rang\$ or level\$ or threshold?)).ti,ab.
24 target\$.ti.
25 target\$.ab. /freq=2
26 ((tight\$ or intens\$ or aggressive\$ or strict\$ or rigid\$ or liberal\$ or conventional\$ or regular or
usual or routin\$ or standard?) adj3 (control\$ or target\$ or goal\$ or rang\$ or therap\$ or
regime\$ or treatment? or interven\$ or manag\$ or monitor\$)).ti,ab.
27 or/21-26
28 and/20,27
29 (("American Diabetic Association" or ADA or "Australasian P?ediatric Endocrine Group" or
APEG or "International Society for P?ediatric and Adolescent Diabetes" or ISPAD) adj3
(value\$ or target\$ or goal\$ or rang\$ or level\$ or threshold?)).ti,ab.
30 (glyc?emi\$ adj3 control\$ adj3 (target\$ or goal\$)).ti,ab.
31 or/28-30
32 TIME FACTORS/
33 ((time or timing or prandial or preprandial or postprandial) adj3 (monitor\$ or test\$ or measur\$
or value\$ or target\$ or goal\$ or rang\$ or level\$ or threshold?)).ti,ab.
34 or/32-33
35 and/20,34
36 or/31,35
37 and/9,13,36

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,tx,kw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or
kindergar\$ or boy? or girl?).tw,tx,kw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx,kw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,tx,kw.
5 or/1-4
6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or
child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw,tx,kw.
7 (IDDM or T1D or TID or DM1 or DMI).tw,tx.
8 or/6-7
9 ((blood or plasma) adj3 (glucose or sugar?)).tw,tx,kw.
10 (F#G or P#G or R#G or BG or HMBG or SMBG or BGM).tw,tx.
11 (normoglyc?emi\$ or euglyc?emi\$).tw,tx.
12 (glyc?emi\$ adj3 (norm\$ or near?norm\$)).tw,tx.
13 or/9-12
14 (REFERENCE STANDARDS or REFERENCE VALUES).kw.
15 GOALS.kw.
16 ((reference? or normal\$ or standard?) adj3 (value\$ or rang\$ or level\$ or threshold?)).tw,tx.
17 target\$.tw,tx,kw.
18 ((tight\$ or intens\$ or aggressive\$ or strict\$ or rigid\$ or liberal\$ or conventional\$ or regular or
usual or routin\$ or standard?) adj3 (control\$ or target\$ or goal\$ or rang\$ or therap\$ or
regime\$ or treatment? or interven\$ or manag\$ or monitor\$)).tw,tx.

- 19 or/14-18
- 20 and/13,19
- 21 (("American Diabetic Association" or ADA or "Australasian P?ediatric Endocrine Group" or APEG or "International Society for P?ediatric and Adolescent Diabetes" or ISPAD) adj3 (value\$ or target\$ or goal\$ or rang\$ or level\$ or threshold?)).tw,tx.
- 22 (glyc?emi\$ adj3 control\$ adj3 (target\$ or goal\$)).tw,tx.
- 23 or/20-22
- 24 TIME.kw.
- 25 ((time or timing or prandial or preprandial or postprandial) adj3 (monitor\$ or test\$ or measur\$ or value\$ or target\$ or goal\$ or rang\$ or level\$ or threshold?)).tw,tx.
- 26 or/24-25
- 27 and/13,26
- 28 or/23,27
- 29 and/5,8,28

Health Technology Assessment

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 1/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw.
- 12 (IDDM or T1D or TID or DM1 or DMI).tw.
- 13 or/10-12
- 14 BLOOD GLUCOSE/
- 15 BLOOD GLUCOSE SELF-MONITORING/
- 16 ((blood or plasma) adj3 (glucose or sugar?)).tw.
- 17 (F#G or P#G or R#G or BG or HMBG or SMBG or BGM).tw.
- 18 (normoglyc?emi\$ or euglyc?emi\$).tw.
- 19 (glyc?emi\$ adj3 (norm\$ or near?norm\$)).tw.
- 20 or/14-19
- 21 REFERENCE STANDARDS/ or REFERENCE VALUES/
- 22 GOALS/
- 23 ((reference? or normal\$ or standard?) adj3 (value\$ or rang\$ or level\$ or threshold?)).tw.
- 24 target\$.tw.
- 25 ((tight\$ or intens\$ or aggressive\$ or strict\$ or rigid\$ or liberal\$ or conventional\$ or regular or usual or routin\$ or standard?) adj3 (control\$ or target\$ or goal\$ or rang\$ or therap\$ or regime\$ or treatment? or interven\$ or manag\$ or monitor\$)).tw.
- 26 or/21-25
- 27 and/20,26
- 28 (("American Diabetic Association" or ADA or "Australasian P?ediatric Endocrine Group" or APEG or "International Society for P?ediatric and Adolescent Diabetes" or ISPAD) adj3 (value\$ or target\$ or goal\$ or rang\$ or level\$ or threshold?)).tw.
- 29 (glyc?emi\$ adj3 control\$ adj3 (target\$ or goal\$)).tw.
- 30 or/27-29
- 31 TIME FACTORS/

- 32 ((time or timing or prandial or preprandial or postprandial) adj3 (monitor\$ or test\$ or measur\$ or value\$ or target\$ or goal\$ or rang\$ or level\$ or threshold?)).tw.
33 or/31-32
34 and/20,33
35 or/30,34
36 and/9,13,35

Embase

- # Searches
1 exp ADOLESCENT/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
5 exp NEWBORN/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
9 or/1-8
10 INSULIN DEPENDENT DIABETES MELLITUS/
11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or Tl or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
13 or/10-12
14 JUVENILE DIABETES MELLITUS/
15 and/9,13
16 or/14-15
17 GLUCOSE BLOOD LEVEL/
18 BLOOD GLUCOSE MONITORING/
19 GLYCEMIC CONTROL/
20 ((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
21 (F#G or P#G or R#G or BG or HMBG or SMBG or BGM).ti,ab.
22 (normoglyc?emi\$ or euglyc?emi\$).ti,ab.
23 (glyc?emi\$ adj3 (norm\$ or near?norm\$)).ti,ab.
24 or/17-23
25 STANDARD/
26 REFERENCE VALUE/ or NORMAL VALUE/
27 MOTIVATION/
28 ((reference? or normal\$ or standard?) adj3 (value\$ or rang\$ or level\$ or threshold?)).ti,ab.
29 target\$.ti.
30 target\$.ab. /freq=2
31 ((tight\$ or intens\$ or aggressive\$ or strict\$ or rigid\$ or liberal\$ or conventional\$ or regular or usual or routin\$ or standard?) adj3 (control\$ or target\$ or goal\$ or rang\$ or therap\$ or regime\$ or treatment? or interven\$ or manag\$ or monitor\$)).ti,ab.
32 or/25-31
33 and/24,32
34 (("American Diabetic Association" or ADA or "Australasian P?ediatric Endocrine Group" or APEG or "International Society for P?ediatric and Adolescent Diabetes" or ISPAD) adj3 (value\$ or target\$ or goal\$ or rang\$ or level\$ or threshold?)).ti,ab.
35 (glyc?emi\$ adj3 control\$ adj3 (target\$ or goal\$)).ti,ab.
36 or/33-35
37 TIME/
38 ((time or timing or prandial or preprandial or postprandial) adj3 (monitor\$ or test\$ or measur\$ or value\$ or target\$ or goal\$ or rang\$ or level\$ or threshold?)).ti,ab.

39 or/37-38
40 and/24,39
41 or/36,40
42 and/16,41
43 limit 42 to english language
44 conference abstract.pt.
45 letter.pt. or LETTER/
46 note.pt.
47 editorial.pt.
48 CASE REPORT/ or CASE STUDY/
49 (letter or comment* or abstracts).ti.
50 or/44-49
51 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
52 50 not 51
53 ANIMAL/ not HUMAN/
54 NONHUMAN/
55 exp ANIMAL EXPERIMENT/
56 exp EXPERIMENTAL ANIMAL/
57 ANIMAL MODEL/
58 exp RODENT/
59 (rat or rats or mouse or mice).ti.
60 or/52-59
61 43 not 60

F.7 Type 1 diabetes – blood glucose monitoring

Review questions:

How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?

What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?

What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?

MEDLINE(R)

Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/

- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 13 or/10-12
- 14 and/9,13
- 15 BLOOD GLUCOSE SELF-MONITORING/
- 16 ((glucose or blood sugar\$ or insulin\$) adj3 (meter\$ or monitor\$ or sensor\$ or capillary)).ti,ab.
- 17 (HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucometer\$ or (glucose adj meter\$)).ti,ab.
- 18 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
- 19 or/15-18
- 20 and/14,19
- 21 limit 20 to english language
- 22 LETTER/
- 23 EDITORIAL/
- 24 NEWS/
- 25 exp HISTORICAL ARTICLE/
- 26 ANECDOTES AS TOPIC/
- 27 COMMENT/
- 28 CASE REPORT/
- 29 (letter or comment* or abstracts).ti.
- 30 or/22-29
- 31 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 32 30 not 31
- 33 ANIMALS/ not HUMANS/
- 34 exp ANIMALS, LABORATORY/
- 35 exp ANIMAL EXPERIMENTATION/
- 36 exp MODELS, ANIMAL/
- 37 exp RODENTIA/
- 38 (rat or rats or mouse or mice).ti.
- 39 or/32-38
- 40 21 not 39

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 7 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 8 or/6-7
- 9 and/5,8
- 10 ((glucose or blood sugar\$ or insulin\$) adj3 (meter\$ or monitor\$ or sensor\$ or capillary)).ti,ab.
- 11 (HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucometer\$ or (glucose adj meter\$)).ti,ab.
- 12 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
- 13 or/10-12
- 14 and/9,13
- 15 limit 14 to english language

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
 - 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
 - 3 exp CHILD/
 - 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
 - 5 exp INFANT/
 - 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
 - 7 exp PEDIATRICS/ or exp PUBERTY/
 - 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
 - 9 or/1-8
 - 10 exp DIABETES MELLITUS, TYPE 1/
 - 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
 - 12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
 - 13 or/10-12
 - 14 and/9,13
 - 15 BLOOD GLUCOSE SELF-MONITORING/
 - 16 ((glucose or blood sugar\$ or insulin\$) adj3 (meter\$ or monitor\$ or sensor\$ or capillary)).ti,ab.
 - 17 (HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucometer\$ or (glucose adj meter\$)).ti,ab.
 - 18 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
 - 19 or/15-18
 - 20 and/14,19

Database of Abstracts of Reviews of Effects

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).kw,ti,ab,jw,rw.
 - 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).kw,ti,ab,jw,rw.
 - 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).kw,ti,ab,jw,rw.
 - 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).kw,ti,ab,jw,rw.
 - 5 or/1-4
 - 6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).kw,ti,ab.
 - 7 (IDDM or T1D or T1D or DM1 or DMI).kw,ti,ab.
 - 8 or/6-7
 - 9 and/5,8
 - 10 ((glucose or blood sugar\$ or insulin) adj3 (meter\$ or monitor\$ or sensor\$ or capillary)).tw,tx,kw.
 - 11 (HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucometer\$ or (glucose adj meter\$)).tw,tx.
 - 12 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").tw,tx.
 - 13 or/10-12
 - 14 and/9,13

Health Technology Assessment

- # Searches
- 1 ADOLESCENT/ or MINORS/
 - 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx,rw.

- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jx,rw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 1/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw.
- 12 (IDDM or T1D or T1D or DM1 or DMI).tw.
- 13 or/10-12
- 14 and/9,13
- 15 BLOOD GLUCOSE SELF-MONITORING/
- 16 ((glucose or blood sugar\$ or insulin) adj3 (meter\$ or monitor\$ or sensor\$ or capillary)).tw.
- 17 (HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucometer\$ or (glucose adj meter\$)).tw.
- 18 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").tw.
- 19 or/15-18
- 20 and/14,19

Embase

- # Searches
- 1 exp ADOLESCENT/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
- 9 or/1-8
- 10 INSULIN DEPENDENT DIABETES MELLITUS/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 13 or/10-12
- 14 JUVENILE DIABETES MELLITUS/
- 15 and/9,13
- 16 or/14-15
- 17 BLOOD GLUCOSE MONITORING/
- 18 ((glucose or blood sugar\$ or insulin\$) adj3 (meter\$ or monitor\$ or sensor\$ or capillary)).ti,ab.
- 19 (HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucometer\$ or (glucose adj meter\$)).ti,ab.
- 20 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
- 21 or/17-20
- 22 and/16,21
- 23 limit 22 to english language
- 24 conference abstract.pt.
- 25 letter.pt. or LETTER/
- 26 note.pt.

27 editorial.pt.
28 CASE REPORT/ or CASE STUDY/
29 (letter or comment* or abstracts).ti.
30 or/24-29
31 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
32 30 not 31
33 ANIMAL/ not HUMAN/
34 NONHUMAN/
35 exp ANIMAL EXPERIMENT/
36 exp EXPERIMENTAL ANIMAL/
37 ANIMAL MODEL/
38 exp RODENT/
39 (rat or rats or mouse or mice).ti.
40 or/32-39
41 23 not 40

F.8 Type 1 diabetes – blood ketone monitoring

Review question: What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis?

Ovid MEDLINE(R)

Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/
11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
13 exp KETOSIS/
14 (ketosis or ketoacid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
15 (DK or DKA).ti,ab.
16 or/10-15
17 exp KETONES/
18 HYDROXYBUTYRATES/
19 (ketone? or acetone? or acetoacetate? or OHB or 3HB or betaOHB or BOHB or 3OHB or hydroxy but\$ or hydroxybut\$ or betahydroxybut\$ or 3hydroxybut\$).ti,ab.
20 or/17-19
21 and/9,16,20
22 limit 21 to english language
23 LETTER/
24 EDITORIAL/
25 NEWS/

- 26 exp HISTORICAL ARTICLE/
- 27 ANECDOTES AS TOPIC/
- 28 COMMENT/
- 29 CASE REPORT/
- 30 (letter or comment* or abstracts).ti.
- 31 or/23-30
- 32 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 33 31 not 32
- 34 ANIMALS/ not HUMANS/
- 35 exp ANIMALS, LABORATORY/
- 36 exp ANIMAL EXPERIMENTATION/
- 37 exp MODELS, ANIMAL/
- 38 exp RODENTIA/
- 39 (rat or rats or mouse or mice).ti.
- 40 or/33-39
- 41 22 not 40

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 7 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 8 (ketosis or ketoacid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
- 9 (DK or DKA).ti,ab.
- 10 or/6-9
- 11 (ketone? or acetone? or acetoacetate? or OHB or 3HB or betaOHB or BOHB or 3OHB or hydroxy but\$ or hydroxybut\$ or betahydroxybut\$ or 3hydroxybut\$).ti,ab.
- 12 and/5,10-11

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 1/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 13 exp KETOSIS/

- 14 (ketosis or ketoacid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
- 15 (DK or DKA).ti,ab.
- 16 or/10-15
- 17 exp KETONES/
- 18 HYDROXYBUTYRATES/
- 19 (ketone? or acetone? or acetoacetate? or OHB or 3HB or betaOHB or BOHB or 3OHB or hydroxy but\$ or hydroxybut\$ or betahydroxybut\$ or 3hydroxybut\$).ti,ab.
- 20 or/17-19
- 21 and/9,16,20

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- | | |
|----|--|
| # | Searches |
| 1 | (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,tx,kw. |
| 2 | (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,tx,kw. |
| 3 | (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx,kw. |
| 4 | (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,tx,kw. |
| 5 | or/1-4 |
| 6 | (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw,tx,kw. |
| 7 | (IDDM or T1D or T1D or DM1 or DMI).tw,tx. |
| 8 | (ketosis or ketoacid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).tw,tx,kw. |
| 9 | (DK or DKA).tw,tx. |
| 10 | or/6-9 |
| 11 | (ketone? or acetone? or acetoacetate? or OHB or 3HB or betaOHB or BOHB or 3OHB or hydroxy but\$ or hydroxybut\$ or betahydroxybut\$ or 3hydroxybut\$).tw,tx,kw. |
| 12 | and/5,10-11 |

Embase

- | | |
|----|---|
| # | Searches |
| 1 | exp ADOLESCENT/ |
| 2 | (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx. |
| 3 | exp CHILD/ |
| 4 | (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx. |
| 5 | exp INFANT/ |
| 6 | (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx. |
| 7 | exp PEDIATRICS/ or exp PUBERTY/ |
| 8 | (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec. |
| 9 | or/1-8 |
| 10 | INSULIN DEPENDENT DIABETES MELLITUS/ |
| 11 | (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab. |
| 12 | (IDDM or T1D or T1D or DM1 or DMI).ti,ab. |
| 13 | KETOACIDOSIS/ or DIABETIC KETOACIDOSIS/ |
| 14 | KETONURIA/ |
| 15 | (ketosis or ketoacid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab. |
| 16 | (DK or DKA).ti,ab. |
| 17 | or/10-16 |
| 18 | and/9,17 |

19 JUVENILE DIABETES MELLITUS/
20 or/18-19
21 exp KETONE/
22 3 HYDROXYBUTYRIC ACID/ or HYDROXYBUTYRIC ACID/
23 (ketone? or acetone? or acetoacetate? or OHB or 3HB or betaOHB or BOHB or 3OHB or
hydroxy but\$ or hydroxybut\$ or betahydroxybut\$ or 3hydroxybut\$).ti,ab.
24 or/21-23
25 and/20,24
26 limit 25 to english language
27 conference abstract.pt.
28 letter.pt. or LETTER/
29 note.pt.
30 editorial.pt.
31 CASE REPORT/ or CASE STUDY/
32 (letter or comment* or abstracts).ti.
33 or/27-32
34 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
35 33 not 34
36 ANIMAL/ not HUMAN/
37 NONHUMAN/
38 exp ANIMAL EXPERIMENT/
39 exp EXPERIMENTAL ANIMAL/
40 ANIMAL MODEL/
41 exp RODENT/
42 (rat or rats or mouse or mice).ti.
43 or/35-42
44 26 not 43

F.9 Type 1 diabetes – dietary advice

Review questions:

What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?

What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?

Ovid MEDLINE(R)

Searches
1 ADOLESCENT/ or MINORS/
2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or
kindergar\$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/

- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 13 or/10-12
- 14 GLYCEMIC INDEX/
- 15 DIETARY CARBOHYDRATES/
- 16 (glyc?emic adj3 (index or indice? or load)).ti,ab.
- 17 ((carbohydrate? or CHO) adj3 (count\$ or quant\$ or exchang\$ or diet\$ or intake)).ti,ab.
- 18 (CHOx or GI).ti,ab.
- 19 or/14-18
- 20 and/9,13,19
- 21 limit 20 to english language
- 22 LETTER/
- 23 EDITORIAL/
- 24 NEWS/
- 25 exp HISTORICAL ARTICLE/
- 26 ANECDOTES AS TOPIC/
- 27 COMMENT/
- 28 CASE REPORT/
- 29 (letter or comment* or abstracts).ti.
- 30 or/22-29
- 31 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 32 30 not 31
- 33 ANIMALS/ not HUMANS/
- 34 exp ANIMALS, LABORATORY/
- 35 exp ANIMAL EXPERIMENTATION/
- 36 exp MODELS, ANIMAL/
- 37 exp RODENTIA/
- 38 (rat or rats or mouse or mice).ti.
- 39 or/32-38
- 40 21 not 39

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescenc\$ or prepubescen\$).ti,ab,jw.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 7 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 8 or/6-7
- 9 (glyc?emic adj3 (index or indice? or load)).ti,ab.
- 10 ((carbohydrate? or CHO) adj3 (count\$ or quant\$ or exchang\$ or diet\$ or intake)).ti,ab.
- 11 (CHOx or GI).ti,ab.
- 12 or/9-11
- 13 and/5,8,12
- 14 limit 13 to english language

Cochrane Central Register of Controlled Trials

- # Searches

- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 1/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 13 or/10-12
- 14 GLYCEMIC INDEX/
- 15 DIETARY CARBOHYDRATES/
- 16 (glyc?emic adj3 (index or indice? or load)).ti,ab.
- 17 ((carbohydrate? or CHO) adj3 (count\$ or quant\$ or exchang\$ or diet\$ or intake)).ti,ab.
- 18 (CHOx or GI).ti,ab.
- 19 or/14-18
- 20 and/9,13,19

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).kw,tw,tx,jw,rw.
 - 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).kw,tw,tx,jw,rw.
 - 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).kw,tw,tx,jw,rw.
 - 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).kw,tw,tx,jw,rw.
 - 5 or/1-4
 - 6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).kw,tw,tx.
 - 7 (IDDM or T1D or T1D or DM1 or DMI).kw,tw,tx.
 - 8 or/6-7
 - 9 (glyc?emic adj3 (index or indice? or load)).tw,tx,kw.
 - 10 ((carbohydrate? or CHO) adj3 (count\$ or quant\$ or exchang\$ or diet\$ or intake)).tw,tx,kw.
 - 11 (CHOx or GI).tw,tx.
 - 12 or/9-11
 - 13 and/5,8,12

Health Technology Assessment

- # Searches
- 1 ADOLESCENT/ or MINORS/
 - 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx,rw.
 - 3 exp CHILD/
 - 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
 - 5 exp INFANT/
 - 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw.
 - 7 exp PEDIATRICS/ or exp PUBERTY/
 - 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jx,rw.

- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 1/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or Tl or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw.
- 12 (IDDM or T1D or TID or DM1 or DMI).tw.
- 13 or/10-12
- 14 GLYCEMIC INDEX/
- 15 DIETARY CARBOHYDRATES/
- 16 (glyc?emic adj3 (index or indice? or load)).tw.
- 17 ((carbohydrate? or CHO) adj3 (count\$ or quant\$ or exchange\$ or diet\$ or intake)).tw.
- 18 (CHOx or GI).tw.
- 19 or/14-18
- 20 and/9,13,19

Embase

- # Searches
- 1 exp ADOLESCENT/
- 2 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
- 9 or/1-8
- 10 INSULIN DEPENDENT DIABETES MELLITUS/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or Tl or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
- 13 or/10-12
- 14 JUVENILE DIABETES MELLITUS/
- 15 and/9,13
- 16 or/14-15
- 17 GLYCEMIC INDEX/
- 18 CARBOHYDRATE DIET/
- 19 exp CARBOHYDRATE INTAKE/
- 20 (glyc?emic adj3 (index or indice? or load)).ti,ab.
- 21 ((carbohydrate? or CHO) adj3 (count\$ or quant\$ or exchange\$ or diet\$ or intake)).ti,ab.
- 22 (CHOx or GI).ti,ab.
- 23 or/17-22
- 24 and/16,23
- 25 limit 24 to english language
- 26 conference abstract.pt.
- 27 letter.pt. or LETTER/
- 28 note.pt.
- 29 editorial.pt.
- 30 CASE REPORT/ or CASE STUDY/
- 31 (letter or comment* or abstracts).ti.
- 32 or/26-31
- 33 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 34 32 not 33
- 35 ANIMAL/ not HUMAN/

- 36 NONHUMAN/
- 37 exp ANIMAL EXPERIMENT/
- 38 exp EXPERIMENTAL ANIMAL/
- 39 ANIMAL MODEL/
- 40 exp RODENT/
- 41 (rat or rats or mouse or mice).ti.
- 42 or/34-41
- 43 25 not 42

PsycINFO

- # Searches
- 1 adolescen\$.ag.
- 2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,id,jw.
- 3 (child\$ or school\$ or preschool\$).ag.
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,id,jw.
- 5 (infan\$ or neonat\$).ag.
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies or p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,id,jw.
- 7 or/1-6
- 8 DIABETES MELLITUS/
- 9 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab,id.
- 10 (IDDM or T1D or TID or DM1 or DMI).ti,ab,id.
- 11 or/8-10
- 12 DIETS/
- 13 exp CARBOHYDRATES/
- 14 (glyc?emic adj3 (index or indice? or load)).ti,ab,id.
- 15 ((carbohydrate? or CHO) adj3 (count\$ or quant\$ or exchang\$ or diet\$ or intake)).ti,ab,id.
- 16 (CHOx or GI).ti,ab,id.
- 17 or/12-16
- 18 and/7,11,17
- 19 limit 18 to english language
- 20 (book or dissertation abstract or encyclopedia).pt.
- 21 19 not 20

CINAHL with Full Text

- # Query Limiters/Expanders
- S21 S6 AND S9 AND S20 Limiters - English Language; Exclude MEDLINE records
- Search modes - Boolean/Phrase
- S20 S16 OR S19 Search modes - Boolean/Phrase
- S19 S17 AND S18 Search modes - Boolean/Phrase
- S18 TI (count* or quant* or exchang* or diet* or intake) or AB (count* or quant* or exchang* or diet* or intake) Search modes - Boolean/Phrase
- S17 TI (carbohydrate* or CHO) or AB (carbohydrate* or CHO) Search modes - Boolean/Phrase
- S16 S10 OR S11 OR S12 OR S13 OR S14 OR S15 Search modes - Boolean/Phrase
- S15 TI (glycaemic load*) or AB (glycaemic load*) Search modes - Boolean/Phrase
- S14 TI (glycemic load*) or AB (glycemic load*) Search modes - Boolean/Phrase
- S13 AB (glycemic index) or AB (glycaemic index) Search modes - Boolean/Phrase
- S12 TI (glycemic index) or TI (glycaemic index) Search modes - Boolean/Phrase
- S11 (MH "Dietary Carbohydrates+") Search modes - Boolean/Phrase
- S10 (MH "Glycemic Load") OR (MH "Glycemic Index") Search modes - Boolean/Phrase

- S9 S7 OR S8 Search modes - Boolean/Phrase
- S8 TI (diabet* N5 ("type one" or "type 1" or "type I" or "insulin depend*" or juvenile or child* or earl* or labile or brittle or "sudden onset" or "auto immun*" or autoimmun* or "auto-immun*")) OR AB (diabet* N5 ("type one" or "type 1" or "type I" or "insulin depend*" or juvenile or child* or earl* or labile or brittle or "sudden onset" or "auto immun*" or autoimmun* or "auto-immun*"))
Search modes - Boolean/Phrase
- S7 (MH "Diabetes Mellitus, Type 1+") Search modes - Boolean/Phrase
- S6 S1 OR S2 OR S3 OR S4 OR S5 Search modes - Boolean/Phrase
- S5 TI (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) OR AB (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) or SO (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*)
Search modes - Boolean/Phrase
- S4 TI (infan* or neonat* or newborn* or baby or babies) OR AB (infan* or neonat* or newborn* or baby or babies) OR SO (infan* or neonat* or newborn* or baby or babies) Search modes - Boolean/Phrase
- S3 TI (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR AB (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR SO (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#)
Search modes - Boolean/Phrase
- S2 TI (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR AB (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR SO (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) Search modes - Boolean/Phrase
- S1 (MH "Infant, Newborn+") OR (MH "Infant+") OR (MH "Child, Preschool") OR (MH "Child+") OR (MH "Adolescence+") Search modes - Boolean/Phrase

F.10 Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

Review question: What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?

Ovid MEDLINE(R)

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$ or high school\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or pre school\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pre pubert\$ or pubescen\$ or prepubescen\$ or pre pubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 DIABETIC KETOACIDOSIS/
- 11 (DK or DKA).ti,ab.
- 12 or/10-11
- 13 exp KETOSIS/
- 14 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
- 15 or/13-14

16 exp DIABETES MELLITUS/
17 diabet\$.mp.
18 or/16-17
19 and/15,18
20 9 and (12 or 19)
21 POLYDIPSIA/
22 DRINKING BEHAVIOR/
23 THIRST/
24 (polyd#psi\$ or dehydrat\$ or ((excess\$ or frequen\$) adj3 (thirst\$ or fluid intake or
drink\$))).ti,ab.
25 or/21-24
26 POLYURIA/
27 (polyuri\$ or ((excess\$ or frequen\$) adj3 (urin\$ or urine))).ti,ab.
28 or/26-27
29 WEIGHT LOSS/
30 (weight adj3 (loss or lost or reduc\$)).ti,ab.
31 or/29-30
32 DEHYDRATION/
33 (dehydrat\$ or rehydrat\$ or re hydrat\$ or hydration status).ti,ab.
34 or/32-33
35 NAUSEA/ or VOMITING/
36 (nausea or emesis or vomit\$).ti,ab.
37 or/35-36
38 ABDOMINAL PAIN/ or ABDOMEN, ACUTE/
39 ((abdom#n\$ adj3 pain\$) or acute abdomen).ti,ab.
40 or/38-39
41 DYSPNEA/
42 TACHYPNEA/
43 HYPERVENTILATION/
44 (respirat\$ adj (distress or rate)).ti,ab.
45 (breath\$ adj3 (difficult\$ or pattern\$ or abnormal\$ or dysfunction\$ or labo?r\$ or deep\$ or
shallow\$ or rapid\$ or short\$ or effort\$)).ti,ab.
46 (gasping or kussmaul or dyspnea or tachypnea or breathless\$ or hyperventilat\$).ti,ab.
47 or/41-46
48 CONSCIOUSNESS DISORDERS/ or exp CONFUSION/
49 (conscious\$ or confus\$ or deliri\$ or mental state\$).ti,ab.
50 or/48-49
51 "SIGNS AND SYMPTOMS"/
52 (sign? or symptom? or indicat\$ or presentation).ti,ab.
53 ((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest\$ or
aspect?)).ti,ab.
54 or/51-53
55 or/25,28,31,34,37,40,47,50,54
56 exp HYPERGLYCEMIA/
57 hyperglyc?emi\$.ti,ab.
58 ((high or elevat\$ or excess\$ or abnormal\$ or above or extreme\$) adj3 (blood glucose or blood
sugar?)).ti,ab.
59 BLOOD GLUCOSE/an
60 (BGM or glucometer or glucometer\$ or (glucose adj meter\$)).ti,ab.
61 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
62 or/56-61
63 exp KETOSIS/

- 64 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuria or hyperketonuria or keton?emi\$ or hyperketon?emi\$ or ketogenesis).ti,ab.
- 65 KETONES/
66 3-HYDROXYBUTYRIC ACID/
67 HYDROXYBUTYRATES/
68 or/65-67
69 URINALYSIS/
70 BLOOD CHEMICAL ANALYSIS/
71 or/69-70
72 and/68,71
73 KETONES/an, bl, ur [Analysis, Blood, Urine]
74 3-HYDROXYBUTYRIC ACID/an, bl, ur [Analysis, Blood, Urine]
75 HYDROXYBUTYRATES/an, bl, ur [Analysis, Blood, Urine]
76 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
77 ((urine or urinary) adj3 (dipstick or dip test)).ti,ab.
78 or/63-64,72-77
79 ACIDOSIS/
80 (acidosis or (blood? adj3 acid\$) or acid?emi\$).ti,ab.
81 HYDROGEN-ION CONCENTRATION/
82 ACID-BASE EQUILIBRIUM/
83 ACID-BASE IMBALANCE/
84 BICARBONATES/
85 ELECTROLYTES/
86 or/81-85
87 BLOOD GAS ANALYSIS/
88 BLOOD CHEMICAL ANALYSIS/
89 or/87-88
90 and/86,89
91 HYDROGEN-ION CONCENTRATION/an, bl, ur [Analysis, Blood, Urine]
92 ACID-BASE EQUILIBRIUM/an, bl [Analysis, Blood]
93 ACID-BASE IMBALANCE/bl, ur [Blood, Urine]
94 BICARBONATES/an, bl, ur [Analysis, Blood, Urine]
95 ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]
96 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate\$ or electrolyte\$)).ti,ab.
97 (blood gas or ABG or blood test\$).ti,ab.
98 or/79-80,90-97
99 (biochemical adj3 (variable? or measur\$ or marker? or parameter? or abnormal\$)).ti,ab.
100 or/62,78,98-99
101 or/55,100
102 exp "SENSITIVITY AND SPECIFICITY"/
103 exp BLOOD CHEMICAL ANALYSIS/
104 URINALYSIS/
105 (detect\$ or diagnos\$ or predict\$ or sensitiv\$ or accuracy or test\$).mp.
106 or/102-105
107 and/20,101,106
108 limit 107 to english language
109 LETTER/
110 EDITORIAL/
111 NEWS/

- 112 exp HISTORICAL ARTICLE/
- 113 ANECDOTES AS TOPIC/
- 114 COMMENT/
- 115 CASE REPORT/
- 116 (letter or comment* or abstracts).ti.
- 117 or/109-116
- 118 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 119 117 not 118
- 120 ANIMALS/ not HUMANS/
- 121 exp ANIMALS, LABORATORY/
- 122 exp ANIMAL EXPERIMENTATION/
- 123 exp MODELS, ANIMAL/
- 124 exp RODENTIA/
- 125 (rat or rats or mouse or mice).ti.
- 126 or/119-125
- 127 108 not 126

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$ or high school\$).ti,ab,jw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or pre school\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pre pubert\$ or pubescen\$ or prepubescen\$ or pre pubescen\$).ti,ab,jw.
- 5 or/1-4
- 6 (diabetic ketoacidosis or DK or DKA).ti,ab.
- 7 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
- 8 diabet\$.mp.
- 9 and/7-8
- 10 5 and (6 or 9)
- 11 (polyd#psi\$ or dehydrat\$ or ((excess\$ or frequen\$) adj3 (thirst\$ or fluid intake or drink\$))).ti,ab.
- 12 (polyuri\$ or ((excess\$ or frequen\$) adj3 (urin\$ or urine))).ti,ab.
- 13 (weight adj3 (loss or lost or reduc\$)).ti,ab.
- 14 (dehydrat\$ or rehydrat\$ or re hydrat\$ or hydration status).ti,ab.
- 15 (nausea or emesis or vomit\$).ti,ab.
- 16 ((abdom#n\$ adj3 pain\$) or acute abdomen).ti,ab.
- 17 (respirat\$ adj (distress or rate)).ti,ab.
- 18 (breath\$ adj3 (difficult\$ or pattern\$ or abnormal\$ or dysfunction\$ or labo?r\$ or deep\$ or shallow\$ or rapid\$ or short\$ or effort\$)).ti,ab.
- 19 (gasping or kussmaul or dyspnea or tchypnea or breathless\$ or hyperventilat\$).ti,ab.
- 20 (conscious\$ or confus\$ or deliri\$ or mental state\$).ti,ab.
- 21 (sign? or symptom? or indicat\$ or presentation).ti,ab.
- 22 ((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest\$ or aspect?)).ti,ab.
- 23 or/11-22
- 24 hyperglyc?emi\$.ti,ab.
- 25 ((high or elevat\$ or excess\$ or abnormal\$ or above or extreme\$) adj3 (blood glucose or blood sugar?)).ti,ab.
- 26 (BGM or glucometer or glucometer\$ or (glucose adj meter\$)).ti,ab.
- 27 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.

- 28 or/24-27
 29 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuria or hyperketonuria or keton?emi\$ or hyperketon?emi\$ or ketogenesis).ti,ab.
 30 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
 31 ((urine or urinary) adj3 (dipstick or dip test)).ti,ab.
 32 or/29-31
 33 (acidosis or (blood? adj3 acid\$) or acid?emi\$).ti,ab.
 34 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate\$ or electrolyte\$)).ti,ab.
 35 (blood gas or ABG or blood test\$).ti,ab.
 36 or/33-35
 37 (biochemical adj3 (variable? or measur\$ or marker? or parameter? or abnormal\$)).ti,ab.
 38 or/23,28,32,36-37
 39 (detect\$ or diagnos\$ or predict\$ or sensitiv\$ or accuracy or test\$).mp.
 40 and/10,38-39

Cochrane Central Register of Controlled Trials

- # Searches
 1 ADOLESCENT/ or MINORS/
 2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$ or high school\$).ti,ab,jw.
 3 exp CHILD/
 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or pre school\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
 5 exp INFANT/
 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
 7 exp PEDIATRICS/ or exp PUBERTY/
 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pre pubert\$ or pubescen\$ or prepubescen\$ or pre pubescen\$).ti,ab,jw.
 9 or/1-8
 10 DIABETIC KETOACIDOSIS/
 11 (DK or DKA).ti,ab.
 12 or/10-11
 13 exp KETOSIS/
 14 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
 15 or/13-14
 16 exp DIABETES MELLITUS/
 17 diabet\$.mp.
 18 or/16-17
 19 and/15,18
 20 9 and (12 or 19)
 21 POLYDIPSIA/
 22 DRINKING BEHAVIOR/
 23 THIRST/
 24 (polyd#psi\$ or dehydrat\$ or ((excess\$ or frequen\$) adj3 (thirst\$ or fluid intake or drink\$))).ti,ab.
 25 or/21-24
 26 POLYURIA/
 27 (polyuri\$ or ((excess\$ or frequen\$) adj3 (urin\$ or urine))).ti,ab.
 28 or/26-27

- 29 WEIGHT LOSS/
30 (weight adj3 (loss or lost or reduc\$)).ti,ab.
31 or/29-30
32 DEHYDRATION/
33 (dehydrat\$ or rehydrat\$ or re hydrat\$ or hydration status).ti,ab.
34 or/32-33
35 NAUSEA/ or VOMITING/
36 (nausea or emesis or vomit\$).ti,ab.
37 or/35-36
38 ABDOMINAL PAIN/ or ABDOMEN, ACUTE/
39 ((abdom#n\$ adj3 pain\$) or acute abdomen).ti,ab.
40 or/38-39
41 DYSPNEA/
42 TACHYPNEA/
43 HYPERVENTILATION/
44 (respirat\$ adj (distress or rate)).ti,ab.
45 (breath\$ adj3 (difficult\$ or pattern\$ or abnormal\$ or dysfunction\$ or labo?r\$ or deep\$ or shallow\$ or rapid\$ or short\$ or effort\$)).ti,ab.
46 (gasping or kussmaul or dyspnea or tchypnea or breathless\$ or hyperventilat\$).ti,ab.
47 or/41-46
48 CONSCIOUSNESS DISORDERS/ or exp CONFUSION/
49 (conscious\$ or confus\$ or deliri\$ or mental state\$).ti,ab.
50 or/48-49
51 "SIGNS AND SYMPTOMS"/
52 (sign? or symptom? or indicat\$ or presentation).ti,ab.
53 ((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest\$ or aspect?)).ti,ab.
54 or/51-53
55 or/25,28,31,34,37,40,47,50,54
56 exp HYPERGLYCEMIA/
57 hyperglyc?emi\$.ti,ab.
58 ((high or elevat\$ or excess\$ or abnormal\$ or above or extreme\$) adj3 (blood glucose or blood sugar?)).ti,ab.
59 BLOOD GLUCOSE/an
60 (BGM or glucometer or glucosemeter\$ or (glucose adj meter\$)).ti,ab.
61 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
62 or/56-61
63 exp KETOSIS/
64 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuria or hyperketonuria or keton?emi\$ or hyperketon?emi\$ or ketogenesis).ti,ab.
65 KETONES/
66 3-HYDROXYBUTYRIC ACID/
67 HYDROXYBUTYRATES/
68 or/65-67
69 URINALYSIS/
70 BLOOD CHEMICAL ANALYSIS/
71 or/69-70
72 and/68,71
73 KETONES/an, bl, ur [Analysis, Blood, Urine]
74 3-HYDROXYBUTYRIC ACID/an, bl, ur [Analysis, Blood, Urine]
75 HYDROXYBUTYRATES/an, bl, ur [Analysis, Blood, Urine]
76 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-

- hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
- 77 ((urine or urinary) adj3 (dipstick or dip test)).ti,ab.
- 78 or/63-64,72-77
- 79 ACIDOSIS/
- 80 (acidosis or (blood? adj3 acid\$) or acid?emi\$).ti,ab.
- 81 HYDROGEN-ION CONCENTRATION/
- 82 ACID-BASE EQUILIBRIUM/
- 83 ACID-BASE IMBALANCE/
- 84 BICARBONATES/
- 85 ELECTROLYTES/
- 86 or/81-85
- 87 BLOOD GAS ANALYSIS/
- 88 BLOOD CHEMICAL ANALYSIS/
- 89 or/87-88
- 90 and/86,89
- 91 HYDROGEN-ION CONCENTRATION/an, bl, ur [Analysis, Blood, Urine]
- 92 ACID-BASE EQUILIBRIUM/an, bl [Analysis, Blood]
- 93 ACID-BASE IMBALANCE/bl, ur [Blood, Urine]
- 94 BICARBONATES/an, bl, ur [Analysis, Blood, Urine]
- 95 ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]
- 96 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate\$ or electrolyte\$)).ti,ab.
- 97 (blood gas or ABG or blood test\$).ti,ab.
- 98 or/79-80,90-97
- 99 (biochemical adj3 (variable? or measur\$ or marker? or parameter? or abnormal\$)).ti,ab.
- 100 or/62,78,98-99
- 101 55 or 100
- 102 20 and 101
- 103 exp "SENSITIVITY AND SPECIFICITY"/
- 104 exp BLOOD CHEMICAL ANALYSIS/
- 105 URINALYSIS/
- 106 (detect\$ or diagnos\$ or predict\$ or sensitiv\$ or accuracy or test\$).mp.
- 107 or/103-106
- 108 102 and 107

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
- 1 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$ or high school\$).kw,tw,tx,jw,rw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or pre school\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).kw,tw,tx,jw,rw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).kw,tw,tx,jw,rw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pre pubert\$ or pubescen\$ or prepubescen\$ or pre pubescen\$).kw,tw,tx,jw,rw.
- 5 or/1-4
- 6 (diabetic ketoacidosis or DK or DKA).kw,tw,tx.
- 7 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).kw,tw,tx.
- 8 diabet\$.kw,tw,tx.
- 9 and/7-8
- 10 5 and (6 or 9)

- 11 POLYDIPSIA.kw.
12 DRINKING BEHAVIOR.kw.
13 THIRST.kw.
14 (polyd#psi\$ or dehydrat\$ or ((excess\$ or frequen\$) adj3 (thirst\$ or fluid intake or drink\$))).tw,tx.
15 or/11-14
16 POLYURIA.kw.
17 (polyuri\$ or ((excess\$ or frequen\$) adj3 (urin\$ or urine))).tw,tx.
18 or/16-17
19 WEIGHT LOSS.kw.
20 (weight adj3 (loss or lost or reduc\$)).tw,tx.
21 or/19-20
22 DEHYDRATION.kw.
23 (dehydrat\$ or rehydrat\$ or re hydrat\$ or hydration status).tw,tx.
24 or/22-23
25 (NAUSEA or VOMITING).kw.
26 (nausea or emesis or vomit\$).tw,tx.
27 or/25-26
28 (ABDOMINAL PAIN or ABDOMEN, ACUTE).kw.
29 ((abdom#n\$ adj3 pain\$) or acute abdomen).tw,tx.
30 or/28-29
31 DYSPNEA.kw.
32 TACHYPNEA.kw.
33 HYPERVENTILATION.kw.
34 (respirat\$ adj (distress or rate)).tw,tx.
35 (breath\$ adj3 (difficult\$ or pattern\$ or abnormal\$ or dysfunction\$ or labo?r\$ or deep\$ or shallow\$ or rapid\$ or short\$ or effort\$)).tw,tx.
36 (gasping or kussmaul or dyspnea or tachypnea or breathless\$ or hyperventilat\$).tw,tx.
37 or/31-36
38 (CONSCIOUSNESS DISORDERS or CONFUSION or DELIRIUM).kw.
39 (conscious\$ or confus\$ or deliri\$ or mental state\$).tw,tx.
40 or/38-39
41 "SIGNS AND SYMPTOMS".kw.
42 (sign? or symptom? or indicat\$ or presentation).tw,tx.
43 ((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest\$ or aspect?)).tw,tx.
44 or/41-43
45 or/15,18,21,24,27,30,37,40,44
46 (HYPERGLYCEMIA or GLUCOSE INTOLERANCE).kw.
47 hyperglyc?emi\$.tw,tx.
48 ((high or elevat\$ or excess\$ or abnormal\$ or above or extreme\$) adj3 (blood glucose or blood sugar?)).tw,tx.
49 (BGM or glucometer or glucometer\$ or (glucose adj meter\$)).tw,tx.
50 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").tw,tx.
51 or/46-50
52 (KETOSIS or DIABETIC KETOACIDOSIS).kw.
53 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuria or hyperketonuria or keton?emi\$ or hyperketon?emi\$ or ketogenesis).tw,tx.
54 KETONES.kw.
55 3-HYDROXYBUTYRIC ACID.kw.
56 HYDROXYBUTYRATES.kw.
57 or/54-56
58 URINALYSIS.kw.

- 59 BLOOD CHEMICAL ANALYSIS.kw.
60 or/58-59
61 and/57,60
62 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw,tx.
63 ((urine or urinary) adj3 (dipstick or dip test)).tw,tx.
64 or/52-53,61-63
65 ACIDOSIS.kw.
66 (acidosis or (blood? adj3 acid\$) or acid?emi\$).tw,tx.
67 HYDROGEN-ION CONCENTRATION.kw.
68 ACID-BASE EQUILIBRIUM.kw.
69 ACID-BASE IMBALANCE.kw.
70 BICARBONATES.kw.
71 ELECTROLYTES.kw.
72 or/67-71
73 BLOOD GAS ANALYSIS.kw.
74 BLOOD CHEMICAL ANALYSIS.kw.
75 or/73-74
76 and/72,75
77 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate\$ or electrolyte\$)).tw,tx.
78 (blood gas or ABG or blood test\$).tw,tx.
79 or/65-66,76-78
80 (biochemical adj3 (variable? or measur\$ or marker? or parameter? or abnormal\$)).tw,tx.
81 or/51,64,79-80
82 or/45,81
83 "SENSITIVITY AND SPECIFICITY".kw.
84 "PREDICTIVE VALUE OF TESTS".kw.
85 BLOOD CHEMICAL ANALYSIS.kw.
86 BLOOD GAS ANALYSIS.kw.
87 URINALYSIS.kw.
88 (detect\$ or diagnos\$ or predict\$ or sensitiv\$ or accuracy or test\$).mp.
89 or/83-88
90 and/10,82,89

Health Technology Assessment

- # Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$ or high school\$).tw,jx,rw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or pre school\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw,jx,rw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pre pubert\$ or pubescen\$ or prepubescen\$ or pre pubescen\$).tw,jx,rw.
9 or/1-8
10 DIABETIC KETOACIDOSIS/
11 (DK or DKA).tw.
12 or/10-11

- 13 exp KETOSIS/
14 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).tw.
15 or/13-14
16 exp DIABETES MELLITUS/
17 diabet\$.mp.
18 or/16-17
19 and/15,18
20 9 and (12 or 19)
21 POLYDIPSIA/
22 DRINKING BEHAVIOR/
23 THIRST/
24 (polyd#psi\$ or dehydrat\$ or ((excess\$ or frequen\$) adj3 (thirst\$ or fluid intake or drink\$))).tw.
25 or/21-24
26 POLYURIA/
27 (polyuri\$ or ((excess\$ or frequen\$) adj3 (urin\$ or urine))).tw.
28 or/26-27
29 WEIGHT LOSS/
30 (weight adj3 (loss or lost or reduc\$)).tw.
31 or/29-30
32 DEHYDRATION/
33 (dehydrat\$ or rehydrat\$ or re hydrat\$ or hydration status).tw.
34 or/32-33
35 NAUSEA/ or VOMITING/
36 (nausea or emesis or vomit\$).tw.
37 or/35-36
38 ABDOMINAL PAIN/ or ABDOMEN, ACUTE/
39 ((abdom#n\$ adj3 pain\$) or acute abdomen).tw.
40 or/38-39
41 DYSPNEA/
42 TACHYPNEA/
43 HYPERVENTILATION/
44 (respirat\$ adj (distress or rate)).tw.
45 (breath\$ adj3 (difficult\$ or pattern\$ or abnormal\$ or dysfunction\$ or labo?r\$ or deep\$ or shallow\$ or rapid\$ or short\$ or effort\$)).tw.
46 (gasping or kussmaul or dyspnea or tachypnea or breathless\$ or hyperventilat\$).tw.
47 or/41-46
48 CONSCIOUSNESS DISORDERS/ or exp CONFUSION/
49 (conscious\$ or confus\$ or deliri\$ or mental state\$).tw.
50 or/48-49
51 "SIGNS AND SYMPTOMS"/
52 (sign? or symptom? or indicat\$ or presentation).tw.
53 ((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest\$ or aspect?)).tw.
54 or/51-53
55 or/25,28,31,34,37,40,47,50,54
56 exp HYPERGLYCEMIA/
57 hyperglyc?emi\$.tw.
58 ((high or elevat\$ or excess\$ or abnormal\$ or above or extreme\$) adj3 (blood glucose or blood sugar?)).tw.
59 BLOOD GLUCOSE/an
60 (BGM or glucometer or glucosemeter\$ or (glucose adj meter\$)).tw.
61 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").tw.

- 62 or/56-61
63 exp KETOSIS/
64 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuria or hyperketonuria or keton?emi\$ or hyperketon?emi\$ or ketogenesis).tw.
65 KETONES/
66 3-HYDROXYBUTYRIC ACID/
67 HYDROXYBUTYRATES/
68 or/65-67
69 URINALYSIS/
70 BLOOD CHEMICAL ANALYSIS/
71 or/69-70
72 and/68,71
73 KETONES/an, bl, ur [Analysis, Blood, Urine]
74 3-HYDROXYBUTYRIC ACID/an, bl, ur [Analysis, Blood, Urine]
75 HYDROXYBUTYRATES/an, bl, ur [Analysis, Blood, Urine]
76 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw.
77 ((urine or urinary) adj3 (dipstick or dip test)).tw.
78 or/63-64,72-77
79 ACIDOSIS/
80 (acidosis or (blood? adj3 acid\$) or acid?emi\$).tw.
81 HYDROGEN-ION CONCENTRATION/
82 ACID-BASE EQUILIBRIUM/
83 ACID-BASE IMBALANCE/
84 BICARBONATES/
85 ELECTROLYTES/
86 or/81-85
87 BLOOD GAS ANALYSIS/
88 BLOOD CHEMICAL ANALYSIS/
89 or/87-88
90 and/86,89
91 HYDROGEN-ION CONCENTRATION/an, bl, ur [Analysis, Blood, Urine]
92 ACID-BASE EQUILIBRIUM/an, bl [Analysis, Blood]
93 ACID-BASE IMBALANCE/bl, ur [Blood, Urine]
94 BICARBONATES/an, bl, ur [Analysis, Blood, Urine]
95 ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]
96 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate\$ or electrolyte\$)).tw.
97 (blood gas or ABG or blood test\$).tw.
98 or/79-80,90-97
99 (biochemical adj3 (variable? or measur\$ or marker? or parameter? or abnormal\$)).tw.
100 or/62,78,98-99
101 55 or 100
102 20 and 101
103 exp "SENSITIVITY AND SPECIFICITY"/
104 exp BLOOD CHEMICAL ANALYSIS/
105 URINALYSIS/
106 (detect\$ or diagnos\$ or predict\$ or sensitiv\$ or accuracy or test\$).mp.
107 or/103-106
108 102 and 107

Embase

- # Searches
- 1 exp ADOLESCENT/
2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
- 3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
- 5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
- 7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
- 9 or/1-8
- 10 KETOACIDOSIS/
11 KETONURIA/
12 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
- 13 or/10-12
- 14 exp DIABETES MELLITUS/
15 diabet\$.mp.
- 16 or/14-15
- 17 and/13,16
- 18 DIABETIC KETOACIDOSIS/
19 (DK or DKA).ti,ab.
- 20 or/18-19
- 21 9 and (17 or 20)
- 22 POLYDIPSIA/
23 THIRST/
24 (polyd#psi\$ or dehydrat\$ or ((excess\$ or frequen\$) adj3 (thirst\$ or fluid intake or drink\$))).ti,ab.
- 25 or/22-24
- 26 POLYURIA/
27 (polyuri\$ or ((excess\$ or frequen\$) adj3 (urin\$ or urine))).ti,ab.
- 28 or/26-27
- 29 WEIGHT REDUCTION/
30 (weight adj3 (loss or lost or reduc\$)).ti,ab.
- 31 or/29-30
- 32 DEHYDRATION/
33 (dehydrat\$ or rehydrat\$ or re hydrat\$ or hydration status).ti,ab.
- 34 or/32-33
- 35 NAUSEA/ or VOMITING/
36 (nausea or emesis or vomit\$).ti,ab.
- 37 or/35-36
- 38 exp ABDOMINAL PAIN/ or ACUTE ABDOMEN/
39 ((abdom#n\$ adj3 pain\$) or acute abdomen).ti,ab.
- 40 or/38-39
- 41 DYSPNEA/ or TACHYPNEA/ or HYPERVENTILATION/
42 (respirat\$ adj (distress or rate)).ti,ab.
- 43 (breath\$ adj3 (difficult\$ or pattern\$ or abnormal\$ or dysfunction\$ or labo?r\$ or deep\$ or shallow\$ or rapid\$ or short\$ or effort\$)).ti,ab.
- 44 (gasping or kussmaul or dyspnea or tachypnea or breathless\$ or hyperventilat\$).ti,ab.
- 45 or/41-44
- 46 CONSCIOUSNESS LEVEL/
47 CONFUSION/ or DELIRIUM/

- 48 (conscious\$ or confus\$ or deliri\$ or mental state\$).ti,ab.
49 or/46-48
50 PHYSICAL DISEASE BY BODY FUNCTION/
51 (sign? or symptom? or indicat\$ or presentation).ti,ab.
52 ((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest\$ or aspect?)).ti,ab.
53 or/50-52
54 or/25,28,31,34,37,40,45,49,53
55 HYPERGLYCEMIA/
56 hyperglyc?emi\$.ti,ab.
57 ((high or elevat\$ or excess\$ or abnormal\$ or above or extreme\$) adj3 (blood glucose or blood sugar?)).ti,ab.
58 GLUCOSE BLOOD LEVEL/
59 BLOOD GLUCOSE MONITORING/
60 BLOOD GLUCOSE METER/
61 (BGM or glucometer or glucometer\$ or (glucose adj meter\$)).ti,ab.
62 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
63 or/55-62
64 KETOACIDOSIS/
65 KETONEMIA/
66 KETONURIA/
67 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuria or hyperketonuria or keton?emi\$ or hyperketon?emi\$ or ketogenesis).ti,ab.
68 KETONE/
69 KETONE BODY/
70 3-HYDROXYBUTYRIC ACID/
71 HYDROXYBUTYRIC ACID/
72 or/68-71
73 URINALYSIS/ or BLOOD ANALYSIS/ or BLOOD CHEMISTRY/
74 and/72-73
75 KETONE/an [Drug Analysis]
76 KETONE BODY/an [Drug Analysis]
77 3-HYDROXYBUTYRIC ACID/an [Drug Analysis]
78 HYDROXYBUTYRIC ACID/an [Drug Analysis]
79 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
80 ((urine or urinary) adj3 (dipstick or dip test)).ti,ab.
81 or/64-67,74-80
82 ACIDOSIS/
83 (acidosis or (blood? adj3 acid\$) or acid?emi\$).ti,ab.
84 ACID BASE BALANCE/
85 BLOOD pH/
86 BICARBONATE/
87 ELECTROLYTE/
88 or/84-87
89 BLOOD ANALYSIS/ or BLOOD CHEMISTRY/ or BLOOD GAS ANALYSIS/
90 and/88-89
91 BICARBONATE BLOOD LEVEL/
92 exp ELECTROLYTE BLOOD LEVEL/
93 ACID BASE BALANCE/an [Drug Analysis]
94 BICARBONATE/an [Drug Analysis]

- 95 ELECTROLYTE/an [Drug Analysis]
96 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate\$ or electrolyte\$)).ti,ab.
97 (blood gas or ABG or blood test\$).ti,ab.
98 or/82-83,90-97
99 (biochemical adj3 (variable? or measur\$ or marker? or parameter? or abnormal\$)).ti,ab.
100 or/63,81,98-99
101 or/54,100
102 "SENSITIVITY AND SPECIFICITY"/
103 DIAGNOSTIC ACCURACY/
104 DIAGNOSTIC TEST/
105 DIAGNOSTIC VALUE/
106 PREDICTIVE VALUE/
107 (detect\$ or diagnos\$ or predict\$ or sensitiv\$ or specificity).tw.
108 or/102-107
109 and/21,101,108
110 limit 109 to english language
111 conference abstract.pt.
112 letter.pt. or LETTER/
113 note.pt.
114 editorial.pt.
115 CASE REPORT/ or CASE STUDY/
116 (letter or comment* or abstracts).ti.
117 or/111-116
118 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
119 117 not 118
120 ANIMAL/ not HUMAN/
121 NONHUMAN/
122 exp ANIMAL EXPERIMENT/
123 exp EXPERIMENTAL ANIMAL/
124 ANIMAL MODEL/
125 exp RODENT/
126 (rat or rats or mouse or mice).ti.
127 or/119-126
128 110 not 127

F.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions:

What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?

Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:

- **general observations (for example, heart and respiratory rate and blood pressure)**
- **body weight**
- **hydration status**
- **fluid balance**
- **neurological observations**
- **electrocardiographic (ECG) monitoring?**

Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:

- **blood glucose**
- **blood or urine ketones**
- **serum urea or electrolytes**
- **acid/base status?**

Ovid MEDLINE(R)

```
# Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high
school$).ti,ab,jw.
3 exp CHILD/
4 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or
toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre
pubescen$).ti,ab,jw.
9 or/1-8
10 DIABETIC KETOACIDOSIS/
11 (DK or DKA).ti,ab.
12 or/10-11
```

- 13 exp KETOSIS/
14 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
15 or/13-14
16 exp DIABETES MELLITUS/
17 diabet\$.mp.
18 or/16-17
19 and/15,18
20 9 and (12 or 19)
21 exp VITAL SIGNS/
22 SYMPTOM ASSESSMENT/
23 exp AIRWAY MANAGEMENT/
24 exp INTUBATION/
25 exp NEUROLOGIC EXAMINATION/
26 BLOOD PRESSURE DETERMINATION/
27 exp CONFUSION/
28 CONSCIOUSNESS DISORDERS/
29 GLASGOW COMA SCALE/
30 ((clinical or physical or physiolog\$ or neurologic\$) adj3 (observ\$ or indication? or indicator? or investigat\$ or assess\$ or status or sign? or symptom? or characteristic? or monitor\$)).ti.
31 ((clinical or physical or physiolog\$ or neurologic\$) adj3 (observ\$ or indication? or indicator? or investigat\$ or assess\$ or status or sign? or symptom? or characteristic? or monitor\$)).ab.
/freq=2
32 (vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat\$ or breathing or airway or nasogastric tube or nasogastric intubat\$ or NG tube or temperature or conscious\$ or glasgow coma or GCS or alert\$ or confusion or confused or delirium or delirious or mental stat\$ or reflex\$ or pupil).ti.
33 (vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat\$ or breathing or airway or nasogastric tube or nasogastric intubat\$ or NG tube or temperature or conscious\$ or glasgow coma or GCS or alert\$ or confusion or confused or delirium or delirious or mental stat\$ or reflex\$ or pupil).ab. /freq=2
34 or/21-33
35 and/20,34
36 exp BODY WEIGHT CHANGES/
37 (body weight or (weight adj3 (gain\$ or increas\$ or raise or raising or rising or lose or lost or loss\$ or decreas\$ or drop\$ or fall\$ or chang\$ or fluctuat\$))).ti.
38 (body weight or (weight adj3 (gain\$ or increas\$ or raise or raising or rising or lose or lost or loss\$ or decreas\$ or drop\$ or fall\$ or chang\$ or fluctuat\$))).ab. /freq=2
39 or/36-38
40 and/20,39
41 DEHYDRATION/
42 (dehydrat\$ or hydration status or rehydrate\$ or re hydrat\$).ti,ab.
43 WATER-ELECTROLYTE BALANCE/
44 WATER-ELECTROLYTE IMBALANCE/
45 exp FLUID THERAPY/
46 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj3 (volume? or balance? or imbalance?)).ti.
47 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj3 (volume? or balance? or imbalance?)).ab. /freq=2
48 (volume adj3 expan\$).ti,ab.
49 OLIGURIA/
50 ((urine or urinary) adj3 (reduc\$ or decreas\$ or drop\$ or fall\$ or produc\$ or output\$)).ti,ab.
51 REGIONAL BLOOD FLOW/ and (FINGERS/bs or CAPILLARIES/ph)
52 capillary refill\$.ti,ab.
53 SKIN/

- 54 (skin turgor or skin color or pinch test).ti,ab.
55 EYE/
56 sunken eye?.ti,ab.
57 exp LOWER EXTREMITY/
58 exp UPPER EXTREMITY/
59 (cold adj3 (extremity\$ or limb? or hand? or finger? or foot or feet or toe?)).ti,ab.
60 MOUTH MUCOSA/
61 (mucosa or mucous membrane?).ti,ab.
62 or/41-61
63 and/20,62
64 ELECTROCARDIOGRAPHY/
65 (electrocardio\$ or ECG).ti,ab.
66 or/64-65
67 and/20,66
68 or/35,40,63,67
69 CLINICAL LABORATORY TECHNIQUES/
70 BLOOD GAS ANALYSIS/
71 URINALYSIS/
72 (laboratory adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ti.
73 (laboratory adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ab. /freq=2
74 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ti.
75 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ab. /freq=2
76 or/69-75
77 and/20,76
78 BLOOD GLUCOSE/an [Analysis]
79 GLUCOSE TOLERANCE TEST/
80 (OGTT or FPG or fasting plasma glucose).ti,ab.
81 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (glucose or blood sugar\$)).ti.
82 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (glucose or blood sugar\$)).ab. /freq=2
83 or/78-82
84 and/20,83
85 KETONES/an, bl, ur [Analysis, Blood, Urine]
86 exp KETONE BODIES/an, bl, ur [Analysis, Blood, Urine]
87 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
88 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
89 or/85-88
90 POINT-OF-CARE SYSTEMS/
91 (near patient or bedside or bed side or point of care).ti,ab.
92 or/89-91
93 and/20,92

94 PLASMA/ and OSMOLAR CONCENTRATION/
95 ((plasma or serum or blood) adj3 (osmola\$ or tonicity)).ti,ab.
96 HYDROGEN-ION CONCENTRATION/
97 ACID-BASE EQUILIBRIUM/
98 ACID-BASE IMBALANCE/
99 BICARBONATES/an, bl, ur [Analysis, Blood, Urine]
100 ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]
101 SODIUM/an, bl, ur [Analysis, Blood, Urine]
102 POTASSIUM/an, bl, ur [Analysis, Blood, Urine]
103 exp CHLORIDES/an, bl, ur [Analysis, Blood, Urine]
104 UREA/an, bl, ur [Analysis, Blood, Urine]
105 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte\$ or sodium or potassium or chloride? or bicarbonate\$ or urea)).ti,ab.
106 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (acid base or pH or bicarbonate\$ or electrolyte\$ or urea)).ti,ab.
107 (blood gas or ABG).ti,ab.
108 or/94-107
109 and/20,108
110 or/77,84,93,109
111 or/68,110
112 *HYPOVOLEMIA/
113 *HYPOGLYCEMIA/
114 *HYPOKALEMIA/
115 *HYPONATREMIA/
116 (hypovol?emi\$ or olig?emi\$ or hypoglyc?emi\$ or hypokal?emi\$ or hyponatr?emi\$).ti.
117 (hypovol?emi\$ or olig?emi\$ or hypoglyc?emi\$ or hypokal?emi\$ or hyponatr?emi\$).ab. /freq=2
118 *ACIDOSIS/
119 (acidosis or (blood? adj3 acid\$) or acid?emi\$).ti.
120 (acidosis or (blood? adj3 acid\$) or acid?emi\$).ab. /freq=2
121 *BRAIN EDEMA/
122 ((cerebral or brain) adj3 (oedema? or edema?)).ti.
123 ((cerebral or brain) adj3 (oedema? or edema?)).ab. /freq=2
124 *VENOUS THROMBOSIS/
125 (DVT or deep vein thrombo\$).ti.
126 (DVT or deep vein thrombo\$).ab. /freq=2
127 exp *RESPIRATORY ASPIRATION/
128 exp *PNEUMONIA, ASPIRATION/
129 aspiration.ti. or aspiration.ab. /freq=2
130 or/112-129
131 exp "SENSITIVITY AND SPECIFICITY"/
132 ((pre test or pretest or post test or posttest) adj probability).ti,ab.
133 (predictive value\$ or PPV or NPV).ti,ab.
134 likelihood ratio\$.ti,ab.
135 LIKELIHOOD FUNCTIONS/
136 (ROC curve\$ or AUC).ti,ab.
137 (detect\$ or diagnos\$ or predict\$ or accuracy or test\$).ti,ab.
138 di.xs.
139 or/131-138
140 and/20,130,139
141 or/111,140
142 LETTER/
143 EDITORIAL/

144 NEWS/
145 exp HISTORICAL ARTICLE/
146 ANECDOTES AS TOPIC/
147 COMMENT/
148 CASE REPORT/
149 (letter or comment* or abstracts).ti.
150 or/142-149
151 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
152 150 not 151
153 ANIMALS/ not HUMANS/
154 exp ANIMALS, LABORATORY/
155 exp ANIMAL EXPERIMENTATION/
156 exp MODELS, ANIMAL/
157 exp RODENTIA/
158 (rat or rats or mouse or mice).ti.
159 or/152-158
160 141 not 159
161 limit 160 to english language

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

Searches
1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$ or high school\$).ti,ab,jw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or pre school\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pre pubert\$ or pubescen\$ or prepubescen\$ or pre pubescen\$).ti,ab,jw.
5 or/1-4
6 (diabetic ketoacidosis or DK or DKA).ti,ab.
7 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
8 diabet\$.mp.
9 and/7-8
10 5 and (6 or 9)
11 ((clinical or physical or physiolog\$ or neurologic\$) adj3 (observ\$ or indication? or indicator? or investigat\$ or assess\$ or status or sign? or symptom? or characteristic? or monitor\$)).ti.
12 ((clinical or physical or physiolog\$ or neurologic\$) adj3 (observ\$ or indication? or indicator? or investigat\$ or assess\$ or status or sign? or symptom? or characteristic? or monitor\$)).ab. /freq=2
13 (vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat\$ or breathing or airway or nasogastric tube or nasogastric intubat\$ or NG tube or temperature or conscious\$ or glasgow coma or GCS or alert\$ or confusion or confused or delirium or delirious or mental stat\$ or reflex\$ or pupil).ti.
14 (vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat\$ or breathing or airway or nasogastric tube or nasogastric intubat\$ or NG tube or temperature or conscious\$ or glasgow coma or GCS or alert\$ or confusion or confused or delirium or delirious or mental stat\$ or reflex\$ or pupil).ab. /freq=2
15 (body weight or (weight adj3 (gain\$ or increas\$ or raise or raising or rising or lose or lost or loss\$ or decreas\$ or drop\$ or fall\$ or chang\$ or fluctuat\$))).ti.
16 (body weight or (weight adj3 (gain\$ or increas\$ or raise or raising or rising or lose or lost or loss\$ or decreas\$ or drop\$ or fall\$ or chang\$ or fluctuat\$))).ab. /freq=2
17 (dehydrat\$ or hydration status or rehydrate\$ or re hydrat\$).ti,ab.
18 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj3 (volume? or balance? or imbalance?)).ti.

- 19 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj3 (volume? or balance? or imbalance?)).ab. /freq=2
- 20 (volume adj3 expans).ti,ab.
- 21 ((urine or urinary) adj3 (reduc\$ or decreas\$ or drop\$ or fall\$ or produc\$ or output\$)).ti,ab.
- 22 capillary refill\$.ti,ab.
- 23 (skin turgor or skin colo?r or pinch test).ti,ab.
- 24 sunken eye?.ti,ab.
- 25 (cold adj3 (extremity\$ or limb? or hand? or finger? or foot or feet or toe?)).ti,ab.
- 26 (mucosa or mucous membrane?).ti,ab.
- 27 (electrocardio\$ or ECG).ti,ab.
- 28 or/11-27
- 29 and/10,28
- 30 (laboratory adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ti.
- 31 (laboratory adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ab. /freq=2
- 32 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ti.
- 33 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ab. /freq=2
- 34 (OGTT or FPG or fasting plasma glucose).ti,ab.
- 35 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (glucose or blood sugar\$)).ti.
- 36 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (glucose or blood sugar\$)).ab. /freq=2
- 37 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
- 38 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
- 39 (near patient or bedside or bed side or point of care).ti,ab.
- 40 ((plasma or serum or blood) adj3 (osmola\$ or tonicity)).ti,ab.
- 41 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte\$ or sodium or potassium or chloride? or bicarbonate\$ or urea)).ti,ab.
- 42 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (acid base or pH or bicarbonate\$ or electrolyte\$ or urea)).ti,ab.
- 43 (blood gas or ABG).ti,ab.
- 44 or/30-43
- 45 and/10,44
- 46 or/29,45
- 47 (hypovol?emi\$ or olig?emi\$ or hypoglyc?emi\$ or hypokal?emi\$ or hyponatr?emi\$).ti.
- 48 (hypovol?emi\$ or olig?emi\$ or hypoglyc?emi\$ or hypokal?emi\$ or hyponatr?emi\$).ab. /freq=2
- 49 (acidosis or (blood? adj3 acid\$) or acid?emi\$).ti.
- 50 (acidosis or (blood? adj3 acid\$) or acid?emi\$).ab. /freq=2
- 51 ((cerebral or brain) adj3 (oedema? or edema?)).ti.
- 52 ((cerebral or brain) adj3 (oedema? or edema?)).ab. /freq=2
- 53 (DVT or deep vein thrombo\$).ti.
- 54 (DVT or deep vein thrombo\$).ab. /freq=2

- 55 aspiration.ti. or aspiration.ab. /freq=2
- 56 or/47-55
- 57 ((pre test or pretest or post test or posttest) adj probability).ti,ab.
- 58 (predictive value\$ or PPV or NPV).ti,ab.
- 59 likelihood ratio\$.ti,ab.
- 60 (ROC curve\$ or AUC).ti,ab.
- 61 (detect\$ or diagnos\$ or predict\$ or accuracy or test\$).ti,ab.
- 62 or/57-61
- 63 and/10,56,62
- 64 or/46,63

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$ or high school\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or pre school\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pre pubert\$ or pubescen\$ or prepubescen\$ or pre pubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 DIABETIC KETOACIDOSIS/
- 11 (DK or DKA).ti,ab.
- 12 or/10-11
- 13 exp KETOSIS/
- 14 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
- 15 or/13-14
- 16 exp DIABETES MELLITUS/
- 17 diabet\$.mp.
- 18 or/16-17
- 19 and/15,18
- 20 9 and (12 or 19)
- 21 exp VITAL SIGNS/
- 22 SYMPTOM ASSESSMENT/
- 23 exp AIRWAY MANAGEMENT/
- 24 exp INTUBATION/
- 25 exp NEUROLOGIC EXAMINATION/
- 26 BLOOD PRESSURE DETERMINATION/
- 27 exp CONFUSION/
- 28 CONSCIOUSNESS DISORDERS/
- 29 GLASGOW COMA SCALE/
- 30 ((clinical or physical or physiolog\$ or neurologic\$) adj3 (observ\$ or indication? or indicator? or investigat\$ or assess\$ or status or sign? or symptom? or characteristic? or monitor\$)).ti.
- 31 ((clinical or physical or physiolog\$ or neurologic\$) adj3 (observ\$ or indication? or indicator? or investigat\$ or assess\$ or status or sign? or symptom? or characteristic? or monitor\$)).ab.
/freq=2
- 32 (vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat\$ or breathing or airway or nasogastric tube or nasogastric intubat\$ or NG tube or temperature or conscious\$

- or glasgow coma or GCS or alert\$ or confusion or confused or delirium or delirious or mental stat\$ or reflex\$ or pupil).ti.
- 33 (vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat\$ or breathing or airway or nasogastric tube or nasogastric intubat\$ or NG tube or temperature or conscious\$ or glasgow coma or GCS or alert\$ or confusion or confused or delirium or delirious or mental stat\$ or reflex\$ or pupil).ab. /freq=2
- 34 or/21-33
- 35 and/20,34
- 36 exp BODY WEIGHT CHANGES/
- 37 (body weight or (weight adj3 (gain\$ or increas\$ or raise or raising or rising or lose or lost or loss\$ or decreas\$ or drop\$ or fall\$ or chang\$ or fluctuat\$)).ti.
- 38 (body weight or (weight adj3 (gain\$ or increas\$ or raise or raising or rising or lose or lost or loss\$ or decreas\$ or drop\$ or fall\$ or chang\$ or fluctuat\$)).ab. /freq=2
- 39 or/36-38
- 40 and/20,39
- 41 DEHYDRATION/
- 42 (dehydrat\$ or hydration status or rehydrate\$ or re hydrat\$).ti,ab.
- 43 WATER-ELECTROLYTE BALANCE/
- 44 WATER-ELECTROLYTE IMBALANCE/
- 45 exp FLUID THERAPY/
- 46 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj3 (volume? or balance? or imbalance?)).ti.
- 47 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj3 (volume? or balance? or imbalance?)).ab. /freq=2
- 48 (volume adj3 expan\$).ti,ab.
- 49 OLIGURIA/
- 50 ((urine or urinary) adj3 (reduc\$ or decreas\$ or drop\$ or fall\$ or produc\$ or output\$)).ti,ab.
- 51 REGIONAL BLOOD FLOW/ and (FINGERS/bs or CAPILLARIES/ph)
- 52 capillary refill\$.ti,ab.
- 53 SKIN/
- 54 (skin turgor or skin colo?r or pinch test).ti,ab.
- 55 EYE/
- 56 sunken eye?.ti,ab.
- 57 exp LOWER EXTREMITY/
- 58 exp UPPER EXTREMITY/
- 59 (cold adj3 (extremit\$ or limb? or hand? or finger? or foot or feet or toe?)).ti,ab.
- 60 MOUTH MUCOSA/
- 61 (mucosa or mucous membrane?).ti,ab.
- 62 or/41-61
- 63 and/20,62
- 64 ELECTROCARDIOGRAPHY/
- 65 (electrocardio\$ or ECG).ti,ab.
- 66 or/64-65
- 67 and/20,66
- 68 or/35,40,63,67
- 69 CLINICAL LABORATORY TECHNIQUES/
- 70 BLOOD GAS ANALYSIS/
- 71 URINALYSIS/
- 72 (laboratory adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ti.
- 73 (laboratory adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ab. /freq=2

- 74 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ti.
- 75 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ab. /freq=2
- 76 or/69-75
- 77 and/20,76
- 78 BLOOD GLUCOSE/an [Analysis]
- 79 GLUCOSE TOLERANCE TEST/
(OGTT or FPG or fasting plasma glucose).ti,ab.
- 81 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (glucose or blood sugar\$)).ti.
- 82 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (glucose or blood sugar\$)).ab. /freq=2
- 83 or/78-82
- 84 and/20,83
- 85 KETONES/an, bl, ur [Analysis, Blood, Urine]
- 86 exp KETONE BODIES/an, bl, ur [Analysis, Blood, Urine]
- 87 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
- 88 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
- 89 or/85-88
- 90 POINT-OF-CARE SYSTEMS/
(near patient or bedside or bed side or point of care).ti,ab.
- 92 or/89-91
- 93 and/20,92
- 94 PLASMA/ and OSMOLAR CONCENTRATION/
((plasma or serum or blood) adj3 (osmola\$ or tonicity)).ti,ab.
- 96 HYDROGEN-ION CONCENTRATION/
ACID-BASE EQUILIBRIUM/
ACID-BASE IMBALANCE/
BICARBONATES/an, bl, ur [Analysis, Blood, Urine]
- 100 ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]
- 101 SODIUM/an, bl, ur [Analysis, Blood, Urine]
- 102 POTASSIUM/an, bl, ur [Analysis, Blood, Urine]
- 103 exp CHLORIDES/an, bl, ur [Analysis, Blood, Urine]
- 104 UREA/an, bl, ur [Analysis, Blood, Urine]
- 105 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte\$ or sodium or potassium or chloride? or bicarbonate\$ or urea)).ti,ab.
- 106 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (acid base or pH or bicarbonate\$ or electrolyte\$ or urea)).ti,ab.
- 107 (blood gas or ABG).ti,ab.
- 108 or/94-107
- 109 and/20,108
- 110 or/77,84,93,109
- 111 or/68,110
- 112 *HYPOVOLEMIA/

113 *HYPOGLYCEMIA/
 114 *HYPOKALEMIA/
 115 *HYPONATREMIA/
 116 (hypovol?emi\$ or olig?emi\$ or hypoglyc?emi\$ or hypokal?emi\$ or hyponatr?emi\$).ti.
 117 (hypovol?emi\$ or olig?emi\$ or hypoglyc?emi\$ or hypokal?emi\$ or hyponatr?emi\$).ab. /freq=2
 118 *ACIDOSIS/
 119 (acidosis or (blood? adj3 acid\$) or acid?emi\$).ti.
 120 (acidosis or (blood? adj3 acid\$) or acid?emi\$).ab. /freq=2
 121 *BRAIN EDEMA/
 122 ((cerebral or brain) adj3 (oedema? or edema?)).ti.
 123 ((cerebral or brain) adj3 (oedema? or edema?)).ab. /freq=2
 124 *VENOUS THROMBOSIS/
 125 (DVT or deep vein thrombo\$).ti.
 126 (DVT or deep vein thrombo\$).ab. /freq=2
 127 exp *RESPIRATORY ASPIRATION/
 128 exp *PNEUMONIA, ASPIRATION/
 129 aspiration.ti. or aspiration.ab. /freq=2
 130 or/112-129
 131 exp "SENSITIVITY AND SPECIFICITY"/
 132 ((pre test or pretest or post test or posttest) adj probability).ti,ab.
 133 (predictive value\$ or PPV or NPV).ti,ab.
 134 likelihood ratio\$.ti,ab.
 135 LIKELIHOOD FUNCTIONS/
 136 (ROC curve\$ or AUC).ti,ab.
 137 (detect\$ or diagnos\$ or predict\$ or accuracy or test\$).ti,ab.
 138 di.xs.
 139 or/131-138
 140 and/20,130,139
 141 or/111,140

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

Searches
 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$ or high school\$).tw,kw,tx,jw,rw.
 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or pre school\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,kw,tx,jw,rw.
 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,kw,tx,jw,rw.
 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pre pubert\$ or pubescen\$ or prepubescen\$ or pre pubescen\$).tw,kw,tx,jw,rw.
 5 or/1-4
 6 (diabetic ketoacidosis or DK or DKA).tw,kw,tx.
 7 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).tw,kw,tx.
 8 diabet\$.tw,kw,tx.
 9 and/7-8
 10 5 and (6 or 9)
 11 SYMPTOM ASSESSMENT.kw.
 12 INTUBATION.kw.
 13 (NEUROLOGIC EXAMINATION or REFLEX).kw.
 14 BLOOD PRESSURE DETERMINATION.kw.
 15 CONSCIOUSNESS DISORDERS.kw.
 16 GLASGOW COMA SCALE.kw.

- 17 ((clinical or physical or physiolog\$ or neurologic\$) adj3 (observ\$ or indication? or indicator? or investigat\$ or assess\$ or status or sign? or symptom? or characteristic? or monitor\$)).tw,tx.
- 18 (vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat\$ or breathing or airway or nasogastric tube or nasogastric intubat\$ or NG tube or temperature or conscious\$ or glasgow coma or GCS or alert\$ or confusion or confused or delirium or delirious or mental stat\$ or reflex\$ or pupil).tw,kw,tx.
- 19 or/11-18
- 20 and/10,19
- 21 (BODY WEIGHT CHANGES or WEIGHT GAIN or WEIGHT LOSS).kw.
- 22 (body weight or (weight adj3 (gain\$ or increas\$ or raise or raising or rising or lose or lost or loss\$ or decreas\$ or drop\$ or fall\$ or chang\$ or fluctuat\$))).tw,tx.
- 23 or/21-22
- 24 and/10,23
- 25 (dehydrat\$ or hydration status or rehydrate\$ or re hydrat\$).tw,kw,tx.
- 26 WATER-ELECTROLYTE BALANCE.kw.
- 27 WATER-ELECTROLYTE IMBALANCE.kw.
- 28 (FLUID THERAPY or HYPODERMOCLYSIS).kw.
- 29 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj3 (volume? or balance? or imbalance?)).tw,tx.
- 30 (volume adj3 expan\$).tw,tx.
- 31 OLIGURIA.kw.
- 32 ((urine or urinary) adj3 (reduc\$ or decreas\$ or drop\$ or fall\$ or produc\$ or output\$)).tw,tx.
- 33 (REGIONAL BLOOD FLOW and (FINGERS or CAPILLARIES)).kw.
- 34 capillary refill\$.tw,tx.
- 35 SKIN.kw.
- 36 (skin turgor or skin colo?r or pinch test).tw,tx.
- 37 EYE.kw.
- 38 sunken eye?.tw,tx.
- 39 (LOWER EXTREMITY or FOOT or TOES).kw.
- 40 (UPPER EXTREMITY or HAND or FINGERS).kw.
- 41 (cold adj3 (extremit\$ or limb? or hand? or finger? or foot or feet or toe?)).tw,tx.
- 42 MOUTH MUCOSA.kw.
- 43 (mucosa or mucous membrane?).tw,tx.
- 44 or/25-43
- 45 and/10,44
- 46 ELECTROCARDIOGRAPHY.kw.
- 47 (electrocardio\$ or ECG).tw,tx.
- 48 or/46-47
- 49 and/10,48
- 50 or/20,24,45,49
- 51 CLINICAL LABORATORY TECHNIQUES.kw.
- 52 BLOOD GAS ANALYSIS.kw.
- 53 URINALYSIS.kw.
- 54 (laboratory adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).tw,tx.
- 55 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).tw,tx.
- 56 or/51-55
- 57 and/10,56
- 58 BLOOD GLUCOSE.kw.
- 59 GLUCOSE TOLERANCE TEST.kw.
- 60 (OGTT or FPG or fasting plasma glucose).tw,tx.

- 61 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (glucose or blood sugar\$)).tw,tx.
62 or/58-61
63 and/10,62
64 KETONES.kw.
65 (KETONE BODIES or 3-HYDROXYBUTYRIC ACID or HYDROXYBUTYRATES or ACETOACETATES or ACETONE).kw.
66 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw,tx.
67 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw,tx.
68 or/64-67
69 POINT-OF-CARE SYSTEMS.kw.
70 (near patient or bedside or bed side or point of care).tw,tx.
71 or/68-70
72 and/10,71
73 (PLASMA and OSMOLAR CONCENTRATION).kw.
74 ((plasma or serum or blood) adj3 (osmola\$ or tonicity)).tw,tx.
75 HYDROGEN-ION CONCENTRATION.kw.
76 ACID-BASE EQUILIBRIUM.kw.
77 ACID-BASE IMBALANCE.kw.
78 BICARBONATES.kw.
79 ELECTROLYTES.kw.
80 SODIUM.kw.
81 POTASSIUM.kw.
82 (CHLORIDES or SODIUM CHLORIDE or POTASSIUM CHLORIDE).kw.
83 UREA.kw.
84 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte\$ or sodium or potassium or chloride? or bicarbonate\$ or urea)).tw,tx.
85 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (acid base or pH or bicarbonate\$ or electrolyte\$ or urea)).tw,tx.
86 (blood gas or ABG).tw,tx.
87 or/73-86
88 and/10,87
89 or/57,63,72,88
90 or/50,89
91 HYPOVOLEMIA.kw.
92 HYPOGLYCEMIA.kw.
93 HYPOKALEMIA.kw.
94 HYPONATREMIA.kw.
95 (hypovol?emi\$ or olig?emi\$ or hypoglyc?emi\$ or hypokal?emi\$ or hyponatr?emi\$).tw,tx.
96 ACIDOSIS.kw.
97 (acidosis or (blood? adj3 acid\$) or acid?emi\$).tw,tx.
98 BRAIN EDEMA.kw.
99 ((cerebral or brain) adj3 (oedema? or edema?)).tw,tx.
100 VENOUS THROMBOSIS.kw.
101 (DVT or deep vein thrombo\$).tw,tx.
102 aspiration.tw,kw,tx.

- 103 or/91-102
- 104 ("SENSITIVITY AND SPECIFICITY" or "PREDICTIVE VALUE OF TESTS").kw.
- 105 ((pre test or pretest or post test or posttest) adj probability).tw,tx.
- 106 (predictive value\$ or PPV or NPV).tw,tx.
- 107 likelihood ratio\$.tw,tx.
- 108 LIKELIHOOD FUNCTIONS.kw.
- 109 (ROC curve\$ or AUC).tw,tx.
- 110 (detect\$ or diagnos\$ or predict\$ or accuracy or test\$).tw,tx.
- 111 or/104-110
- 112 and/10,103,111
- 113 or/90,112

Health Technology Assessment

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$ or high school\$).tw,jx,rw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or pre school\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pre pubert\$ or pubescen\$ or prepubescen\$ or pre pubescen\$).tw,jx,rw.
- 9 or/1-8
- 10 DIABETIC KETOACIDOSIS/
- 11 (DK or DKA).tw.
- 12 or/10-11
- 13 exp KETOSIS/
- 14 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).tw.
- 15 or/13-14
- 16 exp DIABETES MELLITUS/
- 17 diabet\$.mp.
- 18 or/16-17
- 19 and/15,18
- 20 9 and (12 or 19)
- 21 exp VITAL SIGNS/
- 22 SYMPTOM ASSESSMENT/
- 23 exp AIRWAY MANAGEMENT/
- 24 exp INTUBATION/
- 25 exp NEUROLOGIC EXAMINATION/
- 26 BLOOD PRESSURE DETERMINATION/
- 27 exp CONFUSION/
- 28 CONSCIOUSNESS DISORDERS/
- 29 GLASGOW COMA SCALE/
- 30 ((clinical or physical or physiolog\$ or neurologic\$) adj3 (observ\$ or indication? or indicator? or investigat\$ or assess\$ or status or sign? or symptom? or characteristic? or monitor\$)).tw.
- 31 (vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat\$ or breathing or airway or nasogastric tube or nasogastric intubat\$ or NG tube or temperature or conscious\$ or glasgow coma or GCS or alert\$ or confusion or confused or delirium or delirious or mental stat\$ or reflex\$ or pupil).tw.
- 32 or/21-31

- 33 and/20,32
34 exp BODY WEIGHT CHANGES/
35 (body weight or (weight adj3 (gain\$ or increas\$ or raise or raising or rising or lose or lost or loss\$ or decreas\$ or drop\$ or fall\$ or chang\$ or fluctuat\$))).tw.
36 or/34-35
37 and/20,36
38 DEHYDRATION/
39 (dehydrat\$ or hydration status or rehydrate\$ or re hydrat\$).tw.
40 WATER-ELECTROLYTE BALANCE/
41 WATER-ELECTROLYTE IMBALANCE/
42 exp FLUID THERAPY/
43 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj3 (volume? or balance? or imbalance?)).tw.
44 (volume adj3 expan\$).tw.
45 OLIGURIA/
46 ((urine or urinary) adj3 (reduc\$ or decreas\$ or drop\$ or fall\$ or produc\$ or output\$)).tw.
47 REGIONAL BLOOD FLOW/ and (FINGERS/bs or CAPILLARIES/ph)
48 capillary refill\$.tw.
49 SKIN/
50 (skin turgor or skin colo?r or pinch test).tw.
51 EYE/
52 sunken eye?.tw.
53 exp LOWER EXTREMITY/
54 exp UPPER EXTREMITY/
55 (cold adj3 (extremit\$ or limb? or hand? or finger? or foot or feet or toe?)).tw.
56 MOUTH MUCOSA/
57 (mucosa or mucous membrane?).tw.
58 or/38-57
59 and/20,58
60 ELECTROCARDIOGRAPHY/
61 (electrocardio\$ or ECG).tw.
62 or/60-61
63 and/20,62
64 or/33,37,59,63
65 CLINICAL LABORATORY TECHNIQUES/
66 BLOOD GAS ANALYSIS/
67 URINALYSIS/
68 (laboratory adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).tw.
69 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).tw.
70 or/65-69
71 and/20,70
72 BLOOD GLUCOSE/an [Analysis]
73 GLUCOSE TOLERANCE TEST/
74 (OGTT or FPG or fasting plasma glucose).tw.
75 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (glucose or blood sugar\$)).tw.
76 or/72-75
77 and/20,76
78 KETONES/an, bl, ur [Analysis, Blood, Urine]
79 exp KETONE BODIES/an, bl, ur [Analysis, Blood, Urine]

- 80 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw.
- 81 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw.
- 82 or/78-81
- 83 POINT-OF-CARE SYSTEMS/
- 84 (near patient or bedside or bed side or point of care).tw.
- 85 or/82-84
- 86 and/20,85
- 87 PLASMA/ and OSMOLAR CONCENTRATION/
- 88 ((plasma or serum or blood) adj3 (osmola\$ or tonicity)).tw.
- 89 HYDROGEN-ION CONCENTRATION/
- 90 ACID-BASE EQUILIBRIUM/
- 91 ACID-BASE IMBALANCE/
- 92 BICARBONATES/an, bl, ur [Analysis, Blood, Urine]
- 93 ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]
- 94 SODIUM/an, bl, ur [Analysis, Blood, Urine]
- 95 POTASSIUM/an, bl, ur [Analysis, Blood, Urine]
- 96 exp CHLORIDES/an, bl, ur [Analysis, Blood, Urine]
- 97 UREA/an, bl, ur [Analysis, Blood, Urine]
- 98 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte\$ or sodium or potassium or chloride? or bicarbonate\$ or urea)).tw.
- 99 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (acid base or pH or bicarbonate\$ or electrolyte\$ or urea)).tw.
- 100 (blood gas or ABG).tw.
- 101 or/87-100
- 102 and/20,101
- 103 or/71,77,86,102
- 104 or/64,103
- 105 *HYPOVOLEMIA/
- 106 *HYPOGLYCEMIA/
- 107 *HYPOKALEMIA/
- 108 *HYPONATREMIA/
- 109 (hypovol?emi\$ or olig?emi\$ or hypoglyc?emi\$ or hypokal?emi\$ or hyponatr?emi\$).tw.
- 110 *ACIDOSIS/
- 111 (acidosis or (blood? adj3 acid\$) or acid?emi\$).tw.
- 112 *BRAIN EDEMA/
- 113 ((cerebral or brain) adj3 (oedema? or edema?)).tw.
- 114 *VENOUS THROMBOSIS/
- 115 (DVT or deep vein thrombo\$).tw.
- 116 exp *RESPIRATORY ASPIRATION/
- 117 exp *PNEUMONIA, ASPIRATION/
- 118 aspiration.tw.
- 119 or/105-118
- 120 exp "SENSITIVITY AND SPECIFICITY"/
- 121 ((pre test or pretest or post test or posttest) adj probability).tw.
- 122 (predictive value\$ or PPV or NPV).tw.
- 123 likelihood ratio\$.tw.

- 124 LIKELIHOOD FUNCTIONS/
125 (ROC curve\$ or AUC).tw.
126 (detect\$ or diagnos\$ or predict\$ or accuracy or test\$).tw.
127 di.xs.
128 or/120-127
129 and/20,119,128
130 or/104,129

Embase

- # Searches
- 1 exp ADOLESCENT/
2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
9 or/1-8
- 10 INSULIN DEPENDENT DIABETES MELLITUS/
11 (diabet\$ adj5 ("type one" or "type 1" or "type II" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
13 or/10-12
- 14 NON INSULIN DEPENDENT DIABETES MELLITUS/
15 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
16 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
17 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18 or/14-17
- 19 JUVENILE DIABETES MELLITUS/
20 or/13,18-19
- 21 KETOACIDOSIS/
22 KETONURIA/
23 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
24 or/21-23
25 and/20,24
- 26 DIABETIC KETOACIDOSIS/
27 (DK or DKA).ti,ab.
28 or/26-27
29 9 and (25 or 28)
- 30 VITAL SIGN/
31 CLINICAL OBSERVATION/
32 CLINICAL ASSESSMENT/
33 PATIENT ASSESSMENT/
34 SYMPTOM ASSESSMENT/
35 BODY TEMPERATURE MEASUREMENT/
36 BLOOD PRESSURE MEASUREMENT/
37 BLOOD PRESSURE MONITORING/
38 HEART RATE/
39 PULSE RATE/

- 40 BREATHING RATE/
41 RESPIRATION CONTROL/
42 exp RESPIRATORY TRACT INTUBATION/
43 STOMACH INTUBATION/
44 CONSCIOUSNESS LEVEL/
45 CONSCIOUSNESS DISORDER/
46 exp CONFUSION/
47 exp DELIRIUM/
48 NEUROLOGIC EXAMINATION/
49 GLASGOW COMA SCALE/
50 ((clinical or physical or physiolog\$ or neurologic\$) adj3 (observ\$ or indication? or indicator? or investigat\$ or assess\$ or status or sign? or symptom? or characteristic? or monitor\$)).ti.
51 ((clinical or physical or physiolog\$ or neurologic\$) adj3 (observ\$ or indication? or indicator? or investigat\$ or assess\$ or status or sign? or symptom? or characteristic? or monitor\$)).ab.
/freq=2
52 (vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat\$ or breathing or airway or nasogastric tube or nasogastric intubat\$ or NG tube or temperature or conscious\$ or glasgow coma or GCS or alert\$ or confusion or confused or delirium or delirious or mental stat\$ or reflex\$ or pupil).ti.
53 (vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat\$ or breathing or airway or nasogastric tube or nasogastric intubat\$ or NG tube or temperature or conscious\$ or glasgow coma or GCS or alert\$ or confusion or confused or delirium or delirious or mental stat\$ or reflex\$ or pupil).ab. /freq=2
54 or/30-53
55 and/29,54
56 WEIGHT CHANGE/
57 WEIGHT FLUCTUATION/
58 WEIGHT GAIN/
59 WEIGHT REDUCTION/
60 (body weight or (weight adj3 (gain\$ or increas\$ or raise or raising or rising or lose or lost or loss\$ or decreas\$ or drop\$ or fall\$ or chang\$ or fluctuat\$))).ti.
61 (body weight or (weight adj3 (gain\$ or increas\$ or raise or raising or rising or lose or lost or loss\$ or decreas\$ or drop\$ or fall\$ or chang\$ or fluctuat\$))).ab. /freq=2
62 or/56-61
63 and/29,62
64 DEHYDRATION/
65 (dehydrat\$ or hydration status or rehydrate\$ or re hydrat\$).ti,ab.
66 FLUID BALANCE/
67 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj3 (volume? or balance? or imbalance?)).ti.
68 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj3 (volume? or balance? or imbalance?)).ab. /freq=2
69 (volume adj3 expans\$).ti,ab.
70 OLIGURIA/
71 URINE OUTPUT/
72 ((urine or urinary) adj3 (reduc\$ or decreas\$ or drop\$ or fall\$ or produc\$ or output\$)).ti,ab.
73 CAPILLARY FLOW/
74 capillary refill\$.ti,ab.
75 SKIN TURGOR/
76 (skin turgor or skin colo?r or pinch test).ti,ab.
77 EYE/
78 sunken eye?.ti,ab.
79 COLD LIMB/
80 (cold adj3 (extremit\$ or limb? or hand? or finger? or foot or feet or toe?)).ti,ab.

- 81 MUCOSAL DRYNESS/
82 (mucosa or mucous membrane?).ti,ab.
83 or/64-82
84 and/29,83
85 ELECTROCARDIOGRAPHY/
86 (electrocardio\$ or ECG).ti,ab.
87 or/85-86
88 and/29,87
89 or/55,63,84,88
90 exp *LABORATORY DIAGNOSIS/
91 exp *BLOOD GAS ANALYSIS/
92 *URINALYSIS/
93 (laboratory adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ti.
94 (laboratory adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ab. /freq=2
95 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ti.
96 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ\$ or indication? or indicator? or investigat\$ or assess\$ or evaluat\$ or analys\$ or test? or monitor\$)).ab. /freq=2
97 or/90-96
98 and/29,97
99 BLOOD GLUCOSE MONITORING/
100 GLUCOSE BLOOD LEVEL/
101 exp GLUCOSE TOLERANCE TEST/
102 (OGTT or FPG or fasting plasma glucose).ti,ab.
103 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (glucose or blood sugar\$)).ti.
104 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (glucose or blood sugar\$)).ab. /freq=2
105 or/99-104
106 and/29,105
107 KETONE/an [Drug Analysis]
108 KETONE BODY/an [Drug Analysis]
109 3-HYDROXYBUTYRIC ACID/an [Drug Analysis]
110 HYDROXYBUTYRIC ACID/an [Drug Analysis]
111 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
112 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or surveillance or status or level? or check\$) adj5 (ketone? or hydroxy butyr\$ or hydroxybutyr\$ or beta hydroxybutyr\$ or betahydroxybutyr\$ or "3 hydroxybutyr\$" or "3-hydroxybutyr\$" or 3hydroxybutyr\$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
113 "POINT OF CARE TESTING"/
114 (near patient or bedside or bed side or point of care).ti,ab.
115 or/107-114
116 and/29,115
117 exp OSMOLALITY/
118 ((plasma or serum or blood) adj3 (osmola\$ or tonicity)).ti,ab.
119 BLOOD pH/
120 ACID BASE BALANCE/

- 121 BICARBONATE BLOOD LEVEL/
122 exp ELECTROLYTE BLOOD LEVEL/
123 exp URINE LEVEL/
124 UREA BLOOD LEVEL/
125 ((capillar\$ or blood\$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte\$ or sodium or potassium or chloride? or bicarbonate\$ or urea)).ti,ab.
126 ((monitor\$ or measur\$ or test\$ or screen\$ or determin\$ or assess\$ or evaluat\$ or surveillance or status or level? or check\$) adj5 (acid base or pH or bicarbonate\$ or electrolyte\$ or urea)).ti,ab.
127 (blood gas or ABG).ti,ab.
128 or/117-127
129 and/29,128
130 or/98,106,116,129
131 or/89,130
132 exp *HYPOVOLEMIA/
133 *HYPOGLYCAEMIA/
134 *HYPOKALEMIA/
135 *HYPONATREMIA/
136 (hypovol?emi\$ or olig?emi\$ or hypoglyc?emi\$ or hypokal?emi\$ or hyponatr?emi\$).ti.
137 (hypovol?emi\$ or olig?emi\$ or hypoglyc?emi\$ or hypokal?emi\$ or hyponatr?emi\$).ab. /freq=2
138 *ACIDOSIS/
139 (acidosis or (blood? adj3 acid\$) or acid?emi\$).ti.
140 (acidosis or (blood? adj3 acid\$) or acid?emi\$).ab. /freq=2
141 *BRAIN EDEMA/
142 ((cerebral or brain) adj3 (oedema? or edema?)).ti.
143 ((cerebral or brain) adj3 (oedema? or edema?)).ab. /freq=2
144 *DEEP VEIN THROMBOSIS/
145 (DVT or deep vein thrombo\$).ti.
146 (DVT or deep vein thrombo\$).ab. /freq=2
147 *PULMONARY ASPIRATION/
148 *ASPIRATION PNEUMONIA/
149 aspiration.ti. or aspiration.ab. /freq=2
150 or/132-149
151 "SENSITIVITY AND SPECIFICITY"/
152 PREDICTIVE VALUE/
153 DIAGNOSTIC VALUE/
154 DIAGNOSTIC ACCURACY/
155 ((pre test or pretest or post test or posttest) adj probability).ti,ab.
156 (predictive value\$ or PPV or NPV).ti,ab.
157 likelihood ratio\$.ti,ab.
158 di.fs.
159 or/151-158
160 and/29,150,159
161 or/131,160
162 conference abstract.pt.
163 letter.pt. or LETTER/
164 note.pt.
165 editorial.pt.
166 CASE REPORT/ or CASE STUDY/
167 (letter or comment* or abstracts).ti.
168 or/162-167
169 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
170 168 not 169

- 171 ANIMAL/ not HUMAN/
- 172 NONHUMAN/
- 173 exp ANIMAL EXPERIMENT/
- 174 exp EXPERIMENTAL ANIMAL/
- 175 ANIMAL MODEL/
- 176 exp RODENT/
- 177 (rat or rats or mouse or mice).ti.
- 178 or/170-177
- 179 161 not 178
- 180 limit 179 to english language

F.12 Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

Review questions:

What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?

At what rate should children and young people with diabetic ketoacidosis be rehydrated?

What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

Ovid MEDLINE(R)

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$ or high school\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or pre school\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pre pubert\$ or pubescen\$ or prepubescen\$ or pre pubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 DIABETIC KETOACIDOSIS/
- 11 (DK or DKA).ti,ab.
- 12 or/10-11
- 13 exp KETOSIS/
- 14 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
- 15 or/13-14
- 16 exp DIABETES MELLITUS/
- 17 diabet\$.mp.
- 18 or/16-17
- 19 and/15,18
- 20 9 and (12 or 19)
- 21 exp FLUID THERAPY/
- 22 REHYDRATION SOLUTIONS/
- 23 WATER-ELECTROLYTE BALANCE/

24 WATER-ELECTROLYTE IMBALANCE/
25 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj5 (manag\$ or regimen? or resuscit\$ or infusion? or administrat\$ or replac\$ or balanc\$ or imbalanc\$)).ti,ab.
26 or/21-25
27 and/20,26
28 DRUG ADMINISTRATION ROUTES/
29 ADMINISTRATION, ORAL/
30 ADMINISTRATION, INTRAVENOUS/
31 INFUSIONS, INTRAVENOUS/
32 INFUSIONS, INTRAOSSEOUS/
33 exp INFUSIONS, SUBCUTANEOUS/
34 INFUSION PUMP/
35 INTUBATION, GASTROINTESTINAL/
36 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (route? or intravenous\$ or oral or orally or mouth or subcutan\$ or hypodermocl\$ or intraosse\$ or intra osse\$ or intraperiton\$ or intra periton\$ or gavage or nasogastric or naso gastric or rectal or proctocl\$)).ti,ab.
37 (fluid bolus or two bag or ORT).ti,ab.
38 or/28-37
39 and/20,38
40 TIME FACTORS/
41 DRUG ADMINISTRATION SCHEDULE/
42 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (rate? or variable rate? or fixed rate? or volume or fast or faster or quickly or quicker or quick or rapid\$ or slow or slowly or slower or gradual\$ or earlier or early or later or late)).ti,ab.
43 or/40-42
44 and/20,43
45 SODIUM/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
46 exp CHLORIDES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
47 GLUCOSE/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
48 GLUCOSE SOLUTION, HYPERTONIC/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
49 SALINE SOLUTION, HYPERTONIC/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
50 exp BICARBONATES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
51 POTASSIUM/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
52 PHOSPHATES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
53 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (chloride? or sodium chloride? or potassium chloride? or saline? or NaCl or KCl or glucose or dextrose or hydrogen carbonate? or bicarbonate? or carbonic acid or potassium or phosphate? or orthophosphate? or ortho phosphate?)).ti,ab.
54 or/45-53
55 and/20,54
56 or/27,39,44,55
57 LETTER/
58 EDITORIAL/
59 NEWS/
60 exp HISTORICAL ARTICLE/
61 ANECDOTES AS TOPIC/
62 COMMENT/
63 CASE REPORT/
64 (letter or comment* or abstracts).ti.
65 or/57-64

- 66 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 67 65 not 66
- 68 ANIMALS/ not HUMANS/
- 69 exp ANIMALS, LABORATORY/
- 70 exp ANIMAL EXPERIMENTATION/
- 71 exp MODELS, ANIMAL/
- 72 exp RODENTIA/
- 73 (rat or rats or mouse or mice).ti.
- 74 or/67-73
- 75 56 not 74
- 76 limit 75 to english language

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$ or high school\$).ti,ab,jw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or pre school\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pre pubert\$ or pubescen\$ or prepubescen\$ or pre pubescen\$).ti,ab,jw.
- 5 or/1-4
- 6 (diabetic ketoacidosis or DK or DKA).ti,ab.
- 7 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
- 8 diabet\$.mp.
- 9 and/7-8
- 10 5 and (6 or 9)
- 11 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj5 (manag\$ or regimen? or resuscit\$ or infusion? or administrat\$ or replac\$ or balanc\$ or imbalanc\$)).ti,ab.
- 12 and/10-11
- 13 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (route? or intravenous\$ or oral or orally or mouth or subcutan\$ or hypodermocl\$ or intraosse\$ or intra osse\$ or intraperiton\$ or intra periton\$ or gavage or nasogastric or naso gastric or rectal or proctocl\$)).ti,ab.
- 14 (fluid bolus or two bag or ORT).ti,ab.
- 15 or/13-14
- 16 and/10,15
- 17 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (rate? or variable rate? or fixed rate? or volume or fast or faster or quickly or quicker or quick or rapid\$ or slow or slowly or slower or gradual\$ or earlier or early or later or late)).ti,ab.
- 18 and/10,17
- 19 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (chloride? or sodium chloride? or potassium chloride? or saline? or NaCl or KCl or glucose or dextrose or hydrogen carbonate? or bicarbonate? or carbonic acid or potassium or phosphate? or orthophosphate? or ortho phosphate?)).ti,ab.
- 20 and/10,19
- 21 or/12,16,18,20
- 22 limit 21 to english language

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/

2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$ or high
school\$).ti,ab,jw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or pre school\$ or
toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pre pubert\$ or pubescen\$ or prepubescen\$ or pre
pubescen\$).ti,ab,jw.
9 or/1-8
10 DIABETIC KETOACIDOSIS/
11 (DK or DKA).ti,ab.
12 or/10-11
13 exp KETOSIS/
14 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or
ketogenesis).ti,ab.
15 or/13-14
16 exp DIABETES MELLITUS/
17 diabet\$.mp.
18 or/16-17
19 and/15,18
20 9 and (12 or 19)
21 exp FLUID THERAPY/
22 REHYDRATION SOLUTIONS/
23 WATER-ELECTROLYTE BALANCE/
24 WATER-ELECTROLYTE IMBALANCE/
25 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj5 (manag\$ or
regimen? or resuscit\$ or infusion? or administrat\$ or replac\$ or balanc\$ or imbalanc\$)).ti,ab.
26 or/21-25
27 and/20,26
28 DRUG ADMINISTRATION ROUTES/
29 ADMINISTRATION, ORAL/
30 ADMINISTRATION, INTRAVENOUS/
31 INFUSIONS, INTRAVENOUS/
32 INFUSIONS, INTRAOSSEOUS/
33 exp INFUSIONS, SUBCUTANEOUS/
34 INFUSION PUMP/
35 INTUBATION, GASTROINTESTINAL/
36 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or
resuscitat\$) adj5 (route? or intravenous\$ or oral or orally or mouth or subcutan\$ or
hypodermocl\$ or intraosse\$ or intra osse\$ or intraperiton\$ or intra periton\$ or gavage or
nasogastric or naso gastric or rectal or proctocl\$)).ti,ab.
37 (fluid bolus or two bag or ORT).ti,ab.
38 or/28-37
39 and/20,38
40 TIME FACTORS/
41 DRUG ADMINISTRATION SCHEDULE/
42 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or
resuscitat\$) adj5 (rate? or variable rate? or fixed rate? or volume or fast or faster or quickly or
quicker or quick or rapid\$ or slow or slowly or slower or gradual\$ or earlier or early or later or
late)).ti,ab.
43 or/40-42
44 and/20,43

- 45 SODIUM/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
46 exp CHLORIDES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
47 GLUCOSE/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
48 GLUCOSE SOLUTION, HYPERTONIC/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
49 SALINE SOLUTION, HYPERTONIC/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
50 exp BICARBONATES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
51 POTASSIUM/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
52 PHOSPHATES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
53 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (chloride? or sodium chloride? or potassium chloride? or saline? or NaCl or KCl or glucose or dextrose or hydrogen carbonate? or bicarbonate? or carbonic acid or potassium or phosphate? or orthophosphate? or ortho phosphate?)).ti,ab.
54 or/45-53
55 and/20,54
56 or/27,39,44,55

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$ or high school\$).kw,tw,tx,jw,rw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or pre school\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).kw,tw,tx,jw,rw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).kw,tw,tx,jw,rw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pre pubert\$ or pubescen\$ or prepubescen\$ or pre pubescen\$).kw,tw,tx,jw,rw.
5 or/1-4
6 (diabetic ketoacidosis or DK or DKA).kw,tw,tx.
7 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).kw,tw,tx.
8 diabet\$.kw,tw,tx.
9 and/7-8
10 5 and (6 or 9)
11 (FLUID THERAPY or HYPODERMOCLYSIS).kw.
12 REHYDRATION SOLUTIONS.kw.
13 WATER-ELECTROLYTE BALANCE.kw.
14 WATER-ELECTROLYTE IMBALANCE.kw.
15 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj5 (manag\$ or regimen? or resuscit\$ or infusion? or administrat\$ or replac\$ or balanc\$ or imbalanc\$)).tw,tx.
16 or/11-15
17 and/10,16
18 DRUG ADMINISTRATION ROUTES.kw.
19 ADMINISTRATION, ORAL.kw.
20 ADMINISTRATION, INTRAVENOUS.kw.
21 INFUSIONS, INTRAVENOUS.kw.
22 INFUSIONS, INTRAOSSEOUS.kw.
23 INFUSIONS, SUBCUTANEOUS.kw.
24 INFUSION PUMP.kw.
25 INTUBATION, GASTROINTESTINAL.kw.
26 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (route? or intravenous\$ or oral or orally or mouth or subcutan\$ or hypodermocl\$ or intraosse\$ or intra osse\$ or intraperiton\$ or intra periton\$ or gavage or nasogastric or naso gastric or rectal or proctocl\$)).tw,tx.

- 27 (fluid bolus or two bag or ORT).tw,tx.
28 or/18-27
29 and/10,28
30 TIME FACTORS.kw.
31 DRUG ADMINISTRATION SCHEDULE.kw.
32 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (rate? or variable rate? or fixed rate? or volume or fast or faster or quickly or quicker or quick or rapid\$ or slow or slowly or slower or gradual\$ or earlier or early or later or late)).tw,tx.
33 or/30-32
34 and/10,33
35 SODIUM.kw.
36 CHLORIDE?.kw.
37 GLUCOSE.kw.
38 GLUCOSE SOLUTION, HYPERTONIC.kw.
39 SALINE SOLUTION, HYPERTONIC.kw.
40 BICARBONATE?.kw.
41 POTASSIUM.kw.
42 PHOSPHATES.kw.
43 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (chloride? or sodium chloride? or potassium chloride? or saline? or NaCl or KCl or glucose or dextrose or hydrogen carbonate? or bicarbonate? or carbonic acid or potassium or phosphate? or orthophosphate? or ortho phosphate?)).tw,tx.
44 or/35-43
45 and/10,44
46 or/17,29,34,45

Health Technology Assessment

- # Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$ or high school\$).tw,jx,rw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or pre school\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pre pubert\$ or pubescen\$ or prepubescen\$ or pre pubescen\$).tw,jx,rw.
9 or/1-8
10 DIABETIC KETOACIDOSIS/
11 (DK or DKA).tw.
12 or/10-11
13 exp KETOSIS/
14 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).tw.
15 or/13-14
16 exp DIABETES MELLITUS/
17 diabet\$.mp.
18 or/16-17
19 and/15,18
20 9 and (12 or 19)
21 exp FLUID THERAPY/

- 22 REHYDRATION SOLUTIONS/
23 WATER-ELECTROLYTE BALANCE/
24 WATER-ELECTROLYTE IMBALANCE/
25 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj5 (manag\$ or regimen? or resuscit\$ or infusion? or administrat\$ or replac\$ or balanc\$ or imbalanc\$)).tw.
26 or/21-25
27 and/20,26
28 DRUG ADMINISTRATION ROUTES/
29 ADMINISTRATION, ORAL/
30 ADMINISTRATION, INTRAVENOUS/
31 INFUSIONS, INTRAVENOUS/
32 INFUSIONS, INTRAOSSEOUS/
33 exp INFUSIONS, SUBCUTANEOUS/
34 INFUSION PUMP/
35 INTUBATION, GASTROINTESTINAL/
36 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (route? or intravenous\$ or oral or orally or mouth or subcutan\$ or hypodermocl\$ or intraosse\$ or intra osse\$ or intraperiton\$ or intra periton\$ or gavage or nasogastric or naso gastric or rectal or proctocl\$)).tw.
37 (fluid bolus or two bag or ORT).tw.
38 or/28-37
39 and/20,38
40 TIME FACTORS/
41 DRUG ADMINISTRATION SCHEDULE/
42 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (rate? or variable rate? or fixed rate? or volume or fast or faster or quickly or quicker or quick or rapid\$ or slow or slowly or slower or gradual\$ or earlier or early or later or late)).tw.
43 or/40-42
44 and/20,43
45 SODIUM/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
46 exp CHLORIDES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
47 GLUCOSE/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
48 GLUCOSE SOLUTION, HYPERTONIC/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
49 SALINE SOLUTION, HYPERTONIC/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
50 exp BICARBONATES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
51 POTASSIUM/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
52 PHOSPHATES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
53 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (chloride? or sodium chloride? or potassium chloride? or saline? or NaCl or KCl or glucose or dextrose or hydrogen carbonate? or bicarbonate? or carbonic acid or potassium or phosphate? or orthophosphate? or ortho phosphate?)).tw.
54 or/45-53
55 and/20,54
56 or/27,39,44,55

Embase

- # Searches
1 exp ADOLESCENT/
2 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
3 exp CHILD/

- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
9 or/1-8
10 INSULIN DEPENDENT DIABETES MELLITUS/
11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
13 or/10-12
14 NON INSULIN DEPENDENT DIABETES MELLITUS/
15 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
16 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
17 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18 or/14-17
19 JUVENILE DIABETES MELLITUS/
20 or/13,18-19
21 KETOACIDOSIS/
22 KETONURIA/
23 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
24 or/21-23
25 and/20,24
26 DIABETIC KETOACIDOSIS/
27 (DK or DKA).ti,ab.
28 or/26-27
29 9 and (25 or 28)
30 FLUID THERAPY/
31 FLUID RESUSCITATION/
32 exp REHYDRATION/
33 exp ELECTROLYTE BALANCE/
34 exp ELECTROLYTE DISTURBANCE/
35 ((fluid? or solution? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$) adj5 (manag\$ or regimen? or resuscit\$ or infusion? or administrat\$ or replac\$ or balanc\$ or imbalanc\$)).ti,ab.
36 or/30-35
37 and/29,36
38 DRUG ADMINISTRATION ROUTE/
39 INTRAVENOUS ADMINISTRATION/
40 INTRAGASTRIC DRUG ADMINISTRATION/
41 INTRAOSSEOUS DRUG ADMINISTRATION/
42 INTRAPERITONEAL DRUG ADMINISTRATION/
43 SUBCUTANEOUS DRUG ADMINISTRATION/
44 STOMACH INTUBATION/
45 ORAL REHYDRATION THERAPY/
46 ORAL REHYDRATION SOLUTION/
47 INFUSION SYSTEM/
48 INFUSION PUMP/
49 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (route? or intravenous\$ or oral or orally or mouth or subcutan\$ or hypodermocl\$ or intraosse\$ or intra osse\$ or intraperiton\$ or intra periton\$ or gavage or nasogastric or naso gastric or rectal or proctocl\$)).ti,ab.

- 50 (fluid bolus or two bag or ORT).ti,ab.
51 or/38-50
52 and/29,51
53 INFUSION RATE/
54 DRUG DOSE REGIMEN/
55 DRUG ADMINISTRATION/
56 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (rate? or variable rate? or fixed rate? or volume or fast or faster or quickly or quicker or quick or rapid\$ or slow or slowly or slower or gradual\$ or earlier or early or later or late)).ti,ab.
57 or/53-56
58 and/29,57
59 INFUSION FLUID/ad, dt, ig, os, iv, po, pa, sc [Drug Administration, Drug Therapy, Intra gastric Drug Administration, Intraosseous Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Subcutaneous Drug Administration]
60 SODIUM/ad, dt, ip, iv, po, pa, sc, th [Drug Administration, Drug Therapy, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Subcutaneous Drug Administration, Therapy]
61 CHLORIDE/ad, dt, ip, iv, po, pa, sc, th [Drug Administration, Drug Therapy, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Subcutaneous Drug Administration, Therapy]
62 SODIUM CHLORIDE/ad, dt, dl, ig, os, ip, iv, po, pa, rc, sc, th [Drug Administration, Drug Therapy, Intradermal Drug Administration, Intra gastric Drug Administration, Intraosseous Drug Administration, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Rectal Drug Administration, Subcutaneous Drug Administration, Therapy]
63 GLUCOSE/ad, dt, ig, os, ip, iv, po, pa, rc, sc, th [Drug Administration, Drug Therapy, Intra gastric Drug Administration, Intraosseous Drug Administration, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Rectal Drug Administration, Subcutaneous Drug Administration, Therapy]
64 GLUCOSE INFUSION/
65 BICARBONATE/ad, dt, ig, os, ip, iv, po, pa, rc, sc, th [Drug Administration, Drug Therapy, Intra gastric Drug Administration, Intraosseous Drug Administration, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Rectal Drug Administration, Subcutaneous Drug Administration, Therapy]
66 POTASSIUM/ad, dt, ig, os, ip, iv, po, pa, rc, sc, th [Drug Administration, Drug Therapy, Intra gastric Drug Administration, Intraosseous Drug Administration, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Rectal Drug Administration, Subcutaneous Drug Administration, Therapy]
67 PHOSPHATE/ad, dt, ig, ip, iv, po, pa, rc, th [Drug Administration, Drug Therapy, Intra gastric Drug Administration, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Rectal Drug Administration, Therapy]
68 exp ELECTROLYTE BLOOD LEVEL/
69 BICARBONATE BLOOD LEVEL/
70 GLUCOSE BLOOD LEVEL/
71 PHOSPHATE BLOOD LEVEL/
72 ((fluid? or solution? or infusion? or electrolyte? or hydrat\$ or rehydrat\$ or re hydrat\$ or resuscitat\$) adj5 (chloride? or sodium chloride? or potassium chloride? or saline? or NaCl or KCl or glucose or dextrose or hydrogen carbonate? or bicarbonate? or carbonic acid? or potassium or phosphate? or orthophosphate? or ortho phosphate?)).ti,ab.
73 or/59-72
74 and/29,73
75 or/37,52,58,74
76 conference abstract.pt.
77 letter.pt. or LETTER/
78 note.pt.

79 editorial.pt.
80 CASE REPORT/ or CASE STUDY/
81 (letter or comment* or abstracts).ti.
82 or/76-81
83 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
84 82 not 83
85 ANIMAL/ not HUMAN/
86 NONHUMAN/
87 exp ANIMAL EXPERIMENT/
88 exp EXPERIMENTAL ANIMAL/
89 ANIMAL MODEL/
90 exp RODENT/
91 (rat or rats or mouse or mice).ti.
92 or/84-91
93 75 not 92
94 limit 93 to english language

F.13 Type 1 and type 2 diabetes – diabetic ketoacidosis intravenous osmotic agents

Review question: What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?

Ovid MEDLINE(R)

Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
9 or/1-8
10 DIABETIC KETOACIDOSIS/
11 (DK or DKA).ti,ab.
12 or/10-11
13 exp KETOSIS/
14 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
15 or/13-14
16 exp DIABETES MELLITUS/
17 diabet\$.mp.
18 or/16-17
19 and/15,18
20 9 and (12 or 19)
21 BRAIN EDEMA/
22 ((brain or cerebral) adj3 (edema? or oedema? or swell\$)).ti,ab.
23 INTRACRANIAL PRESSURE/
24 INTRACRANIAL HYPERTENSION/

- 25 ((intracranial or intracerebral or subarachnoid or "sub arachnoid") adj3 (pressure or hypertens\$)).ti,ab.
26 ICP.ti,ab.
27 or/21-26
28 DIURETICS, OSMOTIC/
29 osmotherap\$.ti,ab.
30 (osmo\$ adj3 (therap\$ or agent? or solution? or serum or plasma or blood)).ti,ab.
31 SALINE SOLUTION, HYPERTONIC/
32 SODIUM CHLORIDE/
33 (hyperton\$ adj3 (saline or solution?)).ti,ab.
34 (saline or sodium chloride or NaCl).ti,ab.
35 MANNITOL/
36 (mannitol or viaflo or viaflex).ti,ab.
37 or/28-36
38 and/20,27,37
39 limit 38 to english language
40 LETTER/
41 EDITORIAL/
42 NEWS/
43 exp HISTORICAL ARTICLE/
44 ANECDOTES AS TOPIC/
45 COMMENT/
46 CASE REPORT/
47 (letter or comment* or abstracts).ti.
48 or/40-47
49 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
50 48 not 49
51 ANIMALS/ not HUMANS/
52 exp ANIMALS, LABORATORY/
53 exp ANIMAL EXPERIMENTATION/
54 exp MODELS, ANIMAL/
55 exp RODENTIA/
56 (rat or rats or mouse or mice).ti.
57 or/50-56
58 39 not 57

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
5 or/1-4
6 (DK or DKA).ti,ab.
7 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
8 diabet\$.mp.
9 and/7-8
10 5 and (6 or 9)
11 ((brain or cerebral) adj3 (edema? or oedema? or swell\$)).ti,ab.
12 ((intracranial or intracerebral or subarachnoid or "sub arachnoid") adj3 (pressure or hypertens\$)).ti,ab.

- 13 ICP.ti,ab.
- 14 or/11-13
- 15 osmotherap\$.ti,ab.
- 16 (osmo\$ adj3 (therap\$ or agent? or solution? or serum or plasma or blood)).ti,ab.
- 17 (hyperton\$ adj3 (saline or solution?)).ti,ab.
- 18 (saline or sodium chloride or NaCl).ti,ab.
- 19 (mannitol or viaflo or viaflex).ti,ab.
- 20 or/15-19
- 21 and/10,14,20
- 22 limit 21 to english language

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 DIABETIC KETOACIDOSIS/
- 11 (DK or DKA).ti,ab.
- 12 or/10-11
- 13 exp KETOSIS/
- 14 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
- 15 or/13-14
- 16 exp DIABETES MELLITUS/
- 17 diabet\$.mp.
- 18 or/16-17
- 19 and/15,18
- 20 9 and (12 or 19)
- 21 BRAIN EDEMA/
- 22 ((brain or cerebral) adj3 (edema? or oedema? or swell\$)).ti,ab.
- 23 INTRACRANIAL PRESSURE/
- 24 INTRACRANIAL HYPERTENSION/
- 25 ((intracranial or intracerebral or subarachnoid or "sub arachnoid") adj3 (pressure or hypertens\$)).ti,ab.
- 26 ICP.ti,ab.
- 27 or/21-26
- 28 DIURETICS, OSMOTIC/
- 29 osmotherap\$.ti,ab.
- 30 (osmo\$ adj3 (therap\$ or agent? or solution? or serum or plasma or blood)).ti,ab.
- 31 SALINE SOLUTION, HYPERTONIC/
- 32 SODIUM CHLORIDE/
- 33 (hyperton\$ adj3 (saline or solution?)).ti,ab.
- 34 (saline or sodium chloride or NaCl).ti,ab.
- 35 MANNITOL/
- 36 (mannitol or viaflo or viaflex).ti,ab.
- 37 or/28-36

38 and/20,27,37

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

Searches
1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,tx,kw,jw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,tx,kw,jw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx,kw,jw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,tx,kw,jw.
5 or/1-4
6 DIABETIC KETOACIDOSIS.kw.
7 (DK or DKA).tw,tx.
8 or/6-7
9 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).tw,tx,kw.
10 diabet\$.tw,tx,kw.
11 and/9-10
12 5 and (8 or 11)
13 ((brain or cerebral) adj3 (edema? or oedema? or swell\$)).tw,tx,kw.
14 ((intracranial or intracerebral or subarachnoid or "sub arachnoid") adj3 (pressure or hypertens\$)).tw,tx,kw.
15 ICP.tw,tx.
16 or/13-15
17 DIURETICS, OSMOTIC.kw.
18 osmotherap\$.tw,tx.
19 (osmo\$ adj3 (therap\$ or agent? or solution? or serum or plasma or blood)).tw,tx.
20 (hyperton\$ adj3 (saline or solution?)).tw,tx,kw.
21 (saline or sodium chloride or NaCl).tw,tx,kw.
22 (mannitol or viaflo or viaflex).tw,tx,kw.
23 or/17-22
24 and/12,16,23

Health Technology Assessment

Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jx.
9 or/1-8
10 DIABETIC KETOACIDOSIS/
11 (DK or DKA).tw.
12 or/10-11
13 exp KETOSIS/
14 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).tw.
15 or/13-14
16 exp DIABETES MELLITUS/

- 17 diabet\$.mp.
- 18 or/16-17
- 19 and/15,18
- 20 9 and (12 or 19)
- 21 BRAIN EDEMA/
22 ((brain or cerebral) adj3 (edema? or oedema? or swell\$)).tw.
- 23 INTRACRANIAL PRESSURE/
24 INTRACRANIAL HYPERTENSION/
25 ((intracranial or intracerebral or subarachnoid or "sub arachnoid") adj3 (pressure or hypertens\$)).tw.
- 26 ICP.tw.
- 27 or/21-26
- 28 DIURETICS, OSMOTIC/
29 osmotherap\$.tw.
30 (osmo\$ adj3 (therap\$ or agent? or solution? or serum or plasma or blood)).tw.
- 31 SALINE SOLUTION, HYPERTONIC/
32 SODIUM CHLORIDE/
33 (hyperton\$ adj3 (saline or solution?)).tw.
34 (saline or sodium chloride or NaCl).tw.
- 35 MANNITOL/
36 (mannitol or viaflo or viaflex).tw.
- 37 or/28-36
- 38 and/20,27,37

Embase

- # Searches
- 1 exp ADOLESCENT/
2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
- 3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
- 5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
- 7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
- 9 or/1-8
- 10 DIABETIC KETOACIDOSIS/
11 (DK or DKA).ti,ab.
- 12 or/10-11
- 13 KETOACIDOSIS/
14 KETONURIA/
15 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
- 16 or/13-15
- 17 exp DIABETES MELLITUS/
18 diabet\$.mp.
- 19 or/17-18
- 20 and/16,19
- 21 9 and (12 or 20)
- 22 BRAIN EDEMA/
23 ((brain or cerebral) adj3 (edema? or oedema? or swell\$)).ti,ab.
- 24 INTRACRANIAL PRESSURE/
25 INTRACRANIAL HYPERTENSION/

- 26 ((intracranial or intracerebral or subarachnoid or "sub arachnoid") adj3 (pressure or hypertens\$)).ti,ab.
- 27 ICP.ti,ab.
- 28 or/22-27
- 29 exp OSMOTIC AGENT/
30 osmotherap\$.ti,ab.
- 31 (osmo\$ adj3 (therap\$ or agent? or solution? or serum or plasma or blood)).ti,ab.
- 32 HYPERTONIC SOLUTION/
33 SODIUM CHLORIDE/
34 (hyperton\$ adj3 (saline or solution?)).ti,ab.
- 35 (saline or sodium chloride or NaCl).ti,ab.
- 36 MANNITOL/
37 (mannitol or viaflo or viaflex).ti,ab.
- 38 or/29-37
- 39 and/21,28,38
- 40 limit 39 to english language
- 41 conference abstract.pt.
- 42 letter.pt. or LETTER/
43 note.pt.
- 44 editorial.pt.
- 45 CASE REPORT/ or CASE STUDY/
46 (letter or comment* or abstracts).ti.
- 47 or/41-46
- 48 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 49 47 not 48
- 50 ANIMAL/ not HUMAN/
51 NONHUMAN/
52 exp ANIMAL EXPERIMENT/
53 exp EXPERIMENTAL ANIMAL/
54 ANIMAL MODEL/
55 exp RODENT/
56 (rat or rats or mouse or mice).ti.
- 57 or/49-56
- 58 40 not 57

F.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

Review questions:

When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?

How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

Ovid MEDLINE(R)

- # Searches
- 1 randomized controlled trial.pt.
- 2 controlled clinical trial.pt.
- 3 DOUBLE BLIND METHOD/
4 SINGLE BLIND METHOD/
5 RANDOM ALLOCATION/

6 RANDOMIZED CONTROLLED TRIALS AS TOPIC/
7 or/1-6
8 ((single or double or triple or treble) adj5 (blind\$ or mask\$)).tw,sh.
9 clinical trial.pt.
10 exp CLINICAL TRIAL/
11 exp CLINICAL TRIALS AS TOPIC/
12 (clinic\$ adj5 trial\$).tw,sh.
13 PLACEBOS/
14 placebo\$.tw,sh.
15 random\$.tw,sh.
16 or/8-15
17 or/7,16
18 META ANALYSIS/
19 META ANALYSIS AS TOPIC/
20 meta analysis.pt.
21 (metaanaly\$ or meta-analy\$ or (meta adj analy\$)).tw,sh.
22 (systematic\$ adj5 (review\$ or overview\$)).tw,sh.
23 (methodologic\$ adj5 (review\$ or overview\$)).tw,sh.
24 or/18-23
25 review\$.pt.
26 (medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or
27 psyclit or "web of science" or "science citation" or scisearch).tw.
28 ((hand or manual\$) adj2 search\$).tw.
29 (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online
30 database\$).tw,sh.
31 (pooling or pooled or mantel haenszel).tw,sh.
32 (peto or dersimonian or der simonian or fixed effect).tw,sh.
33 or/26-30
34 and/25,31
35 exp CASE-CONTROL STUDIES/
36 (case\$ adj2 control\$).tw.
37 exp COHORT STUDIES/
38 cohort\$.tw.
39 or/33-36
40 or/17,24,32,37
41 letter.pt.
42 comment.pt.
43 editorial.pt.
44 historical article.pt.
45 or/39-42
46 38 not 43
47 ADOLESCENT/ or MINORS/
48 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
49 exp CHILD/
50 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or
51 kindergar\$ or boy? or girl?).ti,ab,jw.
52 exp INFANT/
53 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
54 exp PEDIATRICS/ or exp PUBERTY/
55 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
56 or/45-52
57 exp KETOSIS/

- 55 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
56 (DK or DKA).ti,ab.
57 or/54-56
58 exp DIABETES MELLITUS/
59 diabet\$.mp.
60 or/58-59
61 and/53,57,60
62 exp INSULINS/
63 INSULIN INFUSION SYSTEMS/
64 or/62-63
65 exp DRUG ADMINISTRATION SCHEDULE/
66 TIME FACTORS/
67 DOSE-RESPONSE RELATIONSHIP, DRUG/
68 DRUG DOSAGE CALCULATIONS/
69 or/65-68
70 and/64,69
71 exp INSULINS/ad [Administration & Dosage]
72 (insulin\$ adj5 (early or earli\$ or delay\$ or start? or starting or stop? or stopping or intermittent\$ or time or timing)).ti,ab.
73 (insulin\$ adj5 (high-dose? or high-dosage? or low-dose or low-dosage? or dose? or dosage? or bolus\$ or priming or loading)).ti,ab.
74 or/70-73
75 and/61,74
76 and/44,75
77 LETTER/
78 EDITORIAL/
79 NEWS/
80 exp HISTORICAL ARTICLE/
81 ANECDOTES AS TOPIC/
82 COMMENT/
83 CASE REPORT/
84 (letter or comment* or abstracts).ti.
85 or/77-84
86 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
87 85 not 86
88 ANIMALS/ not HUMANS/
89 exp ANIMALS, LABORATORY/
90 exp ANIMAL EXPERIMENTATION/
91 exp MODELS, ANIMAL/
92 exp RODENTIA/
93 (rat or rats or mouse or mice).ti.
94 or/87-93
95 76 not 94
96 limit 95 to english language

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.

- 5 or/1-4
- 6 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
- 7 (DK or DKA).ti,ab.
- 8 or/6-7
- 9 diabet\$.mp.
- 10 and/5,8-9
- 11 (insulin\$ adj5 (early or earli\$ or delay\$ or start? or starting or stop? or stopping or intermittent\$ or time or timing)).ti,ab.
- 12 (insulin\$ adj5 (high-dose? or high-dosage? or low-dose or low-dosage? or dose? or dosage? or bolus\$ or priming or loading)).ti,ab.
- 13 or/11-12
- 14 and/10,13

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 exp KETOSIS/
- 11 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
- 12 (DK or DKA).ti,ab.
- 13 or/10-12
- 14 exp DIABETES MELLITUS/
- 15 diabet\$.mp.
- 16 or/14-15
- 17 and/9,13,16
- 18 exp INSULINS/
- 19 INSULIN INFUSION SYSTEMS/
- 20 or/18-19
- 21 exp DRUG ADMINISTRATION SCHEDULE/
- 22 TIME FACTORS/
- 23 DOSE-RESPONSE RELATIONSHIP, DRUG/
- 24 DRUG DOSAGE CALCULATIONS/
- 25 or/21-24
- 26 and/20,25
- 27 exp INSULINS/ad [Administration & Dosage]
- 28 (insulin\$ adj5 (early or earli\$ or delay\$ or start? or starting or stop? or stopping or intermittent\$ or time or timing)).ti,ab.
- 29 (insulin\$ adj5 (high-dose? or high-dosage? or low-dose or low-dosage? or dose? or dosage? or bolus\$ or priming or loading)).ti,ab.
- 30 or/26-29
- 31 and/17,30

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).kw,tw,tx,jw,rw.
 - 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,tx,kw,jw,rw.
 - 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx,kw,jw,rw.
 - 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,tx,kw,jw,rw.
 - 5 or/1-4
 - 6 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).tw,tx,kw.
 - 7 (DK or DKA).tw,tx.
 - 8 or/6-7
 - 9 diabet\$.tw,tx,kw.
 - 10 and/5,8-9
 - 11 insulin\$.tw,tx,kw.
 - 12 TIME FACTORS.kw.
 - 13 DOSE-RESPONSE.kw.
 - 14 DRUG DOSAGE CALCULATIONS.kw.
 - 15 or/12-14
 - 16 and/11,15
 - 17 (insulin\$ adj5 (early or earli\$ or delay\$ or start? or starting or stop? or stopping or intermittent\$ or time or timing)).tw,tx.
 - 18 (insulin\$ adj5 (high-dose? or high-dosage? or low-dose or low-dosage? or dose? or dosage? or bolus\$ or priming or loading)).tw,tx.
 - 19 or/16-18
 - 20 and/10,19

NHS Economic Evaluation Database

- # Searches
- 1 ADOLESCENT/ or MINORS/
 - 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx,rw.
 - 3 exp CHILD/
 - 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
 - 5 exp INFANT/
 - 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw.
 - 7 exp PEDIATRICS/ or exp PUBERTY/
 - 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jx,rw.
 - 9 or/1-8
 - 10 DIABETIC KETOACIDOSIS/
 - 11 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).tw.
 - 12 (DK or DKA).tw.
 - 13 or/10-12
 - 14 exp DIABETES MELLITUS/
 - 15 diabet\$.mp.
 - 16 or/14-15
 - 17 and/9,13,16
 - 18 exp INSULIN/
 - 19 INSULIN INFUSION SYSTEMS/
 - 20 or/18-19
 - 21 exp DRUG ADMINISTRATION SCHEDULE/

- 22 TIME FACTORS/
- 23 DOSE-RESPONSE RELATIONSHIP, DRUG/
- 24 DRUG DOSAGE CALCULATIONS/
- 25 or/21-24
- 26 and/20,25
- 27 (insulin\$ adj5 (early or earli\$ or delay\$ or start? or starting or stop? or stopping or intermittent\$ or time or timing)).tw.
- 28 (insulin\$ adj5 (high-dose? or high-dosage? or low-dose or low-dosage? or dose? or dosage? or bolus\$ or priming or loading)).tw.
- 29 or/26-28
- 30 and/17,29

Embase

- # Searches
- 1 CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
- 2 (clinic\$ adj5 trial\$).tw,sh.
- 3 SINGLE BLIND PROCEDURE/
- 4 DOUBLE BLIND PROCEDURE/
- 5 RANDOM ALLOCATION/
- 6 CROSSOVER PROCEDURE/
- 7 PLACEBO/
- 8 placebo\$.tw,sh.
- 9 random\$.tw,sh.
- 10 RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
- 11 ((single or double or triple or treble) adj (blind\$ or mask\$)).tw,sh.
- 12 randomi?ed control\$ trial\$.tw.
- 13 or/1-12
- 14 META ANALYSIS/
- 15 ((meta adj analy\$) or metaanalys\$ or meta-analy\$).tw,sh.
- 16 (systematic\$ adj5 (review\$ or overview\$)).tw,sh.
- 17 (methodologic\$ adj5 (review\$ or overview\$)).tw,sh.
- 18 or/14-17
- 19 review.pt.
- 20 (medline or medlars or embase).ab.
- 21 (scisearch or science citation index).ab.
- 22 (psychlit or psychlit or psychinfo or psycinfo or cinahl or cochrane).ab.
- 23 ((hand or manual\$) adj2 search\$).tw.
- 24 (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online database\$).tw.
- 25 (pooling or pooled or mantel haenszel).tw.
- 26 (peto or dersimonian or "der simonian" or fixed effect).tw.
- 27 or/20-26
- 28 and/19,27
- 29 exp CASE CONTROL STUDY/
- 30 RETROSPECTIVE STUDY/
- 31 (case\$ adj2 control\$).tw.
- 32 COHORT ANALYSIS/
- 33 LONGITUDINAL STUDY/
- 34 FOLLOW UP/
- 35 PROSPECTIVE STUDY/
- 36 cohort\$.tw.
- 37 or/29-36
- 38 or/13,18,28,37

- 39 (book or conference paper or editorial or letter or note or proceeding or short survey).pt.
40 38 not 39
41 exp ADOLESCENT/
42 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
43 exp CHILD/
44 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
45 exp INFANT/
46 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
47 exp PEDIATRICS/ or exp PUBERTY/
48 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
49 or/41-48
50 KETOACIDOSIS/ or DIABETIC KETOACIDOSIS/
51 KETONURIA/
52 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
53 (DK or DKA).ti,ab.
54 or/50-53
55 exp DIABETES MELLITUS/
56 diabet\$.mp.
57 or/55-56
58 and/49,54,57
59 exp INSULIN DERIVATIVE/
60 INSULIN TREATMENT/ or INSULIN INFUSION/
61 or/59-60
62 DRUG DOSE/ or DOSE CALCULATION/ or DOSAGE SCHEDULE COMPARISON/ or DRUG DOSE COMPARISON/ or DRUG DOSE ESCALATION/ or DRUG DOSE INCREASE/ or DRUG DOSE INTENSIFICATION/ or DRUG DOSE REDUCTION/ or DRUG DOSE REGIMEN/ or LOADING DRUG DOSE/ or LOW DRUG DOSE/ or MAINTENANCE DRUG DOSE/ or OPTIMAL DRUG DOSE/
63 EARLY INTERVENTION/
64 TREATMENT DURATION/
65 THERAPY DELAY/
66 or/62-65
67 and/61,66
68 exp INSULIN DERIVATIVE/do, iv [Drug Dose, Intravenous Drug Administration]
69 (insulin\$ adj5 (high-dose? or high-dosage? or low-dose or low-dosage? or dose? or dosage? or bolus\$ or priming or loading)).ti,ab.
70 (insulin\$ adj5 (early or earli\$ or delay\$ or start? or starting or stop? or stopping or time or timing)).ti,ab.
71 or/67-70
72 and/58,71
73 and/40,72
74 conference abstract.pt.
75 letter.pt. or LETTER/
76 note.pt.
77 editorial.pt.
78 CASE REPORT/ or CASE STUDY/
79 (letter or comment* or abstracts).ti.
80 or/74-79
81 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
82 80 not 81
83 ANIMAL/ not HUMAN/
84 NONHUMAN/

- 85 exp ANIMAL EXPERIMENT/
- 86 exp EXPERIMENTAL ANIMAL/
- 87 ANIMAL MODEL/
- 88 exp RODENT/
- 89 (rat or rats or mouse or mice).ti.
- 90 or/82-89
- 91 73 not 90
- 92 limit 91 to english language

F.15 Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis

Review question: What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?

Ovid MEDLINE(R)

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 exp KETOSIS/
- 11 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
- 12 (DK or DKA).ti,ab.
- 13 or/10-12
- 14 exp DIABETES MELLITUS/
- 15 diabet\$.mp.
- 16 or/14-15
- 17 and/9,13,16
- 18 exp ANTICOAGULANTS/
- 19 exp FIBRINOLYTIC AGENTS/
- 20 exp THROMBOLYTIC THERAPY/
- 21 ASPIRIN/
- 22 DICUMAROL/
- 23 WARFARIN/
- 24 exp HEPARIN/
- 25 (anticoagula\$ or aspirin\$ or dalteparin\$ or nadroparin\$ or enoxaparin\$ or dic?umarol or fragmin\$ or heparin\$ or UFH or LMWH or warfarin\$ or fibrinoly\$).ti,ab,nm.
- 26 or/18-25
- 27 exp "EMBOLISM AND THROMBOSIS"/
- 28 exp HEMORRHAGE/
- 29 (mo or ut or ae or co).fs.
- 30 PATIENT SATISFACTION/

- 31 (thromboprophyla\$ or thrombus\$ or thrombi or thrombotic\$ or thrombolic\$ or thromboly\$ or thromboemboli\$ or thrombocyt\$ or thrombos\$ or emboli\$ or bleed\$ or h?emorrag\$ or adverse or complication? or mortalit\$ or utili#ation or satisfaction or satisfied).ti,ab.
- 32 or/27-31
- 33 and/17,26,32
- 34 LETTER/
- 35 EDITORIAL/
- 36 NEWS/
- 37 exp HISTORICAL ARTICLE/
- 38 ANECDOTES AS TOPIC/
- 39 COMMENT/
- 40 CASE REPORT/
- 41 (letter or comment* or abstracts).ti.
- 42 or/34-41
- 43 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 44 42 not 43
- 45 ANIMALS/ not HUMANS/
- 46 exp ANIMALS, LABORATORY/
- 47 exp ANIMAL EXPERIMENTATION/
- 48 exp MODELS, ANIMAL/
- 49 exp RODENTIA/
- 50 (rat or rats or mouse or mice).ti.
- 51 or/44-50
- 52 33 not 51

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 5 or/1-4
- 6 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
- 7 (DK or DKA).ti,ab.
- 8 or/6-7
- 9 diabet\$.mp.
- 10 and/5,8-9
- 11 (anticoagula\$ or aspirin\$ or dalteparin\$ or nadroparin\$ or enoxaparin\$ or dic?umarol or fragmin\$ or heparin\$ or UFH or LMWH or warfarin\$ or fibrinoly\$).ti,ab.
- 12 (thromboprophyla\$ or thrombus\$ or thrombi or thrombotic\$ or thrombolic\$ or thromboly\$ or thromboemboli\$ or thrombocyt\$ or thrombos\$ or emboli\$ or bleed\$ or h?emorrag\$ or adverse or complication? or mortalit\$ or utili#ation or satisfaction or satisfied).ti,ab.
- 13 and/10-12

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/

- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
9 or/1-8
10 exp KETOSIS/
11 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
12 (DK or DKA).ti,ab.
13 or/10-12
14 exp DIABETES MELLITUS/
15 diabet\$.mp.
16 or/14-15
17 and/9,13,16
18 exp ANTICOAGULANTS/
19 exp FIBRINOLYTIC AGENTS/
20 exp THROMBOLYTIC THERAPY/
21 ASPIRIN/
22 DICUMAROL/
23 WARFARIN/
24 exp HEPARIN/
25 (anticoagula\$ or aspirin\$ or dalteparin\$ or nadroparin\$ or enoxaparin\$ or dic?umarol or fragmin\$ or heparin\$ or UFH or LMWH or warfarin\$ or fibrinoly\$).ti,ab.
26 or/18-25
27 exp "EMBOLISM AND THROMBOSIS"/
28 exp HEMORRHAGE/
29 (mo or ut or ae or co).fs.
30 PATIENT SATISFACTION/
31 (thromboprophyla\$ or thrombus\$ or thrombi or thrombotic\$ or thrombolic\$ or thromboly\$ or thromboemboli\$ or thrombocyt\$ or thrombos\$ or emboli\$ or bleed\$ or h?emorrag\$ or adverse or complication? or mortalit\$ or utili#ation or satisfaction or satisfied).ti,ab.
32 or/27-31
33 and/17,26,32

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).kw,tw,tx,jw,rw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).kw,tw,tx,jw,rw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).kw,tw,tx,jw,rw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).kw,tw,tx,jw,rw.
5 or/1-4
6 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).kw,tw,tx.
7 (DK or DKA).kw,tw,tx.
8 or/6-7
9 diabet\$.kw,tw,tx.
10 and/5,8-9
11 ANTICOAGULANT\$.kw.
12 FIBRINOLYTIC\$.kw.
13 (THROMBOL\$ or HIRUDIN).kw.
14 ASPIRIN.kw.
15 DICUMAROL.kw.

- 16 WARFARIN.kw.
17 HEPARIN\$.kw.
18 (anticoagula\$ or aspirin\$ or dalteparin\$ or nadroparin\$ or enoxaparin\$ or dic?umarol or fragmin\$ or heparin\$ or UFH or LMWH or warfarin\$ or fibrinoly\$).tw,tx.
19 or/11-18
20 (EMBOLI\$ or THROMBO\$).kw.
21 HEMORRHAGE.kw.
22 SATISFACTION.kw.
23 (thromboprophyla\$ or thrombus\$ or thrombi or thrombotic\$ or thrombolic\$ or thromboly\$ or thromboemboli\$ or thrombocyt\$ or thrombos\$ or emboli\$ or bleed\$ or h?emorrag\$ or adverse or complication? or mortalit\$ or utili#ation or satisfaction or satisfied).tw,tx.
24 or/20-23
25 and/10,19,24

Health Technology Assessment

- # Searches
1 ADOLESCENT/ or MINORS/
2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx,rw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jx,rw.
9 or/1-8
10 exp KETOSIS/
11 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).tw.
12 (DK or DKA).tw.
13 or/10-12
14 exp DIABETES MELLITUS/
15 diabet\$.mp.
16 or/14-15
17 and/9,13,16
18 exp ANTICOAGULANTS/
19 exp FIBRINOLYTIC AGENTS/
20 exp THROMBOLYTIC THERAPY/
21 ASPIRIN/
22 DICUMAROL/
23 WARFARIN/
24 exp HEPARIN/
25 (anticoagula\$ or aspirin\$ or dalteparin\$ or nadroparin\$ or enoxaparin\$ or dic?umarol or fragmin\$ or heparin\$ or UFH or LMWH or warfarin\$ or fibrinoly\$).tw.
26 or/18-25
27 exp "EMBOLISM AND THROMBOSIS"/
28 exp HEMORRHAGE/
29 (mo or ut or ae or co).fs.
30 PATIENT SATISFACTION/
31 (thromboprophyla\$ or thrombus\$ or thrombi or thrombotic\$ or thrombolic\$ or thromboly\$ or thromboemboli\$ or thrombocyt\$ or thrombos\$ or emboli\$ or bleed\$ or h?emorrag\$ or adverse or complication? or mortalit\$ or utili#ation or satisfaction or satisfied).tw.
32 or/27-31
33 and/17,26,32

Embase

- # Searches
- 1 exp ADOLESCENT/
2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
7 exp PEDIATRICS/ or exp PUBERTY/
8 p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
9 or/1-8
10 INSULIN DEPENDENT DIABETES MELLITUS/
11 (diabet\$ adj5 ("type one" or "type 1" or "type II" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
13 or/10-12
14 NON INSULIN DEPENDENT DIABETES MELLITUS/
15 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
16 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
17 (NIDDM or T2D or T2D or DM2 or DMII).ti,ab.
18 or/14-17
19 or/13,18
20 JUVENILE DIABETES MELLITUS/
21 and/9,19
22 or/20-21
23 KETOACIDOSIS/ or DIABETIC KETOACIDOSIS/
24 KETONURIA/
25 (ketosis or ketoacid\$ or keto acid\$ or ketotic or ketonuri\$ or keton?emi\$ or hyperketon\$ or ketogenesis).ti,ab.
26 (DK or DKA).ti,ab.
27 or/23-26
28 and/22,27
29 exp ANTICOAGULANT AGENT/
30 ANTICOAGULANT THERAPY/
31 FIBRINOLYTIC AGENT/
32 FIBRINOLYTIC THERAPY/
33 EMBOLISM PREVENTION/
34 THROMBOSIS PREVENTION/
35 ACETYLSALICYLIC ACID/
36 DICOUMAROL/
37 WARFARIN/
38 exp HEPARIN DERIVATIVE/
39 (anticoagula\$ or aspirin\$ or dalteparin\$ or nadroparin\$ or enoxaparin\$ or dic?umarol or fragmin\$ or heparin\$ or UFH or LMWH or warfarin\$ or fibrinoly\$).ti,ab,rn.
40 or/29-39
41 exp THROMBOEMBOLISM/
42 exp THROMBOCYTOPENIA/
43 exp BLEEDING/
44 ADVERSE DRUG REACTION/
45 exp COMPLICATION/
46 MORTALITY/

- 47 HEALTH CARE UTILIZATION/
- 48 PATIENT SATISFACTION/
- 49 (thromboprophyla\$ or thrombus\$ or thrombi or thrombotic\$ or thrombolic\$ or thromboly\$ or thromboemboli\$ or thrombocyt\$ or thrombos\$ or emboli\$ or bleed\$ or h?emorrag\$ or adverse or complication? or mortalit\$ or utili#ation or satisfaction or satisfied).ti,ab.
- 50 or/41-49
- 51 and/28,40,50
- 52 conference abstract.pt.
- 53 letter.pt. or LETTER/
- 54 note.pt.
- 55 editorial.pt.
- 56 CASE REPORT/ or CASE STUDY/
- 57 (letter or comment* or abstracts).ti.
- 58 or/52-57
- 59 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 60 58 not 59
- 61 ANIMAL/ not HUMAN/
- 62 NONHUMAN/
- 63 exp ANIMAL EXPERIMENT/
- 64 exp EXPERIMENTAL ANIMAL/
- 65 ANIMAL MODEL/
- 66 exp RODENT/
- 67 (rat or rats or mouse or mice).ti.
- 68 or/60-67
- 69 51 not 68

F.16 Type 1 and type 2 diabetes – retinopathy

Review questions:

What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?

What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?

Ovid MEDLINE(R)

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 1/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or Tl or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
- 13 or/10-12

14 exp DIABETES MELLITUS, TYPE 2/
15 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late
or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
16 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
17 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18 or/14-17
19 or/13,18
20 DIABETIC RETINOPATHY/
21 (diabet\$ adj3 retinopath\$).ti,ab.
22 or/20-21
23 RETINAL DISEASES/
24 retinopath\$.ti,ab.
25 or/23-24
26 DIAGNOSTIC TECHNIQUES, OPHTHALMOLOGICAL/
27 exp OPHTHALMOSCOPY/
28 FUNDUS OCULI/
29 RETINA/ or RETINAL VESSELS/
30 PHOTOGRAPHY/
31 and/29-30
32 ((retina\$ or fundus or ocul\$ or eye?) adj3 (photograph\$ or exam\$)).ti,ab.
33 (op?thalmoscop\$ or retinoscop\$).ti,ab.
34 fundus oculi.ti,ab.
35 or/26-28,31-34
36 MASS SCREENING/
37 VISION SCREENING/
38 exp POPULATION SURVEILLANCE/
39 (undiagnos\$ or estimate\$).ti.
40 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
41 or/36-40
42 SEVERITY OF ILLNESS INDEX/
43 INTERNATIONAL CLASSIFICATION OF DISEASES/
44 CLASSIFICATION/
45 (retinopath\$ adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging)).ti,ab.
46 or/42-45
47 exp EYE HEMORRHAGE/
48 h?emorrhag\$.ti,ab.
49 exp ANEURYSM/
50 (microaneurysm? or micro aneurysm?).ti,ab.
51 "EXUDATES AND TRANSUDATES"/
52 exp EYE/
53 and/51-52
54 SUBRETINAL FLUID/
55 exudate?.ti,ab.
56 PAPILLEDEMA/
57 EDEMA/
58 exp EYE/
59 and/57-58
60 (papill?edem\$ or papillitis or choked dis??).ti,ab.
61 ((retina\$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).ti,ab.
62 RETINAL NEOVASCULARIZATION/
63 NEOVASCULARIZATION, PATHOLOGIC/ or VASCULAR MALFORMATIONS/
64 exp EYE/ or RETINAL VESSELS/
65 and/63-64

66 exp RETINAL VESSELS/pa, pp [Pathology, Physiopathology]
67 neovascular\$.ti,ab.
68 (new adj2 vessel adj2 form\$).ti,ab.
69 ((venous or vascular or microvascular or fibrovascular) adj3 (abnormal\$ or malform\$ or loop\$ or bead\$ or reduplicat\$ or duplicat\$ or proliferat\$)).ti,ab.
70 (IRMA or ((intra retinal or intra retinal) adj microvascular adj abnormal\$)).ti,ab.
71 *MACULAR DEGENERATION/
72 MACULAR EDEMA/
73 (macular adj (degenerat\$ or dysfunction\$)).ti,ab.
74 (maculopath\$ or macular edema? or macular oedema? or CSME or CSMO).ti,ab.
75 exp OCULAR HYPERTENSION/
76 (glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi\$ or pressur\$))).ti,ab.
77 OPTIC NEUROPATHY, ISCHEMIC/
78 (optic adj3 (isch?emi\$ or neuropath\$)).ti,ab.
79 cotton wool spot?.ti,ab.
80 RETINAL DETACHMENT/
81 ((retina\$ or preretina\$) adj3 (detach\$ or tear\$ or scar\$ or thick\$ or lesion? or manifest\$ or fibrosis)).ti,ab.
82 VISION DISORDERS/
83 SCOTOMA/
84 VISION, LOW/
85 (scotoma? or blind spot? or floater? or musca volitante?).ti,ab.
86 ((reduc\$ or impair\$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish\$ or low or blur\$) adj3 (vision or visual or acuity)).ti,ab.
87 or/47-50,53-56,59-62,65-86
88 PREVALENCE/
89 INCIDENCE/
90 CROSS-SECTIONAL STUDIES/
91 exp MODELS, STATISTICAL/
92 LIFE TABLES/
93 exp RISK/
94 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
95 or/88-94
96 AGE FACTORS/
97 AGE DISTRIBUTION/
98 AGE OF ONSET/
99 TIME TO TREATMENT/
100 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
101 (disease adj3 (duration or onset)).ti,ab.
102 or/96-101
103 DIABETIC RETINOPATHY/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
104 22 and (35 or 41 or 46 or 95 or 102)
105 19 and 25 and (35 or 41 or 46 or 95 or 102)
106 19 and 87 and (95 or 102)
107 or/103-106
108 and/9,107
109 limit 108 to english language
110 LETTER/
111 EDITORIAL/
112 NEWS/
113 exp HISTORICAL ARTICLE/
114 ANECDOTES AS TOPIC/

115 COMMENT/
116 (letter or comment* or abstracts).ti.
117 or/110-116
118 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
119 117 not 118
120 ANIMALS/ not HUMANS/
121 exp ANIMALS, LABORATORY/
122 exp ANIMAL EXPERIMENTATION/
123 exp MODELS, ANIMAL/
124 exp RODENTIA/
125 (rat or rats or mouse or mice).ti.
126 or/119-125
127 109 not 126

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

Searches
1 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescens\$ or prepubescens\$).ti,ab,jw.
5 or/1-4
6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
7 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
8 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
9 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
10 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
11 or/6-10
12 (diabet\$ adj3 retinopath\$).ti,ab.
13 retinopath\$.ti,ab.
14 ((retina\$ or fundus or ocul\$ or eye?) adj3 (photograph\$ or exam\$)).ti,ab.
15 (op?thalmoscop\$ or retinoscop\$).ti,ab.
16 fundus oculi.ti,ab.
17 or/14-16
18 (undiagnos\$ or estimate\$).ti.
19 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
20 or/18-19
21 (retinopath\$ adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging)).ti,ab.
22 h?emorrhag\$.ti,ab.
23 (microaneurysm? or micro aneurysm?).ti,ab.
24 exudate?.ti,ab.
25 (papill?edem\$ or papillitis or choked dis??).ti,ab.
26 ((retina\$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).ti,ab.
27 neovascular\$.ti,ab.
28 (new adj2 vessel adj2 form\$).ti,ab.
29 ((venous or vascular or microvascular or fibrovascular) adj3 (abnormal\$ or malform\$ or loop\$ or bead\$ or reduplicat\$ or duplicat\$ or proliferat\$)).ti,ab.
30 (IRMA or ((intraretinal or intra retinal) adj microvascular adj abnormal\$)).ti,ab.
31 (macular adj (degenerat\$ or dysfunction\$)).ti,ab.
32 (maculopath\$ or macular edema? or macular oedema? or CSME or CSMO).ti,ab.
33 (glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi\$ or pressur\$))).ti,ab.

- 34 (optic adj3 (isch?emi\$ or neuropath\$)).ti,ab.
- 35 cotton wool spot?.ti,ab.
- 36 ((retina\$ or preretina\$) adj3 (detach\$ or tear\$ or scar\$ or thick\$ or lesion? or manifest\$ or fibrosis)).ti,ab.
- 37 (scotoma? or blind spot? or floater? or musca volitante?).ti,ab.
- 38 ((reduc\$ or impair\$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish\$ or low or blur\$) adj3 (vision or visual or acuity)).ti,ab.
- 39 or/22-38
- 40 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
- 41 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
- 42 (disease adj3 (duration or onset)).ti,ab.
- 43 or/41-42
- 44 12 and (17 or 20 or 21 or 40 or 43)
- 45 11 and 13 and (17 or 20 or 21 or 40 or 43)
- 46 11 and 39 and (40 or 43)
- 47 or/44-46
- 48 and/5,47

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 1/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
- 13 or/10-12
- 14 exp DIABETES MELLITUS, TYPE 2/
- 15 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
- 16 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
- 17 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
- 18 or/14-17
- 19 or/13,18
- 20 DIABETIC RETINOPATHY/
- 21 (diabet\$ adj3 retinopath\$).ti,ab.
- 22 or/20-21
- 23 RETINAL DISEASES/
- 24 retinopath\$.ti,ab.
- 25 or/23-24
- 26 DIAGNOSTIC TECHNIQUES, OPHTHALMOLOGICAL/
- 27 exp OPHTHALMOSCOPY/
- 28 FUNDUS OCULI/
- 29 RETINA/ or RETINAL VESSELS/
- 30 PHOTOGRAPHY/

31 and/29-30
32 ((retina\$ or fundus or ocul\$ or eye?) adj3 (photograph\$ or exam\$)).ti,ab.
33 (op?thalmoscop\$ or retinoscop\$).ti,ab.
34 fundus oculi.ti,ab.
35 or/26-28,31-34
36 MASS SCREENING/
37 VISION SCREENING/
38 exp POPULATION SURVEILLANCE/
39 (undiagnos\$ or estimate\$).ti.
40 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
41 or/36-40
42 SEVERITY OF ILLNESS INDEX/
43 INTERNATIONAL CLASSIFICATION OF DISEASES/
44 CLASSIFICATION/
45 (retinopath\$ adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging)).ti,ab.
46 or/42-45
47 exp EYE HEMORRHAGE/
48 h?emorrhag\$.ti,ab.
49 exp ANEURYSM/
50 (microaneurysm? or micro aneurysm?).ti,ab.
51 "EXUDATES AND TRANSUDATES"/
52 exp EYE/
53 and/51-52
54 SUBRETINAL FLUID/
55 exudate?.ti,ab.
56 PAPILLEDEMA/
57 EDEMA/
58 exp EYE/
59 and/57-58
60 (papill?edem\$ or papillitis or choked dis??).ti,ab.
61 ((retina\$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).ti,ab.
62 RETINAL NEOVASCULARIZATION/
63 NEOVASCULARIZATION, PATHOLOGIC/ or VASCULAR MALFORMATIONS/
64 exp EYE/ or RETINAL VESSELS/
65 and/63-64
66 exp RETINAL VESSELS/pa, pp [Pathology, Physiopathology]
67 neovascular\$.ti,ab.
68 (new adj2 vessel adj2 form\$).ti,ab.
69 ((venous or vascular or microvascular or fibrovascular) adj3 (abnormal\$ or malform\$ or loop\$ or bead\$ or reduplicat\$ or duplicat\$ or proliferat\$)).ti,ab.
70 (IRMA or ((intra retinal or intra retinal) adj microvascular adj abnormal\$)).ti,ab.
71 *MACULAR DEGENERATION/
72 MACULAR EDEMA/
73 (macular adj (degenerat\$ or dysfunction\$)).ti,ab.
74 (maculopath\$ or macular edema? or macular oedema? or CSME or CSMO).ti,ab.
75 exp OCULAR HYPERTENSION/
76 (glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi\$ or pressur\$))).ti,ab.
77 OPTIC NEUROPATHY, ISCHEMIC/
78 (optic adj3 (isch?emi\$ or neuropath\$)).ti,ab.
79 cotton wool spot?.ti,ab.
80 RETINAL DETACHMENT/
81 ((retina\$ or preretina\$) adj3 (detach\$ or tear\$ or scar\$ or thick\$ or lesion? or manifest\$ or fibrosis)).ti,ab.

- 82 VISION DISORDERS/
83 SCOTOMA/
84 VISION, LOW/
85 (scotoma? or blind spot? or floater? or musca volitante?).ti,ab.
86 ((reduc\$ or impair\$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish\$ or low or blur\$) adj3 (vision or visual or acuity)).ti,ab.
87 or/47-50,53-56,59-62,65-86
88 PREVALENCE/
89 INCIDENCE/
90 CROSS-SECTIONAL STUDIES/
91 exp MODELS, STATISTICAL/
92 LIFE TABLES/
93 exp RISK/
94 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
95 or/88-94
96 AGE FACTORS/
97 AGE DISTRIBUTION/
98 AGE OF ONSET/
99 TIME TO TREATMENT/
100 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
101 (disease adj3 (duration or onset)).ti,ab.
102 or/96-101
103 DIABETIC RETINOPATHY/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
104 22 and (35 or 41 or 46 or 95 or 102)
105 19 and 25 and (35 or 41 or 46 or 95 or 102)
106 19 and 87 and (95 or 102)
107 or/103-106
108 and/9,107

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- | # | Searches |
|----|---|
| 1 | (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,tx,kw,jw,rw. |
| 2 | (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,tx,kw,jw,rw. |
| 3 | (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx,kw,jw,rw. |
| 4 | (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,tx,kw,jw,rw. |
| 5 | or/1-4 |
| 6 | (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw,tx,kw. |
| 7 | (IDDM or T1D or TID or DM1 or DMI).tw,tx. |
| 8 | (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw,tx,kw. |
| 9 | (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw,tx,kw. |
| 10 | (NIDDM or T2D or TIID or DM2 or DMII).tw,tx. |
| 11 | or/6-10 |
| 12 | (diabet\$ adj3 retinopath\$).tw,tx,kw. |
| 13 | RETINAL DISEASES.kw. |
| 14 | retinopath\$.tw,tx,kw. |
| 15 | or/13-14 |
| 16 | DIAGNOSTIC TECHNIQUES, OPHTHALMOLOGICAL.kw. |

- 17 ((retina\$ or fundus or ocul\$ or eye?) adj3 (photograph\$ or exam\$)).tw,tx,kw.
- 18 (op?thalmoscop\$ or retinoscop\$).tw,tx,kw.
- 19 fundus oculi.tw,tx,kw.
- 20 or/16-19
- 21 SCREENING.kw.
- 22 SURVEILLANCE.kw.
- 23 (undiagnos\$ or estimate\$.ti.
- 24 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
- 25 or/21-24
- 26 SEVERITY OF ILLNESS INDEX.kw.
- 27 DISEASE SEVERITY.kw.
- 28 DISEASE COURSE.kw.
- 29 STAGING.kw.
- 30 INTERNATIONAL CLASSIFICATION OF DISEASES.kw.
- 31 RATING SCALE.kw.
- 32 CLASSIFICATION.kw.
- 33 (retinopath\$ adj3 (grad\$ or sever\$ or classific\$ or index\$ or indice? or stage\$ or staging)).tw,tx.
- 34 or/26-33
- 35 h?emorrhag\$.tw,tx,kw.
- 36 ANEURYSM.kw.
- 37 (microaneurysm? or micro aneurysm?).tw,tx,kw.
- 38 SUBRETINAL FLUID.kw.
- 39 exudate?.tw,tx,kw.
- 40 (papill?edem\$ or papillitis or choked dis??).tw,tx,kw.
- 41 ((retina\$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).tw,tx,kw.
- 42 neovascular\$.tw,tx,kw.
- 43 (new adj2 vessel adj2 form\$).tw,tx.
- 44 ((venous or vascular or microvascular or fibrovascular) adj3 (abnormal\$ or malform\$ or loop\$ or bead\$ or reduplicat\$ or duplicat\$ or proliferat\$)).tw,tx,kw.
- 45 (IRMA or ((intraretinal or intra retinal) adj microvascular adj abnormal\$)).tw,tx.
- 46 (macular adj (degenerat\$ or dysfunction\$)).tw,tx,kw.
- 47 (maculopath\$ or macular edema? or macular oedema? or CSME or CSMO).tw,tx,kw.
- 48 (glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi\$ or pressur\$))).tw,tx,kw.
- 49 (optic adj3 (isch?emi\$ or neuropath\$)).tw,tx,kw.
- 50 cotton wool spot?.tw,tx.
- 51 ((retina\$ or preretina\$) adj3 (detach\$ or tear\$ or scar\$ or thick\$ or lesion? or manifest\$ or fibrosis)).tw,tx,kw.
- 52 (VISION DISORDERS or VISUAL DISORDER).kw.
- 53 (scotoma? or blind spot? or floater? or musca volitante?).tw,tx,kw.
- 54 ((reduc\$ or impair\$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish\$ or low or blur\$) adj3 (vision or visual or acuity)).tw,tx,kw.
- 55 or/35-54
- 56 PREVALENCE.kw.
- 57 INCIDENCE.kw.
- 58 CROSS-SECTIONAL STUDIES.kw.
- 59 MODELS, STATISTICAL.kw.
- 60 LIFE TABLE\$.kw.
- 61 RISK.kw.
- 62 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
- 63 or/56-62
- 64 AGE.kw.
- 65 TIME TO TREATMENT.kw.
- 66 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).tw,tx,kw.

67 (disease adj3 (duration or onset)).tw,tx,kw.
68 or/64-67
69 12 and (20 or 25 or 34 or 63 or 68)
70 11 and 15 and (20 or 25 or 34 or 63 or 68)
71 11 and 55 and (63 or 68)
72 or/69-71
73 and/5,72

Health Technology Assessment

Searches
1 ADOLESCENT/ or MINORS/
2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx,rw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jw,rw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jw,rw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jw,rw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/
11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw.
12 (IDDM or T1D or TID or DM1 or DMI).tw.
13 or/10-12
14 exp DIABETES MELLITUS, TYPE 2/
15 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw.
16 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw.
17 (NIDDM or T2D or TIID or DM2 or DMII).tw.
18 or/14-17
19 or/13,18
20 DIABETIC RETINOPATHY/
21 (diabet\$ adj3 retinopath\$).tw.
22 or/20-21
23 RETINAL DISEASES/
24 retinopath\$.tw.
25 or/23-24
26 DIAGNOSTIC TECHNIQUES, OPHTHALMOLOGICAL/
27 exp OPHTHALMOSCOPY/
28 FUNDUS OCULI/
29 RETINA/ or RETINAL VESSELS/
30 PHOTOGRAPHY/
31 and/29-30
32 ((retina\$ or fundus or ocul\$ or eye?) adj3 (photograph\$ or exam\$)).tw.
33 (op?thalmoscop\$ or retinoscop\$).tw.
34 fundus oculi.tw.
35 or/26-28,31-34
36 MASS SCREENING/
37 VISION SCREENING/
38 exp POPULATION SURVEILLANCE/
39 (undiagnos\$ or estimate\$).ti.
40 (screen\$ or surveill\$ or predict\$ or detect\$).ti.

41 or/36-40
42 SEVERITY OF ILLNESS INDEX/
43 INTERNATIONAL CLASSIFICATION OF DISEASES/
44 CLASSIFICATION/
45 (retinopath\$ adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging)).tw.
46 or/42-45
47 exp EYE HEMORRHAGE/
48 h?emorrhag\$.tw.
49 exp ANEURYSM/
50 (microaneurysm? or micro aneurysm?).tw.
51 "EXUDATES AND TRANSUDATES"/
52 exp EYE/
53 and/51-52
54 SUBRETINAL FLUID/
55 exudate?.tw.
56 PAPILLEDEMA/
57 EDEMA/
58 exp EYE/
59 and/57-58
60 (papill?edem\$ or papillitis or choked dis??).tw.
61 ((retina\$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).tw.
62 RETINAL NEOVASCULARIZATION/
63 NEOVASCULARIZATION, PATHOLOGIC/ or VASCULAR MALFORMATIONS/
64 exp EYE/ or RETINAL VESSELS/
65 and/63-64
66 exp RETINAL VESSELS/pa, pp [Pathology, Physiopathology]
67 neovascular\$.tw.
68 (new adj2 vessel adj2 form\$).tw.
69 ((venous or vascular or microvascular or fibrovascular) adj3 (abnormal\$ or malform\$ or loop\$ or bead\$ or reduplicat\$ or duplicat\$ or proliferat\$)).tw.
70 (IRMA or ((intra retinal or intra retinal) adj microvascular adj abnormal\$)).tw.
71 MACULAR DEGENERATION/
72 MACULAR EDEMA/
73 (macular adj (degenerat\$ or dysfunction\$)).tw.
74 (maculopath\$ or macular edema? or macular oedema? or CSME or CSMO).tw.
75 exp OCULAR HYPERTENSION/
76 (glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi\$ or pressur\$))).tw.
77 OPTIC NEUROPATHY, ISCHEMIC/
78 (optic adj3 (isch?emi\$ or neuropath\$)).tw.
79 cotton wool spot?.tw.
80 RETINAL DETACHMENT/
81 ((retina\$ or preretina\$) adj3 (detach\$ or tear\$ or scar\$ or thick\$ or lesion? or manifest\$ or fibrosis)).tw.
82 VISION DISORDERS/
83 SCOTOMA/
84 VISION, LOW/
85 (scotoma? or blind spot? or floater? or musca volitante?).tw.
86 ((reduc\$ or impair\$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish\$ or low or blur\$) adj3 (vision or visual or acuity)).tw.
87 or/47-50,53-56,59-62,65-86
88 PREVALENCE/
89 INCIDENCE/
90 CROSS-SECTIONAL STUDIES/

- 91 exp MODELS, STATISTICAL/
- 92 LIFE TABLES/
- 93 exp RISK/
- 94 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
- 95 or/88-94
- 96 AGE FACTORS/
- 97 AGE DISTRIBUTION/
- 98 AGE OF ONSET/
- 99 TIME TO TREATMENT/
- 100 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).tw.
- 101 (disease adj3 (duration or onset)).tw.
- 102 or/96-101
- 103 DIABETIC RETINOPATHY/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
- 104 22 and (35 or 41 or 46 or 95 or 102)
- 105 19 and 25 and (35 or 41 or 46 or 95 or 102)
- 106 19 and 87 and (95 or 102)
- 107 or/103-106
- 108 and/9,107

Embase

- # Searches
- 1 exp ADOLESCENT/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
- 9 or/1-8
- 10 INSULIN DEPENDENT DIABETES MELLITUS/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
- 13 or/10-12
- 14 NON INSULIN DEPENDENT DIABETES MELLITUS/
- 15 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
- 16 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
- 17 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
- 18 or/14-17
- 19 or/13,18
- 20 JUVENILE DIABETES MELLITUS/
- 21 DIABETIC RETINOPATHY/
- 22 (diabet\$ adj3 retinopath\$).ti,ab.
- 23 or/21-22
- 24 RETINOPATHY/
- 25 PROLIFERATIVE RETINOPATHY/
- 26 retinopath\$.ti,ab.
- 27 or/24-26
- 28 EYE PHOTOGRAPHY/

29 exp RETINA EXAMINATION/
30 OPHTHALMOSCOPY/
31 RETINA/ or exp RETINA BLOOD VESSEL/
32 PHOTOGRAPHY/
33 and/31-32
34 exp OPHTHALMIC CAMERA/
35 ((retina\$ or fundus or ocul\$ or eye?) adj3 (photograph\$ or exam\$)).ti,ab.
36 (op?thalmoscop\$ or retinoscop\$).ti,ab.
37 fundus oculi.ti,ab.
38 or/28-30,33-37
39 SCREENING/
40 MASS SCREENING/
41 SCREENING TEST/
42 RESCREENING/
43 exp DISEASE SURVEILLANCE/
44 (undiagnos\$ or estimate\$).ti.
45 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
46 or/39-45
47 SEVERITY OF ILLNESS INDEX/
48 DISEASE SEVERITY/
49 STAGING/
50 exp INTERNATIONAL CLASSIFICATION OF DISEASES/
51 RATING SCALE/
52 CLASSIFICATION/
53 DISEASE CLASSIFICATION/
54 (retinopath\$ adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging)).ti,ab.
55 or/47-54
56 exp INTRAOCULAR HEMORRHAGE/
57 h?emorrhag\$.ti,ab.
58 MICROANEURYSM/
59 (microaneurysm? or micro aneurysm?).ti,ab.
60 RETINA EXUDATE/
61 SUBRETINAL FLUID/
62 exudate?.ti,ab.
63 PAPILLEDEMA/
64 RETINAL EDEMA/
65 (papill?edem\$ or papillitis or choked dis??).ti,ab.
66 ((retina\$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).ti,ab.
67 RETINA NEOVASCULARIZATION/
68 "NEOVASCULARIZATION (PATHOLOGY)"/
69 RETINA/ or exp RETINA BLOOD VESSEL/
70 and/68-69
71 neovascular\$.ti,ab.
72 (new adj2 vessel adj2 form\$).ti,ab.
73 ((venous or vascular or microvascular or fibrovascular) adj3 (abnormal\$ or malform\$ or loop\$ or bead\$ or reduplicat\$ or duplicat\$ or proliferat\$)).ti,ab.
74 (IRMA or ((intra retinal or intra retinal) adj microvascular adj abnormal\$)).ti,ab.
75 RETINA DEGENERATION/
76 RETINA MACULA DEGENERATION/
77 RETINA MACULOPATHY/
78 exp MACULAR EDEMA/
79 (macular adj (degenerat\$ or dysfunction\$)).ti,ab.
80 (maculopath\$ or macular edema? or macular oedema? or CSME or CSMO).ti,ab.

81 exp GLAUCOMA/
82 (glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi\$ or pressur\$))).ti,ab.
83 exp ISCHEMIC OPTIC NEUROPATHY/
84 (optic adj3 (isch?emi\$ or neuropath\$)).ti,ab.
85 cotton wool spot?.ti,ab.
86 RETINA DETACHMENT/
87 RETINA TEAR/
88 ((retina\$ or preretina\$) adj3 (detach\$ or tear\$ or scar\$ or thick\$ or lesion? or manifest\$ or fibrosis)).ti,ab.
89 VISUAL DISORDER/
90 VISUAL IMPAIRMENT/
91 SCOTOMA/
92 VITREOUS FLOATERS/
93 (scotoma? or blind spot? or floater? or musca volitante?).ti,ab.
94 ((reduc\$ or impair\$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish\$ or low or blur\$) adj3 (vision or visual or acuity)).ti,ab.
95 or/56-67,70-94
96 PREVALENCE/
97 INCIDENCE/
98 STATISTICAL MODEL/
99 LIFE TABLE/
100 exp RISK/
101 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
102 or/96-101
103 AGE/
104 AGE DISTRIBUTION/
105 ONSET AGE/
106 DISEASE DURATION/
107 TIME TO TREATMENT/
108 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
109 (disease adj3 (duration or onset)).ti,ab.
110 or/103-109
111 DIABETIC RETINOPATHY/di, ep, pc [Diagnosis, Epidemiology, Prevention]
112 23 and (38 or 46 or 55 or 102 or 110)
113 19 and 27 and (38 or 46 or 55 or 102 or 110)
114 19 and 95 and (102 or 110)
115 or/111-114
116 and/9,115
117 20 and 23 and (38 or 46 or 55 or 102 or 110)
118 20 and 27 and (38 or 46 or 55 or 102 or 110)
119 20 and 95 and (102 or 110)
120 or/116-119
121 limit 120 to english language
122 conference abstract.pt.
123 letter.pt. or LETTER/
124 note.pt.
125 editorial.pt.
126 (letter or comment* or abstracts).ti.
127 or/122-126
128 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
129 127 not 128
130 ANIMAL/ not HUMAN/
131 NONHUMAN/

- 132 exp ANIMAL EXPERIMENT/
- 133 exp EXPERIMENTAL ANIMAL/
- 134 ANIMAL MODEL/
- 135 exp RODENT/
- 136 (rat or rats or mouse or mice).ti.
- 137 or/129-136
- 138 121 not 137

F.17 Type 1 and type 2 diabetes – nephropathy

Review questions:

What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?

What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

Ovid MEDLINE(R)

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 1/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
- 13 or/10-12
- 14 exp DIABETES MELLITUS, TYPE 2/
- 15 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
- 16 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
- 17 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
- 18 or/14-17
- 19 or/13,18
- 20 DIABETIC NEPHROPATHIES/
- 21 nephropath\$.ti,ab.
- 22 glomerulosclerosis.ti,ab.
- 23 (Kimmelstie?l Wilson adj (syndrome? or disease?)).ti,ab.
- 24 ALBUMINURIA/
- 25 PROTEINURIA/
- 26 SERUM ALBUMIN/
- 27 CREATININE/bl, ur [Blood, Urine]
- 28 (albuminuri\$ or microalbuminuri\$ or proteinuri\$).ti,ab.
- 29 ((albumin\$ or creatinine\$) adj3 (serum or sera or blood or urin\$ or ratio or concentration?)).ti,ab.

30 exp RENAL INSUFFICIENCY, CHRONIC/
31 ((kidney? or renal) adj3 (fail\$ or insufficien\$ or disease?)).ti,ab.
32 or/20-31
33 SEVERITY OF ILLNESS INDEX/
34 DISEASE PROGRESSION/
35 INTERNATIONAL CLASSIFICATION OF DISEASES/
36 CLASSIFICATION/
37 or/33-36
38 or/20-28
39 and/37-38
40 ((nephropath\$ or microalbuminuria or proteinuria) adj3 (grad\$ or sever\$ or classif\$ or index\$
or indice? or stage\$ or staging or progress\$ or degree\$)).ti,ab.
41 or/39-40
42 MASS SCREENING/
43 exp POPULATION SURVEILLANCE/
44 (undiagnos\$ or estimate\$).ti.
45 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
46 or/42-45
47 PREVALENCE/
48 INCIDENCE/
49 CROSS-SECTIONAL STUDIES/
50 exp MODELS, STATISTICAL/
51 LIFE TABLES/
52 exp RISK/
53 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
54 or/47-53
55 AGE FACTORS/
56 AGE DISTRIBUTION/
57 AGE OF ONSET/
58 TIME TO TREATMENT/
59 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
60 (disease adj3 (duration or onset)).ti,ab.
61 or/55-60
62 ALBUMINURIA/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
63 32 and (46 or 54 or 61)
64 or/41,62-63
65 and/19,64
66 DIABETIC NEPHROPATHIES/cl, di, ep, pc [Classification, Diagnosis, Epidemiology,
Prevention & Control]
67 or/65-66
68 and/9,67
69 limit 68 to english language
70 LETTER/
71 EDITORIAL/
72 NEWS/
73 exp HISTORICAL ARTICLE/
74 ANECDOTES AS TOPIC/
75 COMMENT/
76 (letter or comment* or abstracts).ti.
77 or/70-76
78 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
79 77 not 78
80 ANIMALS/ not HUMANS/

- 81 exp ANIMALS, LABORATORY/
- 82 exp ANIMAL EXPERIMENTATION/
- 83 exp MODELS, ANIMAL/
- 84 exp RODENTIA/
- 85 (rat or rats or mouse or mice).ti.
- 86 or/79-85
- 87 69 not 86

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 7 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
- 8 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
- 9 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
- 10 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
- 11 or/6-10
- 12 nephropath\$.ti,ab.
- 13 glomerulosclerosis.ti,ab.
- 14 (Kimmelstie?l Wilson adj (syndrome? or disease?)).ti,ab.
- 15 (albuminuri\$ or microalbuminuri\$ or proteinuri\$).ti,ab.
- 16 ((albumin\$ or creatinine\$) adj3 (serum or sera or blood or urin\$ or ratio or concentration?)).ti,ab.
- 17 ((kidney? or renal) adj3 (fail\$ or insufficien\$ or disease?)).ti,ab.
- 18 or/12-17
- 19 ((nephropath\$ or microalbuminuria or proteinuria) adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging or progress\$ or degree\$)).ti,ab.
- 20 (undiagnos\$ or estimate\$).ti.
- 21 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
- 22 or/20-21
- 23 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
- 24 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
- 25 (disease adj3 (duration or onset)).ti,ab.
- 26 or/24-25
- 27 18 and (22 or 23 or 26)
- 28 or/19,27
- 29 and/5,11,28

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/

6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/
11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or
child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
13 or/10-12
14 exp DIABETES MELLITUS, TYPE 2/
15 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late
or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
16 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
17 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18 or/14-17
19 or/13,18
20 DIABETIC NEPHROPATHIES/
21 nephropath\$.ti,ab.
22 glomerulosclerosis.ti,ab.
23 (Kimmelstie?l Wilson adj (syndrome? or disease?)).ti,ab.
24 ALBUMINURIA/
25 PROTEINURIA/
26 SERUM ALBUMIN/
27 CREATININE/bl, ur [Blood, Urine]
28 (albuminuri\$ or microalbuminuri\$ or proteinuri\$).ti,ab.
29 ((albumin\$ or creatinine\$) adj3 (serum or sera or blood or urin\$ or ratio or
concentration?)).ti,ab.
30 exp RENAL INSUFFICIENCY, CHRONIC/
31 ((kidney? or renal) adj3 (fail\$ or insufficien\$ or disease?)).ti,ab.
32 or/20-31
33 SEVERITY OF ILLNESS INDEX/
34 DISEASE PROGRESSION/
35 INTERNATIONAL CLASSIFICATION OF DISEASES/
36 CLASSIFICATION/
37 or/33-36
38 or/20-28
39 and/37-38
40 ((nephropath\$ or microalbuminuria or proteinuria) adj3 (grad\$ or sever\$ or classif\$ or index\$
or indice? or stage\$ or staging or progress\$ or degree\$)).ti,ab.
41 or/39-40
42 MASS SCREENING/
43 exp POPULATION SURVEILLANCE/
44 (undiagnos\$ or estimate\$).ti.
45 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
46 or/42-45
47 PREVALENCE/
48 INCIDENCE/
49 CROSS-SECTIONAL STUDIES/
50 exp MODELS, STATISTICAL/
51 LIFE TABLES/
52 exp RISK/
53 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
54 or/47-53

- 55 AGE FACTORS/
- 56 AGE DISTRIBUTION/
- 57 AGE OF ONSET/
- 58 TIME TO TREATMENT/
- 59 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
- 60 (disease adj3 (duration or onset)).ti,ab.
- 61 or/55-60
- 62 ALBUMINURIA/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
- 63 32 and (46 or 54 or 61)
- 64 or/41,62-63
- 65 and/19,64
- 66 DIABETIC NEPHROPATHIES/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
- 67 or/65-66
- 68 and/9,67

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,tx,kw,jw,rw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,tx,kw,jw,rw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx,kw,jw,rw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,tx,kw,jw,rw.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw,tx,kw.
- 7 (IDDM or T1D or TID or DM1 or DMI).tw,tx.
- 8 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw,tx,kw.
- 9 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw,tx,kw.
- 10 (NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
- 11 or/6-10
- 12 nephropath\$.tw,tx,kw.
- 13 glomerulosclerosis.tw,tx.
- 14 (Kimmelstie?l Wilson adj (syndrome? or disease?)).tw,tx.
- 15 (albuminuri\$ or microalbuminuri\$ or proteinuri\$).tw,tx,kw.
- 16 ((albumin\$ or creatinine\$) adj3 (serum or sera or blood or urin\$ or ratio or concentration?)).tw,tx,kw.
- 17 ((kidney? or renal) adj3 (fail\$ or insufficien\$ or disease?)).tw,tx,kw.
- 18 or/12-17
- 19 SEVERITY OF ILLNESS INDEX.kw.
- 20 (DISEASE PROGRESSION or DISEASE COURSE).kw.
- 21 INTERNATIONAL CLASSIFICATION OF DISEASES.kw.
- 22 RATING SCALE.kw.
- 23 CLASSIFICATION.kw.
- 24 or/19-23
- 25 or/12-15
- 26 and/24-25
- 27 ((nephropath\$ or microalbuminuria or proteinuria) adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging or progress\$ or degree\$)).tw,tx.
- 28 or/26-27
- 29 (SCREENING or RESCREENING).kw.

- 30 SURVEILLANCE.kw.
- 31 (undiagnos\$ or estimate\$).ti.
- 32 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
- 33 or/29-32
- 34 PREVALENCE.kw.
- 35 INCIDENCE.kw.
- 36 (MODELS, STATISTICAL or STATISTICAL MODEL).kw.
- 37 LIFE TABLE?.kw.
- 38 RISK.kw.
- 39 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
- 40 or/34-39
- 41 AGE.kw.
- 42 TIME TO TREATMENT.kw.
- 43 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).tw,tx,kw.
- 44 (disease adj3 (duration or onset)).tw,tx,kw.
- 45 or/41-44
- 46 18 and (33 or 40 or 45)
- 47 or/28,46
- 48 and/5,11,47

Health Technology Assessment

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx,rw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jw,rw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jw,rw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jw,rw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 1/
- 11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw.
- 12 (IDDM or T1D or T1D or DM1 or DMI).tw.
- 13 or/10-12
- 14 exp DIABETES MELLITUS, TYPE 2/
- 15 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw.
- 16 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw.
- 17 (NIDDM or T2D or TIID or DM2 or DMII).tw.
- 18 or/14-17
- 19 or/13,18
- 20 DIABETIC NEPHROPATHIES/
- 21 nephropath\$.tw.
- 22 glomerulosclerosis.tw.
- 23 (Kimmelstie?l Wilson adj (syndrome? or disease?)).tw.
- 24 ALBUMINURIA/
- 25 PROTEINURIA/
- 26 SERUM ALBUMIN/
- 27 CREATININE/bl, ur [Blood, Urine]
- 28 (albuminuri\$ or microalbuminuri\$ or proteinuri\$).tw.

- 29 ((albumin\$ or creatinine\$) adj3 (serum or sera or blood or urin\$ or ratio or concentration?)).tw.
30 exp RENAL INSUFFICIENCY, CHRONIC/
31 ((kidney? or renal) adj3 (fail\$ or insufficien\$ or disease?)).tw.
32 or/20-31
33 SEVERITY OF ILLNESS INDEX/
34 DISEASE PROGRESSION/
35 INTERNATIONAL CLASSIFICATION OF DISEASES/
36 CLASSIFICATION/
37 or/33-36
38 or/20-28
39 and/37-38
40 ((nephropath\$ or microalbuminuria or proteinuria) adj3 (grad\$ or sever\$ or classif\$ or index\$
or indice? or stage\$ or staging or progress\$ or degree\$)).tw.
41 or/39-40
42 MASS SCREENING/
43 exp POPULATION SURVEILLANCE/
44 (undiagnos\$ or estimate\$).ti.
45 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
46 or/42-45
47 PREVALENCE/
48 INCIDENCE/
49 CROSS-SECTIONAL STUDIES/
50 exp MODELS, STATISTICAL/
51 LIFE TABLES/
52 exp RISK/
53 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
54 or/47-53
55 AGE FACTORS/
56 AGE DISTRIBUTION/
57 AGE OF ONSET/
58 TIME TO TREATMENT/
59 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).tw.
60 (disease adj3 (duration or onset)).tw.
61 or/55-60
62 ALBUMINURIA/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
63 32 and (46 or 54 or 61)
64 or/41,62-63
65 and/19,64
66 DIABETIC NEPHROPATHIES/cl, di, ep, pc [Classification, Diagnosis, Epidemiology,
Prevention & Control]
67 or/65-66
68 and/9,67

Embase

- # Searches
1 exp ADOLESCENT/
2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or
kindergar\$ or boy? or girl?).ti,ab,jx.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
7 exp PEDIATRICS/ or exp PUBERTY/

8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
9 or/1-8
10 INSULIN DEPENDENT DIABETES MELLITUS/
11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or
child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
13 or/10-12
14 NON INSULIN DEPENDENT DIABETES MELLITUS/
15 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late
or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
16 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
17 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18 or/14-17
19 or/13,18
20 and/9,19
21 JUVENILE DIABETES MELLITUS/
22 or/20-21
23 DIABETIC NEPHROPATHY/
24 nephropath\$.ti,ab.
25 glomerulosclerosis.ti,ab.
26 (Kimmelstie?l Wilson adj (syndrome? or disease?)).ti,ab.
27 exp ALBUMINURIA/
28 PROTEINURIA/
29 PROTEIN URINE LEVEL/
30 SERUM ALBUMIN/
31 ALBUMIN BLOOD LEVEL/
32 CREATININE URINE LEVEL/
33 CREATININE BLOOD LEVEL/
34 (albuminuri\$ or microalbuminuri\$ or proteinuri\$).ti,ab.
35 ((albumin\$ or creatinine\$) adj3 (serum or sera or blood or urin\$ or ratio or
concentration?)).ti,ab.
36 KIDNEY DISEASE/
37 KIDNEY FAILURE/
38 CHRONIC KIDNEY FAILURE/
39 ((kidney? or renal) adj3 (fail\$ or insufficien\$ or disease?)).ti,ab.
40 or/23-39
41 SEVERITY OF ILLNESS INDEX/
42 DISEASE SEVERITY/
43 DISEASE COURSE/
44 STAGING/
45 exp INTERNATIONAL CLASSIFICATION OF DISEASES/
46 RATING SCALE/
47 CLASSIFICATION/
48 DISEASE CLASSIFICATION/
49 or/41-48
50 or/23-34
51 and/49-50
52 ((nephropath\$ or microalbuminuria or proteinuria) adj3 (grad\$ or sever\$ or classif\$ or index\$
or indice? or stage\$ or staging or progress\$ or degree\$)).ti,ab.
53 or/51-52
54 SCREENING/
55 MASS SCREENING/
56 SCREENING TEST/

57 RESCREENING/
58 exp DISEASE SURVEILLANCE/
59 (undiagnos\$ or estimate\$).ti.
60 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
61 or/54-60
62 PREVALENCE/
63 INCIDENCE/
64 STATISTICAL MODEL/
65 LIFE TABLE/
66 exp RISK/
67 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
68 or/62-67
69 AGE/
70 AGE DISTRIBUTION/
71 ONSET AGE/
72 DISEASE DURATION/
73 TIME TO TREATMENT/
74 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
75 (disease adj3 (duration or onset)).ti,ab.
76 or/69-75
77 MICROALBUMINURIA/di, ep, pc [Diagnosis, Epidemiology, Prevention]
78 40 and (61 or 68 or 76)
79 or/53,77-78
80 and/22,79
81 DIABETIC NEPHROPATHY/di, ep, pc [Diagnosis, Epidemiology, Prevention]
82 and/9,81
83 or/80,82
84 limit 83 to english language
85 conference abstract.pt.
86 letter.pt. or LETTER/
87 note.pt.
88 editorial.pt.
89 (letter or comment* or abstracts).ti.
90 or/85-89
91 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
92 90 not 91
93 ANIMAL/ not HUMAN/
94 NONHUMAN/
95 exp ANIMAL EXPERIMENT/
96 exp EXPERIMENTAL ANIMAL/
97 ANIMAL MODEL/
98 exp RODENT/
99 (rat or rats or mouse or mice).ti.
100 or/92-99
101 84 not 100

F.18 Type 2 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?

Database(s): Ovid MEDLINE(R)

#	Searches
1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	DOUBLE BLIND METHOD/
4	SINGLE BLIND METHOD/
5	RANDOM ALLOCATION/
6	RANDOMIZED CONTROLLED TRIALS AS TOPIC/
7	or/1-6
8	((single or double or triple or treble) adj5 (blind\$ or mask\$)).tw,sh.
9	clinical trial.pt.
10	exp CLINICAL TRIAL/
11	exp CLINICAL TRIALS AS TOPIC/
12	(clinic\$ adj5 trial\$).tw,sh.
13	PLACEBOS/
14	placebo\$.tw,sh.
15	random\$.tw,sh.
16	or/8-15
17	or/7,16
18	META ANALYSIS/
19	META ANALYSIS AS TOPIC/
20	meta analysis.pt.
21	(metaanaly\$ or meta-analy\$ or (meta adj analy\$)).tw,sh.
22	(systematic\$ adj5 (review\$ or overview\$)).tw,sh.
23	(methodologic\$ adj5 (review\$ or overview\$)).tw,sh.
24	or/18-23
25	review\$.pt.
26	(medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.
27	((hand or manual\$) adj2 search\$).tw.
28	(electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online database\$).tw,sh.
29	(pooling or pooled or mantel haenszel).tw,sh.
30	(peto or dersimonian or der simonian or fixed effect).tw,sh.
31	or/26-30
32	and/25,31
33	or/24,32
34	letter.pt.
35	case report.tw.
36	comment.pt.
37	editorial.pt.
38	historical article.pt.
39	or/34-38
40	17 not 39
41	33 not 39
42	or/40-41

43 ADOLESCENT/ or MINORS/
44 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
45 exp CHILD/
46 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or
kindergar\$ or boy? or girl?).ti,ab,jw.
47 exp INFANT/
48 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
49 exp PEDIATRICS/ or exp PUBERTY/
50 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
51 or/43-50
52 exp DIABETES MELLITUS, TYPE 2/
53 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late
or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
54 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
55 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
56 or/52-55
57 PATIENT EDUCATION AS TOPIC/
58 PROBLEM SOLVING/
59 ed.fs.
60 ((educat\$ or training) adj6 (intervention\$ or program? or programme or programmes)).ti,ab.
61 (problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
62 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or
families) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or
instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
63 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or
families) adj3 information).ti,ab.
64 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-
monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or
cope or coping) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e
or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
65 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-
monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or
cope or coping) adj3 information).ti,ab.
66 ((diabet\$ or insulin\$ or glyco?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj6
(educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$
or program? or programme or programmes)).ti,ab.
67 ((diabet\$ or insulin\$ or glyco?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj3
information).ti,ab.
68 or/57-67
69 and/51,56,68
70 limit 69 to english language
71 LETTER/
72 EDITORIAL/
73 NEWS/
74 exp HISTORICAL ARTICLE/
75 ANECDOTES AS TOPIC/
76 COMMENT/
77 CASE REPORT/
78 (letter or comment* or abstracts).ti.
79 or/71-78
80 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
81 79 not 80
82 ANIMALS/ not HUMANS/
83 exp ANIMALS, LABORATORY/

84 exp ANIMAL EXPERIMENTATION/
85 exp MODELS, ANIMAL/
86 exp RODENTIA/
87 (rat or rats or mouse or mice).ti.
88 or/81-87
89 70 not 88
90 and/42,89

Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

Searches
1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
5 or/1-4
6 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
7 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
8 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
9 or/6-8
10 ((educat\$ or training) adj6 (intervention\$ or program? or programme or programmes)).ti,ab.
11 (problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
12 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
13 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj3 information).ti,ab.
14 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
15 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
16 ((diabet\$ or insulin\$ or glyc?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
17 ((diabet\$ or insulin\$ or glyc?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
18 or/10-17
19 and/5,9,18
20 limit 19 to english language

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials

Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
3 exp CHILD/

- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 2/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14 or/10-13
15 PATIENT EDUCATION AS TOPIC/
16 PROBLEM SOLVING/
17 ed.fs.
18 ((educat\$ or training) adj6 (intervention\$ or program? or programme or programmes)).ti,ab.
19 (problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
20 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
21 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj3 information).ti,ab.
22 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
23 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
24 ((diabet\$ or insulin\$ or glyc?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
25 ((diabet\$ or insulin\$ or glyc?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
26 or/15-25
27 and/9,14,26

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).kw,tw,tx,jw,rw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).kw,tw,tx,jw,rw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).kw,tw,tx,jw,rw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).kw,tw,tx,jw,rw.
5 or/1-4
6 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).kw,tw,tx.
7 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).kw,tw,tx.
8 (NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
9 or/6-8
10 PATIENT EDUCATION AS TOPIC.kw.
11 PROBLEM SOLVING.kw.

- 12 ((educat\$ or training) adj6 (intervention\$ or program? or programme or programmes)).tw,tx.
13 (problem-solving or "problem solving" or problem-based or "problem based").tw,tx.
14 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).tw,tx.
15 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj3 information).tw,tx.
16 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).tw,tx.
17 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).tw,tx.
18 ((diabet\$ or insulin\$ or glyco?emi\$ or hypoglyco?emi\$ or "blood glucose" or "blood sugar") adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).tw,tx.
19 ((diabet\$ or insulin\$ or glyco?emi\$ or hypoglyco?emi\$ or "blood glucose" or "blood sugar") adj3 information).tw,tx.
20 or/10-19
21 and/5,9,20

Health Technology Assessment

- # Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx,rw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jx,rw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 2/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw.
13 (NIDDM or T2D or TIID or DM2 or DMII).tw.
14 or/10-13
15 PATIENT EDUCATION AS TOPIC/
16 PROBLEM SOLVING/
17 ed.fs.
18 ((educat\$ or training) adj6 (intervention\$ or program? or programme or programmes)).tw.
19 (problem-solving or "problem solving" or problem-based or "problem based").tw.
20 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).tw.
21 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj3 information).tw.
22 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).tw.

- 23 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).tw.
- 24 ((diabet\$ or insulin\$ or glyc?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).tw.
- 25 ((diabet\$ or insulin\$ or glyc?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj3 information).tw.
- 26 or/15-25
- 27 and/9,14,26

Embase

- # Searches
- 1 CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
- 2 (clinic\$ adj5 trial\$).ti,ab,sh.
- 3 SINGLE BLIND PROCEDURE/
- 4 DOUBLE BLIND PROCEDURE/
- 5 RANDOM ALLOCATION/
- 6 CROSSOVER PROCEDURE/
- 7 PLACEBO/
- 8 placebo\$.ti,ab,sh.
- 9 random\$.ti,ab,sh.
- 10 RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
- 11 ((single or double or triple or treble) adj (blind\$ or mask\$)).ti,ab,sh.
- 12 randomi?ed control\$ trial\$.tw.
- 13 or/1-12
- 14 META ANALYSIS/
- 15 ((meta adj analy\$) or metaanalys\$ or meta-analy\$).ti,ab,sh.
- 16 (systematic\$ adj5 (review\$ or overview\$)).ti,sh,ab.
- 17 (methodologic\$ adj5 (review\$ or overview\$)).ti,ab,sh.
- 18 or/14-17
- 19 review.pt.
- 20 (medline or medlars or embase).ab.
- 21 (scisearch or science citation index).ab.
- 22 (psychlit or psychlit or psychinfo or psycinfo or cinahl or cochrane).ab.
- 23 ((hand or manual\$) adj2 search\$).tw.
- 24 (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online database\$).tw.
- 25 (pooling or pooled or mantel haenszel).tw.
- 26 (peto or dersimonian or "der simonian" or fixed effect).tw.
- 27 or/20-26
- 28 and/19,27
- 29 or/18,28
- 30 (book or conference paper or editorial or letter or note or proceeding or short survey).pt.
- 31 13 not 30
- 32 29 not 30
- 33 or/31-32
- 34 exp ADOLESCENT/
- 35 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
- 36 exp CHILD/
- 37 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
- 38 exp INFANT/
- 39 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.

40 exp PEDIATRICS/ or exp PUBERTY/
41 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
42 or/34-41
43 NON INSULIN DEPENDENT DIABETES MELLITUS/
44 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late
or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
45 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
46 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
47 or/43-46
48 JUVENILE DIABETES MELLITUS/
49 and/42,47
50 or/48-49
51 PATIENT EDUCATION/
52 DIABETES EDUCATION/
53 DIABETES EDUCATOR/
54 EDUCATION PROGRAM/
55 PROBLEM SOLVING/
56 ((educat\$ or training) adj6 (intervention\$ or program? or programme or programmes)).ti,ab.
57 (problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
58 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or
families) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or
instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
59 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or
families) adj3 information).ti,ab.
60 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-
monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or
cope or coping) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e
or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab.
61 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-
monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or
cope or coping) adj3 information).ti,ab.
62 ((diabet\$ or insulin\$ or glyc?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj6
(educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$
or program? or programme or programmes)).ti,ab.
63 ((diabet\$ or insulin\$ or glyc?emi\$ or hypoglyc?emi\$ or "blood glucose" or "blood sugar") adj3
information).ti,ab.
64 or/51-63
65 and/50,64
66 limit 65 to english language
67 conference abstract.pt.
68 letter.pt. or LETTER/
69 note.pt.
70 editorial.pt.
71 CASE REPORT/ or CASE STUDY/
72 (letter or comment* or abstracts).ti.
73 or/67-72
74 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
75 73 not 74
76 ANIMAL/ not HUMAN/
77 NONHUMAN/
78 exp ANIMAL EXPERIMENT/
79 exp EXPERIMENTAL ANIMAL/
80 ANIMAL MODEL/
81 exp RODENT/

- 82 (rat or rats or mouse or mice).ti.
- 83 or/75-82
- 84 66 not 83
- 85 and/33,84

PsycINFO

- # Searches
- 1 LITERATURE REVIEW/
- 2 EXPERIMENTAL DESIGN/
- 3 RANDOM SAMPLING/
- 4 META-ANALYSIS/
- 5 exp TREATMENT/
- 6 (random\$ or search\$ or control\$ or risk\$).tw.
- 7 (meta-analys#s or metaanalys#s).ti.
- 8 (systematic\$ adj (review\$ or overview\$)).ti.
- 9 ((single or double or triple) adj (blind\$ or mask\$)).ti.
- 10 rct.tw.
- 11 or/1-10
- 12 adolescen\$.ag.
- 13 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,id,jw.
- 14 (child\$ or school\$ or preschool\$).ag.
- 15 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,id,jw.
- 16 (infan\$ or neonat\$).ag.
- 17 (infan\$ or neonat\$ or newborn\$ or baby or babies or p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,id,jw.
- 18 or/12-17
- 19 DIABETES MELLITUS/
- 20 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab,id.
- 21 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab,id.
- 22 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab,id.
- 23 BLOOD SUGAR/
- 24 or/19-23
- 25 EDUCATIONAL THERAPY/
- 26 CLIENT EDUCATION/
- 27 EDUCATIONAL PROGRAMS/
- 28 PROBLEM SOLVING/
- 29 ((educat\$ or training) adj6 (intervention\$ or program? or programme or programmes)).ti,ab,id.
- 30 (problem-solving or "problem solving" or problem-based or "problem based").ti,ab,id.
- 31 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab,id.
- 32 ((patient? or parent? or parental or child\$ or adolescen\$ or young or youth? or family\$ or families) adj3 information).ti,ab,id.
- 33 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab,id.
- 34 ((self-help or "self help" or self-care or "self care" or self-regulat\$ or "self regulat\$" or self-monitor\$ or "self monitor\$" or self-manag\$ or "self manag\$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab,id.

- 35 ((diabet\$ or insulin\$ or glyco?emi\$ or hypoglyco?emi\$ or "blood glucose" or "blood sugar") adj6 (educat\$ or train\$ or teach\$ or knowledge or aware\$ or skill\$ or advi?e or instruct\$ or learn\$ or program? or programme or programmes)).ti,ab,id.
- 36 ((diabet\$ or insulin\$ or glyco?emi\$ or hypoglyco?emi\$ or "blood glucose" or "blood sugar") adj3 information).ti,ab,id.
- 37 or/25-36
- 38 and/18,24,37
- 39 and/11,38
- 40 limit 39 to english language

CINAHL with Full Text

- # Query Limiters/Expanders
- S36 S6 AND S34 Limiters - English Language; Exclude MEDLINE records
 Search modes - Boolean/Phrase
- S35 S6 AND S34 Search modes - Boolean/Phrase
- S34 S21 AND S33 Search modes - Boolean/Phrase
- S33 S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32
 Search modes - Boolean/Phrase
- S32 T1 ((diabet* or insulin* or glyco#emi* or hypoglyco#emi* or "blood glucose" or "blood sugar") N3 information) OR AB ((diabet* or insulin* or glyco#emi* or hypoglyco#emi* or "blood glucose" or "blood sugar") N3 information) Search modes - Boolean/Phrase
- S31 T1 ((diabet* or insulin* or glyco#emi* or hypoglyco#emi* or "blood glucose" or "blood sugar") N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) OR AB ((diabet* or insulin* or glyco#emi* or hypoglyco#emi* or "blood glucose" or "blood sugar") N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) Search modes - Boolean/Phrase
- S30 T1 ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N3 information) OR AB ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N3 information) Search modes - Boolean/Phrase
- S29 T1 ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) OR AB ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat*" or self-monitor* or "self monitor*" or self-manag* or "self manag*" or self-efficacy or "self efficacy" or cope or coping) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) Search modes - Boolean/Phrase
- S28 T1 ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N3 information) OR AB ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N3 information) Search modes - Boolean/Phrase
- S27 T1 ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) OR AB ((patient# or parent# or parental or child* or adolescen* or young or youth# or family* or families) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) Search modes - Boolean/Phrase
- S26 T1 (problem-solving or "problem solving" or problem-based or "problem based") OR AB (problem-solving or "problem solving" or problem-based or "problem based") Search modes - Boolean/Phrase
- S25 T1 ((educat* or training) N6 (intervention* or program# or programme or programmes)) OR AB ((educat* or training) N6 (intervention* or program# or programme or programmes))
 Search modes - Boolean/Phrase
- S24 MW "ED" Search modes - Boolean/Phrase
- S23 (MH "Problem Solving+") Search modes - Boolean/Phrase

S22	(MH "Patient Education") OR (MH "Diabetes Education") Boolean/Phrase	Search modes -
S21	S12 AND S20	Search modes - Boolean/Phrase
S20	S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19	Search modes - Boolean/Phrase
S19	AB (NIDDM or T2D or TIID or DM2 or DMII)	Search modes - Boolean/Phrase
S18	TI (NIDDM or T2D or TIID or DM2 or DMII)	Search modes - Boolean/Phrase
S17	AB (diabet* adj5 non insulin or non-insulin)	Search modes - Boolean/Phrase
S16	TI (diabet* adj5 non insulin or non-insulin)	Search modes - Boolean/Phrase
S15	AB (diabet* N5 "type two" or "type 2" or "type II" or T2 or slow or late or stable or ketosis resistant or keto resist* or keto-resist* or non keto* or non-keto*)	Search modes - Boolean/Phrase
S14	TI (diabet* N5 "type two" or "type 2" or "type II" or T2 or slow or late or stable or ketosis resistant or keto resist* or keto-resist* or non keto* or non-keto*)	Search modes - Boolean/Phrase
S13	(MH "Diabetes Mellitus, Type 2")	Search modes - Boolean/Phrase
S12	S7 OR S8 OR S9 OR S10 OR S11	Search modes - Boolean/Phrase
S11	TI (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) OR AB (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) or SO (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*)	Search modes - Boolean/Phrase
S10	TI (infan* or neonat* or newborn* or baby or babies) OR AB (infan* or neonat* or newborn* or baby or babies) OR SO (infan* or neonat* or newborn* or baby or babies)	Search modes - Boolean/Phrase
S9	TI (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR AB (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR SO (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#)	Search modes - Boolean/Phrase
S8	TI (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR AB (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR SO (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*)	Search modes - Boolean/Phrase
S7	(MH "Infant, Newborn+") OR (MH "Infant+") OR (MH "Child, Preschool") OR (MH "Child+") OR (MH "Adolescence+")	Search modes - Boolean/Phrase
S6	S1 OR S2 OR S3 OR S4 OR S5	Search modes - Boolean/Phrase
S5	PT systematic review	Search modes - Boolean/Phrase
S4	PT review	Search modes - Boolean/Phrase
S3	TX meta-analysis OR "meta analysis"	Search modes - Boolean/Phrase
S2	TX random*	Search modes - Boolean/Phrase
S1	(MH "Treatment Outcomes+") OR (MH "Experimental Studies+")	Search modes - Boolean/Phrase

F.19 Type 2 diabetes – behavioural interventions

Review questions:

What is the effectiveness of behavioural interventions to promote engagement with clinical services in children and young people with type 2 diabetes?

What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 2 diabetes?

Ovid MEDLINE(R)

Searches

1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or
kindergar\$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 2/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late
or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14 or/10-13
15 and/9,14
16 BEHAVIOR THERAPY/
17 COGNITIVE THERAPY/
18 PSYCHOTHERAPY/
19 PSYCHOTHERAPY, GROUP/
20 FAMILY THERAPY/
21 (psychotherap\$ or BFST or CBT).ti,ab.
22 ((cogniti\$ or psycho\$) adj5 (intervention\$ or treatment\$ or therap\$)).ti,ab.
23 ((behavio?r\$ or motivation\$) adj5 (intervention\$ or treatment\$ or therap\$ or chang\$ or
modif\$)).ti,ab.
24 ((family\$ or families or parent?) adj5 (intervention\$ or treatment\$ or therap\$ or team? or
teamwork\$ or team-work\$)).ti,ab.
25 COUNSELING/
26 MOTIVATIONAL INTERVIEWING/
27 MENTORS/
28 SOCIAL SUPPORT/
29 SELF-HELP GROUPS/
30 (motivation\$ or counsel?ing or mentor\$).ti,ab.
31 ((peer or social\$ or self help or self-help) adj3 (group? or support?)).ti,ab.
32 or/16-31
33 and/15,32
34 limit 33 to english language
35 LETTER/
36 EDITORIAL/
37 NEWS/
38 exp HISTORICAL ARTICLE/
39 ANECDOTES AS TOPIC/
40 COMMENT/
41 CASE REPORT/
42 (letter or comment* or abstracts).ti.
43 or/35-42
44 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
45 43 not 44
46 ANIMALS/ not HUMANS/
47 exp ANIMALS, LABORATORY/
48 exp ANIMAL EXPERIMENTATION/
49 exp MODELS, ANIMAL/

- 50 exp RODENTIA/
- 51 (rat or rats or mouse or mice).ti.
- 52 or/45-51
- 53 34 not 52

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
- 7 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
- 8 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
- 9 or/6-8
- 10 and/5,9
- 11 (psychotherap\$ or BFST or CBT).ti,ab.
- 12 ((cogniti\$ or psycho\$) adj5 (intervention\$ or treatment\$ or therap\$)).ti,ab.
- 13 ((behavio?\$ or motivation\$) adj5 (intervention\$ or treatment\$ or therap\$ or chang\$ or modif\$)).ti,ab.
- 14 ((family\$ or families or parent?) adj5 (intervention\$ or treatment\$ or therap\$ or team? or teamwork\$ or team-work\$)).ti,ab.
- 15 (motivation\$ or counsel?ing or mentor\$).ti,ab.
- 16 ((peer or social\$ or self help or self-help) adj3 (group? or support?)).ti,ab.
- 17 or/11-16
- 18 and/10,17
- 19 limit 18 to english language

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 2/
- 11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
- 12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
- 13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
- 14 or/10-13
- 15 and/9,14
- 16 BEHAVIOR THERAPY/
- 17 COGNITIVE THERAPY/
- 18 PSYCHOTHERAPY/

- 19 PSYCHOTHERAPY, GROUP/
20 FAMILY THERAPY/
21 (psychotherap\$ or BFST or CBT).ti,ab.
22 ((cogniti\$ or psycho\$) adj5 (intervention\$ or treatment\$ or therap\$)).ti,ab.
23 ((behavio?r\$ or motivation\$) adj5 (intervention\$ or treatment\$ or therap\$ or chang\$ or modif\$)).ti,ab.
24 ((family\$ or families or parent?) adj5 (intervention\$ or treatment\$ or therap\$ or team? or teamwork\$ or team-work\$)).ti,ab.
25 COUNSELING/
26 MOTIVATIONAL INTERVIEWING/
27 MENTORS/
28 SOCIAL SUPPORT/
29 SELF-HELP GROUPS/
30 (motivation\$ or counsel?ing or mentor\$).ti,ab.
31 ((peer or social\$ or self help or self-help) adj3 (group? or support?)).ti,ab.
32 or/16-31
33 and/15,32

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).kw,ti,ab,jw,rw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).kw,ti,ab,jw,rw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).kw,ti,ab,jw,rw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).kw,ti,ab,jw,rw.
5 or/1-4
6 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab,kw.
7 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab,kw.
8 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
9 or/6-8
10 GROUP THERAPY.kw.
11 (psychotherap\$ or BFST or CBT).tw,tx,kw.
12 ((cogniti\$ or psycho\$) adj5 (intervention\$ or treatment\$ or therap\$)).tw,tx,kw.
13 ((behavio?r\$ or motivation\$) adj5 (intervention\$ or treatment\$ or therap\$ or chang\$ or modif\$)).tw,tx,kw.
14 ((family\$ or families or parent?) adj5 (intervention\$ or treatment\$ or therap\$ or team? or teamwork\$ or team-work\$)).tw,tx,kw.
15 TEACHER.kw.
16 SUPPORT GROUP.kw.
17 SELF HELP.kw.
18 (motivation\$ or counsel?ing or mentor\$).tw,tx,kw.
19 ((peer or social\$ or self help or self-help) adj3 (group? or support?)).tw,tx,kw.
20 or/10-19
21 and/5,9,20

Health Technology Assessment

- # Searches
- 1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx,rw.
3 exp CHILD/

- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jx,rw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 2/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw.
13 (NIDDM or T2D or TIID or DM2 or DMII).tw.
14 or/10-13
15 BEHAVIOR THERAPY/
16 COGNITIVE THERAPY/
17 PSYCHOTHERAPY/
18 PSYCHOTHERAPY, GROUP/
19 FAMILY THERAPY/
20 (psychotherap\$ or BFST or CBT).tw.
21 ((cogniti\$ or psycho\$) adj5 (intervention\$ or treatment\$ or therap\$)).tw.
22 ((behavior?r\$ or motivation\$) adj5 (intervention\$ or treatment\$ or therap\$ or chang\$ or modif\$)).tw.
23 ((family\$ or families or parent?) adj5 (intervention\$ or treatment\$ or therap\$ or team? or teamwork\$ or team-work\$)).tw.
24 COUNSELING/
25 MOTIVATIONAL INTERVIEWING/
26 MENTORS/
27 SOCIAL SUPPORT/
28 SELF-HELP GROUPS/
29 (motivation\$ or counsel?ing or mentor\$).tw.
30 ((peer or social\$ or self help or self-help) adj3 (group? or support?)).tw.
31 or/15-30
32 and/9,14,31

Embase

- # Searches
1 exp ADOLESCENT/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
9 or/1-8
10 NON INSULIN DEPENDENT DIABETES MELLITUS/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14 or/10-13
15 JUVENILE DIABETES MELLITUS/

- 16 and/9,14
- 17 or/15-16
- 18 BEHAVIOR THERAPY/
- 19 BEHAVIOR MODIFICATION/
- 20 COGNITIVE THERAPY/
- 21 PSYCHOTHERAPY/
- 22 FAMILY THERAPY/
- 23 GROUP THERAPY/
- 24 MOTIVATIONAL INTERVIEWING/
- 25 (psychotherap\$ or BFST or CBT).ti,ab.
- 26 ((cogniti\$ or psycho\$) adj5 (intervention\$ or treatment\$ or therap\$)).ti,ab.
- 27 ((behavio?\$ or motivation\$) adj5 (intervention\$ or treatment\$ or therap\$ or chang\$ or modif\$)).ti,ab.
- 28 ((family\$ or families or parent\$) adj5 (intervention\$ or treatment\$ or therap\$ or team? or teamwork\$ or team-work\$)).ti,ab.
- 29 COUNSELING/
- 30 FAMILY COUNSELING/
- 31 PARENT COUNSELING/
- 32 PATIENT COUNSELING/
- 33 PEER COUNSELING/
- 34 TEACHER/
- 35 SOCIAL SUPPORT/
- 36 SUPPORT GROUP/
- 37 SELF HELP/
- 38 (motivation\$ or counsel?ing or mentor\$).ti,ab.
- 39 ((peer or social\$ or self help or self-help) adj3 (group? or support?)).ti,ab.
- 40 or/18-39
- 41 and/17,40
- 42 limit 41 to english language
- 43 conference abstract.pt.
- 44 letter.pt. or LETTER/
- 45 note.pt.
- 46 editorial.pt.
- 47 CASE REPORT/ or CASE STUDY/
- 48 (letter or comment* or abstracts).ti.
- 49 or/43-48
- 50 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 51 49 not 50
- 52 ANIMAL/ not HUMAN/
- 53 NONHUMAN/
- 54 exp ANIMAL EXPERIMENT/
- 55 exp EXPERIMENTAL ANIMAL/
- 56 ANIMAL MODEL/
- 57 exp RODENT/
- 58 (rat or rats or mouse or mice).ti.
- 59 or/51-58
- 60 42 not 59

PsycINFO

- # Searches
- 1 adolescen\$.ag.
- 2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,id,jw.
- 3 (child\$ or school\$ or preschool\$).ag.

- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,id,jw.
- 5 (infan\$ or neonat\$).ag.
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies or p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,id,jw.
- 7 or/1-6
- 8 DIABETES MELLITUS/
- 9 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab,id.
- 10 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab,id.
- 11 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab,id.
- 12 or/8-11
- 13 BEHAVIOR THERAPY/
- 14 COGNITIVE THERAPY/
- 15 COGNITIVE BEHAVIOR THERAPY/
- 16 PSYCHOTHERAPY/
- 17 ADOLESCENT PSYCHOTHERAPY/
- 18 CHILD PSYCHOTHERAPY/
- 19 GROUP PSYCHOTHERAPY/
- 20 FAMILY THERAPY/
- 21 FAMILY INTERVENTION/
- 22 MOTIVATIONAL INTERVIEWING/
- 23 (psychotherap\$ or BFST or CBT).ti,ab.
- 24 ((cogniti\$ or psycho\$) adj5 (intervention\$ or treatment\$ or therap\$)).ti,ab.
- 25 ((behavio?r\$ or motivation\$) adj5 (intervention\$ or treatment\$ or therap\$ or chang\$ or modif\$)).ti,ab.
- 26 ((family\$ or families or parent\$) adj5 (intervention\$ or treatment\$ or therap\$ or team? or teamwork\$ or team-work\$)).ti,ab.
- 27 COUNSELING/
- 28 GROUP COUNSELING/
- 29 PEER COUNSELING/
- 30 MENTOR/
- 31 SOCIAL SUPPORT/
- 32 SUPPORT GROUPS/
- 33 SELF HELP TECHNIQUES/
- 34 (motivation\$ or counsel?ing or mentor\$).ti,ab.
- 35 ((peer or social\$ or self help or self-help) adj3 (group? or support?)).ti,ab.
- 36 or/13-35
- 37 and/7,12,36
- 38 limit 37 to english language
- 39 limit 38 to yr="2013 -Current"

CINAHL with Full Text

- | # | Query | Limiters/Expanders |
|-----|--|---|
| S24 | S6 AND S9 AND S23 | Limiters - English Language; Exclude MEDLINE records
Search modes - Boolean/Phrase |
| S23 | S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 | Search modes - Boolean/Phrase |
| S22 | T1 ((peer or social* or "self help" or self-help) N3 (group# or support#)) OR AB ((peer or social* or "self help" or self-help) N3 (group# or support#)) | Search modes - Boolean/Phrase |
| S21 | T1 (motivation* or counsel#ing or mentor*) OR AB (motivation* or counsel#ing or mentor*) | Search modes - Boolean/Phrase |
| S20 | (MH "Support Groups") | Search modes - Boolean/Phrase |

- S19 (MH "Mentorship") Search modes - Boolean/Phrase
S18 (MH "Counseling") OR (MH "Peer Counseling") Search modes - Boolean/Phrase
S17 TI ((family* or families or parent#) N5 (intervention* or treatment* or therap* or team# or teamwork* or team-work*)) OR AB ((family* or families or parent#) N5 (intervention* or treatment* or therap* or team# or teamwork* or team-work*)) Search modes - Boolean/Phrase
S16 TI ((behavio#r* or motivation*) N5 (intervention* or treatment* or therap* or chang* or modif*)) OR AB ((behavio#r* or motivation*) N5 (intervention* or treatment* or therap* or chang* or modif*)) Search modes - Boolean/Phrase
S15 TI ((cogniti* or psycho*) N5 (intervention* or treatment* or therap*)) OR AB ((cogniti* or psycho*) N5 (intervention* or treatment* or therap*)) Search modes - Boolean/Phrase
S14 TI (psychotherap* or BFST or CBT) OR AB (psychotherap* or BFST or CBT) Search modes - Boolean/Phrase
S13 (MH "Motivational Interviewing") Search modes - Boolean/Phrase
S12 (MH "Psychotherapy, Group") OR (MH "Family Therapy") Search modes - Boolean/Phrase
S11 (MH "Psychotherapy") Search modes - Boolean/Phrase
S10 (MH "Behavior Therapy+") OR (MH "Cognitive Therapy") Search modes - Boolean/Phrase
S9 S7 OR S8 Search modes - Boolean/Phrase
S8 TI (diabet* N5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)) OR AB (diabet* N5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)) Search modes - Boolean/Phrase
S7 (MH "Diabetes Mellitus, Type 2") Search modes - Boolean/Phrase
S6 S1 OR S2 OR S3 OR S4 OR S5 Search modes - Boolean/Phrase
S5 TI (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) OR AB (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) or SO (pediatric* or paediatric* or pubert* or prepubert* or pre-pubert* or pubescen* or prepubescen* or pre-pubescen*) Search modes - Boolean/Phrase
S4 TI (infan* or neonat* or newborn* or baby or babies) OR AB (infan* or neonat* or newborn* or baby or babies) OR SO (infan* or neonat* or newborn* or baby or babies) Search modes - Boolean/Phrase
S3 TI (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR AB (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR SO (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) Search modes - Boolean/Phrase
S2 TI (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR AB (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR SO (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) Search modes - Boolean/Phrase
S1 (MH "Infant, Newborn+") OR (MH "Infant+") OR (MH "Child, Preschool") OR (MH "Child+") OR (MH "Adolescence+") Search modes - Boolean/Phrase

F.20 Type 2 diabetes – dietary advice

Review question: What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?

Ovid MEDLINE(R)

- # Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.

3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 2/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14 or/10-13
15 exp DIET THERAPY/
16 NUTRITION THERAPY/
17 dh.fs.
18 or/15-17
19 exp FOOD HABITS/
20 exp DIET/
21 DIETETICS/
22 (diet\$ or nutrition\$ or food or feed\$).ti,ab.
23 or/19-22
24 HEMOGLOBIN A, GLYCOSYLATED/
25 (h?emoglobin? adj3 (glyc\$ or A1?)).ti,ab.
26 (glycoh?emoglobin? or HbA1c or HbA1c or HbA 1c or HbA 1c or Hb A1c or Hb A1c).ti,ab.
27 "hemoglobin A1c protein, human".nm.
28 BLOOD GLUCOSE/
29 ((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
30 (glyc?emi\$ adj3 (control\$ or parameter\$ or status\$)).ti,ab.
31 exp HYPERGLYCEMIA/
32 hyperglyc?emi\$.ti,ab.
33 REMISSION INDUCTION/
34 remission?.ti,ab.
35 ((revers\$ or regress\$) adj5 diabet\$).ti,ab.
36 or/24-35
37 and/23,36
38 or/18,37
39 and/9,14,38
40 limit 39 to english language
41 LETTER/
42 EDITORIAL/
43 NEWS/
44 exp HISTORICAL ARTICLE/
45 ANECDOTES AS TOPIC/
46 COMMENT/
47 CASE REPORT/
48 (letter or comment* or abstracts).ti.
49 or/41-48
50 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
51 49 not 50
52 ANIMALS/ not HUMANS/
53 exp ANIMALS, LABORATORY/

- 54 exp ANIMAL EXPERIMENTATION/
- 55 exp MODELS, ANIMAL/
- 56 exp RODENTIA/
- 57 (rat or rats or mouse or mice).ti.
- 58 or/51-57
- 59 40 not 58

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
- 7 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
- 8 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
- 9 or/6-8
- 10 (diet\$ or nutrition\$ or food or feed\$).ti,ab.
- 11 (h?emoglobin? adj3 (glyc\$ or A1?)).ti,ab.
- 12 (glycoh?emoglobin? or HbA1c or HbA1c or HbA 1c or HbA 1c or Hb A1c or Hb A1c).ti,ab.
- 13 ((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
- 14 (glyc?emi\$ adj3 (control\$ or parameter\$ or status\$)).ti,ab.
- 15 hyperglyc?emi\$.ti,ab.
- 16 remission?.ti,ab.
- 17 ((revers\$ or regress\$) adj5 diabet\$).ti,ab.
- 18 or/11-17
- 19 and/5,9-10,18
- 20 limit 19 to english language

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 2/
- 11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
- 12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
- 13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
- 14 or/10-13
- 15 exp DIET THERAPY/
- 16 NUTRITION THERAPY/
- 17 dh.fs.

18 or/15-17
19 exp FOOD HABITS/
20 exp DIET/
21 DIETETICS/
22 (diet\$ or nutrition\$ or food or feed\$).ti,ab.
23 or/19-22
24 HEMOGLOBIN A, GLYCOSYLATED/
25 (h?emoglobin? adj3 (glyc\$ or A1?)).ti,ab.
26 (glycoh?emoglobin? or HbA1c or HbA1c or HbA 1c or HbA 1c or Hb A1c or Hb Alc).ti,ab.
27 ["hemoglobin A1c protein, human".nm.]
28 BLOOD GLUCOSE/
29 ((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
30 (glyc?emi\$ adj3 (control\$ or parameter\$ or status\$)).ti,ab.
31 exp HYPERGLYCEMIA/
32 hyperglyc?emi\$.ti,ab.
33 REMISSION INDUCTION/
34 remission?.ti,ab.
35 ((revers\$ or regress\$) adj5 diabet\$).ti,ab.
36 or/24-35
37 and/23,36
38 or/18,37
39 and/9,14,38

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

Searches
1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).kw,tw,tx,jw,rw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).kw,tw,tx,jw,rw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).kw,tw,tx,jw,rw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).kw,tw,tx,jw,rw.
5 or/1-4
6 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw,tx,kw.
7 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw,tx,kw.
8 (NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
9 or/6-8
10 DIET THERAPY.kw.
11 NUTRITION THERAPY.kw.
12 or/10-11
13 (diet\$ or nutrition\$ or food or feed\$).tw,tx,kw.
14 (h?emoglobin? adj3 (glyc\$ or A1?)).tw,tx,kw.
15 (glycoh?emoglobin? or HbA1c or HbA1c or HbA 1c or HbA 1c or Hb A1c or Hb Alc).tw,tx,kw.
16 ((blood or plasma) adj3 (glucose or sugar?)).tw,tx,kw.
17 (glyc?emi\$ adj3 (control\$ or parameter\$ or status\$)).tw,tx,kw.
18 hyperglyc?emi\$.tw,tx,kw.
19 remission?.tw,tx,kw.
20 ((revers\$ or regress\$) adj5 diabet\$).tw,tx.
21 or/14-20
22 and/13,21
23 or/12,22
24 and/5,9,23

Health Technology Assessment

- # Searches
- 1 ADOLESCENT/ or MINORS/
 - 2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx,rw.
 - 3 exp CHILD/
 - 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
 - 5 exp INFANT/
 - 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw.
 - 7 exp PEDIATRICS/ or exp PUBERTY/
 - 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jx,rw.
 - 9 or/1-8
 - 10 exp DIABETES MELLITUS, TYPE 2/
 - 11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw.
 - 12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw.
 - 13 (NIDDM or T2D or TIID or DM2 or DMII).tw.
 - 14 or/10-13
 - 15 exp DIET THERAPY/
 - 16 NUTRITION THERAPY/
 - 17 dh.fs.
 - 18 or/15-17
 - 19 exp FOOD HABITS/
 - 20 exp DIET/
 - 21 DIETETICS/
 - 22 (diet\$ or nutrition\$ or food or feed\$).tw.
 - 23 or/19-22
 - 24 HEMOGLOBIN A, GLYCOSYLATED/
 - 25 (h?emoglobin? adj3 (glyc\$ or A1?)).tw.
 - 26 (glycoh?emoglobin? or HbA1c or HbA1c or HbA 1c or HbA 1c or Hb A1c or Hb A1c).tw.
 - 27 BLOOD GLUCOSE/
 - 28 ((blood or plasma) adj3 (glucose or sugar?)).tw.
 - 29 (glyc?emi\$ adj3 (control\$ or parameter\$ or status\$)).tw.
 - 30 exp HYPERGLYCEMIA/
 - 31 hyperglyc?emi\$.tw.
 - 32 REMISSION INDUCTION/
 - 33 remission?.tw.
 - 34 ((revers\$ or regress\$) adj5 diabet\$).tw.
 - 35 or/24-34
 - 36 and/23,35
 - 37 or/18,36
 - 38 and/9,14,37

Embase

- # Searches
- 1 exp ADOLESCENT/
 - 2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
 - 3 exp CHILD/
 - 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
 - 5 exp INFANT/
 - 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
 - 7 exp PEDIATRICS/ or exp PUBERTY/

8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
9 or/1-8
10 NON INSULIN DEPENDENT DIABETES MELLITUS/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late
or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14 or/10-13
15 JUVENILE DIABETES MELLITUS/
16 and/9,14
17 or/15-16
18 exp DIET THERAPY/
19 exp FEEDING BEHAVIOR/
20 exp DIET/ or DIETARY COMPLIANCE/
21 DIETETICS/
22 (diet\$ or nutrition\$ or food or feed\$).ti,ab.
23 or/19-22
24 HEMOGLOBIN A1C/
25 GLYCOSYLATED HEMOGLOBIN/
26 (h?emoglobin? adj3 (glyc\$ or A1?)).ti,ab.
27 (glycoh?emoglobin? or HbA1c or HbA1c or HbA 1c or HbA 1c or Hb A1c or Hb A1c).ti,ab.
28 GLUCOSE BLOOD LEVEL/
29 ((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
30 GLYCEMIC CONTROL/
31 (glyc?emi\$ adj3 (control\$ or parameter\$ or status\$)).ti,ab.
32 HYPERGLYCEMIA/
33 hyperglyc?emi\$.ti,ab.
34 REMISSION/ or DISEASE CLEARANCE/
35 remission?.ti,ab.
36 ((revers\$ or regress\$) adj5 diabet\$).ti,ab.
37 or/24-36
38 and/23,37
39 or/18,38
40 and/17,39
41 limit 40 to english language
42 conference abstract.pt.
43 letter.pt. or LETTER/
44 note.pt.
45 editorial.pt.
46 CASE REPORT/ or CASE STUDY/
47 (letter or comment* or abstracts).ti.
48 or/42-47
49 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
50 48 not 49
51 ANIMAL/ not HUMAN/
52 NONHUMAN/
53 exp ANIMAL EXPERIMENT/
54 exp EXPERIMENTAL ANIMAL/
55 ANIMAL MODEL/
56 exp RODENT/
57 (rat or rats or mouse or mice).ti.
58 or/50-57
59 41 not 58

PsycINFO

- # Searches
- 1 adolescen\$.ag.
- 2 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,id,jw.
- 3 (child\$ or school\$ or preschool\$).ag.
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,id,jw.
- 5 (infan\$ or neonat\$).ag.
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies or p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,id,jw.
- 7 or/1-6
- 8 DIABETES MELLITUS/
- 9 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab,id.
- 10 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab,id.
- 11 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab,id.
- 12 or/8-11
- 13 DIETS/ or DIETARY RESTRAINT/ or EATING BEHAVIOUR/ or WEIGHT CONTROL/
- 14 (diet\$ or nutrition\$ or food or feed\$).ti,ab,id.
- 15 or/13-14
- 16 BLOOD SUGAR/
- 17 (h?emoglobin? adj3 (glyc\$ or A1?)).ti,ab,id.
- 18 (glycoh?emoglobin? or HbA1c or HbA1c or HbA 1c or HbA 1c or Hb A1c or Hb A1c).ti,ab,id.
- 19 ((blood or plasma) adj3 (glucose or sugar?)).ti,ab,id.
- 20 (glyc?emi\$ adj3 (control\$ or parameter\$ or status\$)).ti,ab,id.
- 21 HYPERGLYCEMIA/
- 22 hyperglyc?emi\$.ti,ab,id.
- 23 exp "REMISSION (DISORDERS)"/
- 24 remission?.ti,ab,id.
- 25 ((revers\$ or regress\$) adj5 diabet\$).ti,ab.
- 26 or/16-25
- 27 and/7,12,15,26
- 28 limit 27 to english language
- 29 (book or dissertation abstract or encyclopedia).pt.
- 30 28 not 29

F.21 Type 2 diabetes – weight loss

Review question: Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?

Ovid MEDLINE(R)

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.

9 or/1-8
10 exp DIABETES MELLITUS, TYPE 2/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late
or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14 or/10-13
15 exp OVERWEIGHT/
16 exp OBESITY/
17 (obes\$ or overweight or over weight).ti,ab.
18 or/15-17
19 exp BODY WEIGHT CHANGES/
20 ((weight or BMI or body mass index) adj3 (gain\$ or los# or lose? or losing or chang\$ or r#se?
or rising or raise? or f#ll\$ or drop\$ or up or down or reduc\$ or increas\$ or control\$ or
maintain\$ or maintenance)).ti,ab.
21 SERVING SIZE/
22 PORTION SIZE/
23 ((serving? or portion?) adj3 (size? or sizing)).ti,ab.
24 or/19-23
25 HEMOGLOBIN A, GLYCOSYLATED/
26 (h?emoglobin? adj3 (glyc\$ or A1?)).ti,ab.
27 (glycoh?emoglobin? or HbA1c or HbAlc or HbA 1c or HbA 1c or Hb A1c or Hb Alc).ti,ab.
28 "hemoglobin A1c protein, human".nm.
29 BLOOD GLUCOSE/
30 ((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
31 (glyc?emi\$ adj3 (control\$ or parameter\$ or status\$)).ti,ab.
32 exp HYPERGLYCEMIA/
33 hyperglyc?emi\$.ti,ab.
34 exp HYPOGLYCEMIA/
35 hypoglyc?emi\$.ti,ab.
36 REMISSION INDUCTION/
37 remission?.ti,ab.
38 ((revers\$ or regress\$) adj5 diabet\$).ti,ab.
39 or/25-38
40 and/9,14,18,24,39
41 limit 40 to english language
42 LETTER/
43 EDITORIAL/
44 NEWS/
45 exp HISTORICAL ARTICLE/
46 ANECDOTES AS TOPIC/
47 COMMENT/
48 (letter or comment* or abstracts).ti.
49 or/42-48
50 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
51 49 not 50
52 ANIMALS/ not HUMANS/
53 exp ANIMALS, LABORATORY/
54 exp ANIMAL EXPERIMENTATION/
55 exp MODELS, ANIMAL/
56 exp RODENTIA/
57 (rat or rats or mouse or mice).ti.
58 or/51-57

59 41 not 58

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- | # | Searches |
|----|--|
| 1 | (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab. |
| 2 | (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab. |
| 3 | (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab. |
| 4 | (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab. |
| 5 | or/1-4 |
| 6 | (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab. |
| 7 | (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab. |
| 8 | (NIDDM or T2D or TIID or DM2 or DMII).ti,ab. |
| 9 | or/6-8 |
| 10 | (obes\$ or overweight or over weight).ti,ab. |
| 11 | ((weight or BMI or body mass index) adj3 (gain\$ or los# or lose? or losing or chang\$ or r#se? or rising or raise? or f#ll\$ or drop\$ or up or down or reduc\$ or increas\$ or control\$ or maintain\$ or maintenance)).ti,ab. |
| 12 | ((serving? or portion?) adj3 (size? or sizing)).ti,ab. |
| 13 | or/11-12 |
| 14 | (h?emoglobin? adj3 (glyc\$ or A1?)).ti,ab. |
| 15 | (glycoh?emoglobin? or HbA1c or HbA1c or HbA 1c or HbA 1c or Hb A1c or Hb A1c).ti,ab. |
| 16 | ((blood or plasma) adj3 (glucose or sugar?)).ti,ab. |
| 17 | (glyc?emi\$ adj3 (control\$ or parameter\$ or status\$)).ti,ab. |
| 18 | hyperglyc?emi\$.ti,ab. |
| 19 | hypoglyc?emi\$.ti,ab. |
| 20 | remission?.ti,ab. |
| 21 | ((revers\$ or regress\$) adj5 diabet\$).ti,ab. |
| 22 | or/14-21 |
| 23 | and/5,9-10,13,22 |

Cochrane Central Register of Controlled Trials

- | # | Searches |
|----|--|
| 1 | ADOLESCENT/ or MINORS/ |
| 2 | (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab. |
| 3 | exp CHILD/ |
| 4 | (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab. |
| 5 | exp INFANT/ |
| 6 | (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab. |
| 7 | exp PEDIATRICS/ or exp PUBERTY/ |
| 8 | (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab. |
| 9 | or/1-8 |
| 10 | exp DIABETES MELLITUS, TYPE 2/ |
| 11 | (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab. |
| 12 | (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab. |
| 13 | (NIDDM or T2D or TIID or DM2 or DMII).ti,ab. |
| 14 | or/10-13 |
| 15 | exp OVERWEIGHT/ |
| 16 | exp OBESITY/ |
| 17 | (obes\$ or overweight or over weight).ti,ab. |

- 18 or/15-17
- 19 exp BODY WEIGHT CHANGES/
- 20 ((weight or BMI or body mass index) adj3 (gain\$ or los# or lose? or losing or chang\$ or r#se? or rising or raise? or f#l\$ or drop\$ or up or down or reduc\$ or increas\$ or control\$ or maintain\$ or maintenance)).ti,ab.
- 21 SERVING SIZE/
- 22 PORTION SIZE/
- 23 ((serving? or portion?) adj3 (size? or sizing)).ti,ab.
- 24 or/19-23
- 25 HEMOGLOBIN A, GLYCOSYLATED/
- 26 (h?emoglobin? adj3 (glyc\$ or A1?)).ti,ab.
- 27 (glycoh?emoglobin? or HbA1c or HbA1c or HbA 1c or HbA 1c or Hb A1c or Hb Alc).ti,ab.
- 28 BLOOD GLUCOSE/
- 29 ((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
- 30 (glyc?emi\$ adj3 (control\$ or parameter\$ or status\$)).ti,ab.
- 31 exp HYPERGLYCEMIA/
- 32 hyperglyc?emi\$.ti,ab.
- 33 exp HYPOGLYCEMIA/
- 34 hypoglyc?emi\$.ti,ab.
- 35 REMISSION INDUCTION/
- 36 remission?.ti,ab.
- 37 ((revers\$ or regress\$) adj5 diabet\$).ti,ab.
- 38 or/25-37
- 39 and/9,14,18,24,38

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,tx,kw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,tx,kw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx,kw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,tx,kw.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw,tx,kw.
- 7 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw,tx,kw.
- 8 (NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
- 9 or/6-8
- 10 (obes\$ or overweight or over weight).tw,tx,kw.
- 11 ((weight or BMI or body mass index) adj3 (gain\$ or los# or lose? or losing or chang\$ or r#se? or rising or raise? or f#l\$ or drop\$ or up or down or reduc\$ or increas\$ or control\$ or maintain\$ or maintenance)).tw,tx,kw.
- 12 (portion? or serv?).tw,tx,kw.
- 13 or/11-12
- 14 (h?emoglobin? adj3 (glyc\$ or A1?)).tw,tx,kw.
- 15 (glycoh?emoglobin? or HbA1c or HbA1c or HbA 1c or HbA 1c or Hb A1c or Hb Alc).tw,tx.
- 16 ((blood or plasma) adj3 (glucose or sugar?)).tw,tx,kw.
- 17 (glyc?emi\$ adj3 (control\$ or parameter\$ or status\$)).tw,tx,kw.
- 18 hyperglyc?emi\$.tw,tx,kw.
- 19 hypoglyc?emi\$.tw,tx,kw.
- 20 remission?.tw,tx,kw.
- 21 ((revers\$ or regress\$) adj5 diabet\$).tw,tx.

22 or/14-21
23 and/5,9-10,13,22

Health Technology Assessment

Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 2/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw.
13 (NIDDM or T2D or TIID or DM2 or DMII).tw.
14 or/10-13
15 exp OVERWEIGHT/
16 exp OBESITY/
17 (obes\$ or overweight or over weight).tw.
18 or/15-17
19 exp BODY WEIGHT CHANGES/
20 (portion? or serv?).tw.
21 ((weight or BMI or body mass index) adj3 (gain\$ or los# or lose? or losing or chang\$ or r#se? or rising or raise? or f#II\$ or drop\$ or up or down or reduc\$ or increas\$ or control\$ or maintain\$ or maintenance)).tw.
22 or/19-20
23 HEMOGLOBIN A, GLYCOSYLATED/
24 (h?emoglobin? adj3 (glyc\$ or A1?)).tw.
25 (glycoh?emoglobin? or HbA1c or HbA1c or HbA 1c or HbA 1c or Hb A1c or Hb A1c).tw.
26 BLOOD GLUCOSE/
27 ((blood or plasma) adj3 (glucose or sugar?)).tw.
28 (glyc?emi\$ adj3 (control\$ or parameter\$ or status\$)).tw.
29 exp HYPERGLYCEMIA/
30 hyperglyc?emi\$.tw.
31 exp HYPOGLYCEMIA/
32 hypoglyc?emi\$.tw.
33 REMISSION INDUCTION/
34 remission?.tw.
35 ((revers\$ or regress\$) adj5 diabet\$).tw.
36 or/23-35
37 and/9,14,18,22,36

Embase 1974 to 2014 April 03

Searches
1 exp ADOLESCENT/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
3 exp CHILD/

4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or
kindergar\$ or boy? or girl?).ti,ab,jx.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
9 or/1-8
10 NON INSULIN DEPENDENT DIABETES MELLITUS/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late
or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14 or/10-13
15 JUVENILE DIABETES MELLITUS/
16 and/9,14
17 or/15-16
18 exp OBESITY/
19 (obes\$ or overweight or over weight).ti,ab.
20 or/18-19
21 WEIGHT CHANGE/ or WEIGHT CONTROL/ or WEIGHT GAIN/ or WEIGHT REDUCTION/
22 ((weight or BMI or body mass index) adj3 (gain\$ or los# or lose? or losing or chang\$ or r#se?
or rising or raise? or f#II\$ or drop\$ or up or down or reduc\$ or increas\$ or control\$ or
maintain\$ or maintenance)).ti,ab.
23 ((serving? or portion?) adj3 (size? or sizing)).ti,ab.
24 or/21-23
25 HEMOGLOBIN A1C/
26 GLYCOSYLATED HEMOGLOBIN/
27 (h?emoglobin? adj3 (glyc\$ or A1?)).ti,ab.
28 (glycoh?emoglobin? or HbA1c or HbA1c or HbA 1c or HbA 1c or Hb A1c or Hb A1c).ti,ab.
29 GLUCOSE BLOOD LEVEL/
30 ((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
31 GLYCEMIC CONTROL/
32 (glyc?emi\$ adj3 (control\$ or parameter\$ or status\$)).ti,ab.
33 HYPERGLYCEMIA/
34 hyperglyc?emi\$.ti,ab.
35 HYPOGLYCEMIA/
36 hypoglyc?emi\$.ti,ab.
37 REMISSION/
38 remission?.ti,ab.
39 ((revers\$ or regress\$) adj5 diabet\$).ti,ab.
40 or/25-39
41 and/17,20,24,40
42 limit 41 to english language
43 conference abstract.pt.
44 letter.pt. or LETTER/
45 note.pt.
46 editorial.pt.
47 (letter or comment* or abstracts).ti.
48 or/43-47
49 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
50 48 not 49
51 ANIMAL/ not HUMAN/
52 NONHUMAN/

53 exp ANIMAL EXPERIMENT/
54 exp EXPERIMENTAL ANIMAL/
55 ANIMAL MODEL/
56 exp RODENT/
57 (rat or rats or mouse or mice).ti.
58 or/50-57
59 42 not 58

F.22 Type 2 diabetes – metformin

Review question: What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?

Ovid MEDLINE(R)

Searches
1 randomized controlled trial.pt.
2 controlled clinical trial.pt.
3 DOUBLE BLIND METHOD/
4 SINGLE BLIND METHOD/
5 RANDOM ALLOCATION/
6 or/1-5
7 ((single or double or triple or treble) adj5 (blind\$ or mask\$)).tw,sh.
8 clinical trial.pt.
9 exp CLINICAL TRIAL/
10 exp CLINICAL TRIALS AS TOPIC/
11 (clinic\$ adj5 trial\$).tw,sh.
12 PLACEBOS/
13 placebo\$.tw,sh.
14 random\$.tw,sh.
15 or/7-14
16 or/6,15
17 META ANALYSIS/
18 META ANALYSIS AS TOPIC/
19 meta analysis.pt.
20 (metaanaly\$ or meta-analy\$ or (meta adj analy\$)).tw,sh.
21 (systematic\$ adj5 (review\$ or overview\$)).tw,sh.
22 (methodologic\$ adj5 (review\$ or overview\$)).tw,sh.
23 or/17-22
24 review\$.pt.
25 (medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.
26 ((hand or manual\$) adj2 search\$).tw.
27 (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online database\$).tw,sh.
28 (pooling or pooled or mantel haenszel).tw,sh.
29 (peto or dersimonian or der simonian or fixed effect).tw,sh.
30 or/25-29
31 and/24,30
32 or/16,23,31
33 letter.pt.
34 case report.tw.

35 comment.pt.
36 editorial.pt.
37 historical article.pt.
38 or/33-37
39 32 not 38
40 ADOLESCENT/ or MINORS/
41 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
42 exp CHILD/
43 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
44 exp INFANT/
45 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
46 exp PEDIATRICS/ or exp PUBERTY/
47 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
48 or/40-47
49 exp DIABETES MELLITUS, TYPE 2/
50 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
51 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
52 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
53 or/49-52
54 METFORMIN/
55 (metformin or glucophage or glucient or metsol or bolamyn or metabet).ti,ab.
56 or/54-55
57 and/48,53,56
58 and/39,57
59 limit 58 to english language
60 LETTER/
61 EDITORIAL/
62 NEWS/
63 exp HISTORICAL ARTICLE/
64 ANECDOTES AS TOPIC/
65 COMMENT/
66 CASE REPORT/
67 (letter or comment* or abstracts).ti.
68 or/60-67
69 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
70 68 not 69
71 ANIMALS/ not HUMANS/
72 exp ANIMALS, LABORATORY/
73 exp ANIMAL EXPERIMENTATION/
74 exp MODELS, ANIMAL/
75 exp RODENTIA/
76 (rat or rats or mouse or mice).ti.
77 or/70-76
78 59 not 77

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

Searches
1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.

- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
- 7 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
- 8 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
- 9 or/6-8
- 10 (metformin or glucophage or glucient or metsol or bolamyn or metabet).ti,ab.
- 11 and/5,9-10

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,kw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,kw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,kw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,kw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 2/
- 11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab,kw.
- 12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab,kw.
- 13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
- 14 or/10-13
- 15 METFORMIN/
- 16 (metformin or glucophage or glucient or metsol or bolamyn or metabet).ti,ab,kw.
- 17 or/15-16
- 18 and/9,14,17

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
- 1 (adolescenc\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,tx,kw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,tx,kw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx,kw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,tx,kw.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw,tx,kw.
- 7 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab,kw.
- 8 (NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
- 9 or/6-8
- 10 (metformin or glucophage or glucient or metsol or bolamyn or metabet).tw,tx,kw.
- 11 and/5,9-10

Health Technology Assessment

- # Searches

- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 2/
- 11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw.
- 12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw.
- 13 (NIDDM or T2D or TIID or DM2 or DMII).tw.
- 14 or/10-13
- 15 METFORMIN/
- 16 (metformin or glucophage or glucient or metsol or bolamyn or metabet).tw.
- 17 or/15-16
- 18 and/9,14,17

Embase

- # Searches
- 1 CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
- 2 (clinic\$ adj5 trial\$).ti,ab,sh.
- 3 SINGLE BLIND PROCEDURE/
- 4 DOUBLE BLIND PROCEDURE/
- 5 RANDOM ALLOCATION/
- 6 CROSSOVER PROCEDURE/
- 7 PLACEBO/
- 8 placebo\$.ti,ab,sh.
- 9 random\$.ti,ab,sh.
- 10 RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
- 11 ((single or double or triple or treble) adj (blind\$ or mask\$)).ti,ab,sh.
- 12 randomi?ed control\$ trial\$.tw.
- 13 or/1-12
- 14 META ANALYSIS/
- 15 ((meta adj analy\$) or metaanalys\$ or meta-analy\$).ti,ab,sh.
- 16 (systematic\$ adj5 (review\$ or overview\$)).ti,sh,ab.
- 17 (methodologic\$ adj5 (review\$ or overview\$)).ti,ab,sh.
- 18 or/14-17
- 19 review.pt.
- 20 (medline or medlars or embase).ab.
- 21 (scisearch or science citation index).ab.
- 22 (psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
- 23 ((hand or manual\$) adj2 search\$).tw.
- 24 (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online database\$).tw.
- 25 (pooling or pooled or mantel haenszel).tw.
- 26 (peto or dersimonian or "der simonian" or fixed effect).tw.
- 27 or/20-26
- 28 and/19,27
- 29 or/18,28

30 (book or conference paper or editorial or letter or note or proceeding or short survey).pt.
31 13 not 30
32 29 not 30
33 or/31-32
34 exp ADOLESCENT/
35 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
36 exp INFANT/
37 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
38 exp NEWBORN/
39 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
40 exp PEDIATRICS/ or exp PUBERTY/
41 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
42 or/34-41
43 NON INSULIN DEPENDENT DIABETES MELLITUS/
44 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
45 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
46 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
47 or/43-46
48 JUVENILE DIABETES MELLITUS/
49 and/42,47
50 or/48-49
51 METFORMIN/
52 (metformin or glucophage or glucient or metsol or bolamyn or metabet).ti,ab.
53 or/51-52
54 and/50,53
55 limit 54 to english language
56 conference abstract.pt.
57 letter.pt. or LETTER/
58 note.pt.
59 editorial.pt.
60 CASE REPORT/ or CASE STUDY/
61 (letter or comment* or abstracts).ti.
62 or/56-61
63 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
64 62 not 63
65 ANIMAL/ not HUMAN/
66 NONHUMAN/
67 exp ANIMAL EXPERIMENT/
68 exp EXPERIMENTAL ANIMAL/
69 ANIMAL MODEL/
70 exp RODENT/
71 (rat or rats or mouse or mice).ti.
72 or/64-71
73 55 not 72
74 and/33,73

F.23 Type 2 diabetes – HbA1c targets

Review question: What is the optimal HbA1c target for children and young people with type 2 diabetes?

Ovid MEDLINE(R)

```
# Searches
1 randomized controlled trial.pt.
2 controlled clinical trial.pt.
3 DOUBLE BLIND METHOD/
4 SINGLE BLIND METHOD/
5 RANDOM ALLOCATION/
6 or/1-5
7 ((single or double or triple or treble) adj5 (blind$ or mask$)).tw,sh.
8 clinical trial.pt.
9 exp CLINICAL TRIAL/
10 exp CLINICAL TRIALS AS TOPIC/
11 (clinic$ adj5 trial$).tw,sh.
12 PLACEBOS/
13 placebo$.tw,sh.
14 random$.tw,sh.
15 or/7-14
16 or/6,15
17 META ANALYSIS/
18 META ANALYSIS AS TOPIC/
19 meta analysis.pt.
20 (metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.
21 (systematic$ adj5 (review$ or overview$)).tw,sh.
22 (methodologic$ adj5 (review$ or overview$)).tw,sh.
23 or/17-22
24 review$.pt.
25 (medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or
    psyclit or "web of science" or "science citation" or scisearch).tw.
26 ((hand or manual$) adj2 search$).tw.
27 (electronic database$ or bibliographic database$ or computeri?ed database$ or online
    database$).tw,sh.
28 (pooling or pooled or mantel haenszel).tw,sh.
29 (peto or dersimonian or der simonian or fixed effect).tw,sh.
30 or/25-29
31 and/24,30
32 exp CASE-CONTROL STUDIES/
33 (case$ adj2 control$).tw.
34 exp COHORT STUDIES/
35 cohort$.tw.
36 or/32-35
37 comparative study.pt.
38 (compar$ adj3 stud$).tw.
39 or/37-38
40 or/16,23,31,36,39
41 ADOLESCENT/ or MINORS/
42 (adolescenc$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
43 exp CHILD/
```

44 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or
kindergar\$ or boy? or girl?).ti,ab,jw.
45 exp INFANT/
46 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
47 exp PEDIATRICS/ or exp PUBERTY/
48 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
49 or/41-48
50 exp DIABETES MELLITUS, TYPE 2/
51 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late
or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
52 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
53 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
54 or/50-53
55 and/49,54
56 HEMOGLOBIN A, GLYCOSYLATED/
57 (h?emoglobin? adj3 glycosylat\$).ti,ab.
58 (glycated adj3 h?emoglobin?).ti,ab.
59 (glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).ti,ab.
60 "hemoglobin A1c protein, human".nm.
61 or/56-60
62 and/55,61
63 REFERENCE STANDARDS/ or REFERENCE VALUES/
64 ((reference? or normal\$ or standard?) adj3 (value? or target\$ or rang\$ or level\$ or
threshold?)).ti,ab.
65 or/63-64
66 ((F#G or BG) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold\$)).ti,ab.
67 ((normogly?emi\$ or euglyc?emi\$ or glyc?emi\$) adj3 (value\$ or target\$ or rang\$ or level\$ or
threshold?)).ti,ab.
68 or/65-67
69 and/62,68
70 and/55,69
71 LETTER/
72 EDITORIAL/
73 NEWS/
74 exp HISTORICAL ARTICLE/
75 ANECDOTES AS TOPIC/
76 COMMENT/
77 CASE REPORT/
78 (letter or comment* or abstracts).ti.
79 or/71-78
80 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
81 79 not 80
82 ANIMALS/ not HUMANS/
83 exp ANIMALS, LABORATORY/
84 exp ANIMAL EXPERIMENTATION/
85 exp MODELS, ANIMAL/
86 exp RODENTIA/
87 (rat or rats or mouse or mice).ti.
88 or/81-87
89 70 not 88
90 limit 89 to english language

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab.
 - 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab.
 - 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
 - 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab.
 - 5 or/1-4
 - 6 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$ or mellitus)).ti,ab.
 - 7 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
 - 8 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
 - 9 or/6-8
 - 10 (h?emoglobin? adj3 glycosylat\$).ti,ab.
 - 11 (glycated adj3 h?emoglobin?).ti,ab.
 - 12 (glycoh?emoglobin? or HbA1c or HbA1c or Hb A1c or Hb A1c).ti,ab.
 - 13 or/10-12
 - 14 ((reference? or normal\$ or standard?) adj3 (value? or target\$ or rang\$ or level\$ or threshold?)).ti,ab.
 - 15 ((F#G or BG) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold\$)).ti,ab.
 - 16 ((normogly?emi\$ or euglyc?emi\$ or glyc?emi\$) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold?)).ti,ab.
 - 17 or/14-16
 - 18 and/5,9,13,17

Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
 - 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab.
 - 3 exp CHILD/
 - 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab.
 - 5 exp INFANT/
 - 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
 - 7 exp PEDIATRICS/ or exp PUBERTY/
 - 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab.
 - 9 or/1-8
 - 10 exp DIABETES MELLITUS, TYPE 2/
 - 11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
 - 12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
 - 13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
 - 14 or/10-13
 - 15 and/9,14
 - 16 HEMOGLOBIN A, GLYCOSYLATED/
 - 17 (h?emoglobin? adj3 glycosylat\$).ti,ab.
 - 18 (glycated adj3 h?emoglobin?).ti,ab.
 - 19 (glycoh?emoglobin? or HbA1c or HbA1c or Hb A1c or Hb A1c).ti,ab.
 - 20 or/16-19
 - 21 REFERENCE STANDARDS/ or REFERENCE VALUES/
 - 22 ((reference? or normal\$ or standard?) adj3 (value? or target\$ or rang\$ or level\$ or threshold?)).ti,ab.
 - 23 or/21-22

- 24 ((F#G or BG) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold\$)).ti,ab.
- 25 ((normogly?emi\$ or euglyc?emi\$ or glyc?emi\$) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold?)).ti,ab.
- 26 or/23-25
- 27 and/20,26
- 28 and/15,27

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
- 1 (ADOLESCENT or MINORS).kw.
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,tx.
- 3 CHILD.kw.
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,tx.
- 5 INFANT.kw.
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx.
- 7 (PEDIATRICS or PUBERTY).kw.
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,tx.
- 9 or/1-8
- 10 DIABETES MELLITUS, TYPE 2.kw.
- 11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw,tx.
- 12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw,tx.
- 13 (NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
- 14 or/10-13
- 15 and/9,14
- 16 HEMOGLOBIN A, GLYCOSYLATED.kw.
- 17 (h?emoglobin? adj3 glycosylat\$).tw,tx.
- 18 (glycated adj3 h?emoglobin?).tw,tx.
- 19 (glycoh?emoglobin? or HbA1c or HbA1c or Hb A1c or Hb A1c).tw,tx.
- 20 or/16-19
- 21 (REFERENCE STANDARDS or REFERENCE VALUES).kw.
- 22 ((reference? or normal\$ or standard?) adj3 (value? or target\$ or rang\$ or level\$ or threshold?)).tw,tx.
- 23 or/21-22
- 24 ((F#G or BG) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold\$)).tw,tx.
- 25 ((normogly?emi\$ or euglyc?emi\$ or glyc?emi\$) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold?)).tw,tx.
- 26 or/23-25
- 27 and/20,26
- 28 and/15,27

Health Technology Assessment

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw.
- 7 exp PEDIATRICS/ or exp PUBERTY/

8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 2/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late
or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw.
13 (NIDDM or T2D or TIID or DM2 or DMII).tw.
14 or/10-13
15 and/9,14
16 HEMOGLOBIN A, GLYCOSYLATED/
17 (h?emoglobin? adj3 glycosylat\$).tw.
18 (glycated adj3 h?emoglobin?).tw.
19 (glycoh?emoglobin? or HbA1c or HbA1c or Hb A1c or Hb A1c).tw.
20 or/16-19
21 REFERENCE STANDARDS/ or REFERENCE VALUES/
22 ((reference? or normal\$ or standard?) adj3 (value? or target\$ or rang\$ or level\$ or
threshold?)).tw.
23 or/21-22
24 ((F#G or BG) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold\$)).tw.
25 ((normogly?emi\$ or euglyc?emi\$ or glyc?emi\$) adj3 (value\$ or target\$ or rang\$ or level\$ or
threshold?)).tw.
26 or/23-25
27 and/20,26
28 and/15,27

Embase

Searches
1 CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)"/
2 (clinic\$ adj5 trial\$).tw,sh.
3 SINGLE BLIND PROCEDURE/
4 DOUBLE BLIND PROCEDURE/
5 RANDOM ALLOCATION/
6 CROSSOVER PROCEDURE/
7 PLACEBO/
8 placebo\$.tw,sh.
9 random\$.tw,sh.
10 RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)"/
11 ((single or double or triple or treble) adj (blind\$ or mask\$)).tw,sh.
12 randomi?ed control\$ trial\$.tw.
13 or/1-12
14 META ANALYSIS/
15 ((meta adj analy\$) or metaanalys\$ or meta-analy\$).tw,sh.
16 (systematic\$ adj5 (review\$ or overview\$)).tw,sh.
17 (methodologic\$ adj5 (review\$ or overview\$)).tw,sh.
18 or/14-17
19 review.pt.
20 (medline or medlars or embase).ab.
21 (scisearch or science citation index).ab.
22 (psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
23 ((hand or manual\$) adj2 search\$).tw.
24 (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online
database\$).tw.
25 (pooling or pooled or mantel haenszel).tw.

26 (peto or dersimonian or "der simonian" or fixed effect).tw.
27 or/20-26
28 and/19,27
29 exp CASE CONTROL STUDY/
30 RETROSPECTIVE STUDY/
31 (case\$ adj2 control\$).tw.
32 COHORT ANALYSIS/
33 LONGITUDINAL STUDY/
34 FOLLOW UP/
35 PROSPECTIVE STUDY/
36 cohort\$.tw.
37 or/29-36
38 or/13,18,28,37
39 (book or conference paper or editorial or letter or note or proceeding or short survey).pt.
40 38 not 39
41 COMPARATIVE STUDY/
42 (compar\$ adj3 stud\$).tw.
43 or/41-42
44 or/40,43
45 exp ADOLESCENT/
46 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
47 exp CHILD/
48 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
49 exp INFANT/
50 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
51 exp PEDIATRICS/ or exp PUBERTY/
52 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
53 or/45-52
54 NON INSULIN DEPENDENT DIABETES MELLITUS/
55 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
56 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
57 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
58 or/54-57
59 JUVENILE DIABETES MELLITUS/
60 and/53,58
61 or/59-60
62 HEMOGLOBIN A1c/
63 (glycoh?emoglobin? or HbA1c or HbA1c or Hb A1c or Hb A1c).ti,ab.
64 (h?emoglobin? adj3 glycosylat\$).ti,ab.
65 (glycated adj3 h?emoglobin?).ti,ab.
66 or/62-65
67 and/61,66
68 STANDARD/
69 REFERENCE VALUE/
70 ((reference? or normal\$ or standard?) adj3 (value? or target\$ or rang\$ or level\$ or threshold?)).ti,ab.
71 or/68-70
72 ((F#G or BG) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold\$)).ti,ab.
73 ((normogly?emi\$ or euglyc?emi\$ or glyco?emi\$) adj3 (value\$ or target\$ or rang\$ or level\$ or threshold?)).ti,ab.
74 or/71-73

- 75 and/67,74
- 76 and/44,75
- 77 conference abstract.pt.
- 78 letter.pt. or LETTER/
- 79 note.pt.
- 80 editorial.pt.
- 81 CASE REPORT/ or CASE STUDY/
- 82 (letter or comment* or abstracts).ti.
- 83 or/77-82
- 84 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 85 83 not 84
- 86 ANIMAL/ not HUMAN/
- 87 NONHUMAN/
- 88 exp ANIMAL EXPERIMENT/
- 89 exp EXPERIMENTAL ANIMAL/
- 90 ANIMAL MODEL/
- 91 exp RODENT/
- 92 (rat or rats or mouse or mice).ti.
- 93 or/85-92
- 94 76 not 93
- 95 limit 94 to english language

F.24 Type 2 diabetes – hypertension

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Ovid MEDLINE(R)

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 2/
- 11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
- 12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
- 13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
- 14 or/10-13
- 15 HYPERTENSION/
- 16 PREHYPERTENSION/
- 17 (hypertens\$ or prehypertens\$).ti,ab.
- 18 ((high or elevat\$ or increas\$) adj3 blood pressur\$).ti,ab.
- 19 or/15-18
- 20 BLOOD PRESSURE/
- 21 exp BLOOD PRESSURE DETERMINATION/

- 22 ((blood or systol\$ or diastol\$ or arterial) adj3 pressur\$).ti,ab.
- 23 or/20-22
- 24 SEVERITY OF ILLNESS INDEX/
- 25 DISEASE PROGRESSION/
- 26 INTERNATIONAL CLASSIFICATION OF DISEASES/
- 27 CLASSIFICATION/
- 28 ((hypertens\$ or prehypertens\$) adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging or defin\$)).ti,ab.
- 29 or/24-28
- 30 MASS SCREENING/
- 31 exp POPULATION SURVEILLANCE/
- 32 (undiagnos\$ or estimate\$).ti.
- 33 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
- 34 or/30-33
- 35 PREVALENCE/
- 36 INCIDENCE/
- 37 exp COHORT STUDIES/
- 38 CROSS-SECTIONAL STUDIES/
- 39 exp MODELS, STATISTICAL/
- 40 LIFE TABLES/
- 41 exp RISK/
- 42 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
- 43 or/35-42
- 44 AGE FACTORS/
- 45 AGE DISTRIBUTION/
- 46 AGE OF ONSET/
- 47 TIME TO TREATMENT/
- 48 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
- 49 (disease adj3 (duration or onset)).ti,ab.
- 50 or/44-49
- 51 19 and (23 or 29 or 34 or 43 or 50)
- 52 *HYPERTENSION/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
- 53 *PREHYPERTENSION/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
- 54 or/51-53
- 55 and/9,14,54
- 56 *DIABETIC ANGIOPATHIES/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
- 57 and/9,56
- 58 *DIABETES MELLITUS, TYPE 2/co, ep [Complications, Epidemiology]
- 59 *DIABETES COMPLICATIONS/ep [Epidemiology]
- 60 or/58-59
- 61 9 and (35 or 36) and 60
- 62 (diabet\$ adj10 (characteristic? or feature? or presentation? or complication? or comorbidit\$)).ti.
- 63 9 and 14 and (43 or 50) and 62
- 64 or/55,57,61,63
- 65 limit 64 to english language
- 66 LETTER/
- 67 EDITORIAL/
- 68 NEWS/
- 69 exp HISTORICAL ARTICLE/

70 ANECDOTES AS TOPIC/
71 COMMENT/
72 (letter or comment* or abstracts).ti.
73 or/66-72
74 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
75 73 not 74
76 ANIMALS/ not HUMANS/
77 exp ANIMALS, LABORATORY/
78 exp ANIMAL EXPERIMENTATION/
79 exp MODELS, ANIMAL/
80 exp RODENTIA/
81 (rat or rats or mouse or mice).ti.
82 or/75-81
83 65 not 82
84 limit 83 to yr="2013 -Current"

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

Searches
1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
5 or/1-4
6 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
7 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
8 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
9 or/6-8
10 (hypertens\$ or prehypertens\$).ti,ab.
11 ((high or elevat\$ or increas\$) adj3 blood pressur\$).ti,ab.
12 or/10-11
13 ((blood or systol\$ or diastol\$ or arterial) adj3 pressur\$).ti,ab.
14 ((hypertens\$ or prehypertens\$) adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging or defin\$)).ti,ab.
15 (undiagnos\$ or estimate\$).ti.
16 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
17 or/15-16
18 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
19 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
20 (disease adj3 (duration or onset)).ti,ab.
21 or/19-20
22 12 and (13 or 14 or 17 or 18 or 21)
23 and/5,9,22
24 (diabet\$ adj10 (characteristic? or feature? or presentation? or complication? or comorbit\$)).ti.
25 5 and 9 and (18 or 21) and 24
26 or/23,25

Cochrane Central Register of Controlled Trials

Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.

3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 2/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14 or/10-13
15 HYPERTENSION/
16 PREHYPERTENSION/
17 (hypertens\$ or prehypertens\$).ti,ab.
18 ((high or elevat\$ or increas\$) adj3 blood pressur\$).ti,ab.
19 or/15-18
20 BLOOD PRESSURE/
21 exp BLOOD PRESSURE DETERMINATION/
22 ((blood or systol\$ or diastol\$ or arterial) adj3 pressur\$).ti,ab.
23 or/20-22
24 SEVERITY OF ILLNESS INDEX/
25 DISEASE PROGRESSION/
26 INTERNATIONAL CLASSIFICATION OF DISEASES/
27 CLASSIFICATION/
28 ((hypertens\$ or prehypertens\$) adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging or defin\$)).ti,ab.
29 or/24-28
30 MASS SCREENING/
31 exp POPULATION SURVEILLANCE/
32 (undiagnos\$ or estimate\$).ti.
33 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
34 or/30-33
35 PREVALENCE/
36 INCIDENCE/
37 exp COHORT STUDIES/
38 CROSS-SECTIONAL STUDIES/
39 exp MODELS, STATISTICAL/
40 LIFE TABLES/
41 exp RISK/
42 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
43 or/35-42
44 AGE FACTORS/
45 AGE DISTRIBUTION/
46 AGE OF ONSET/
47 TIME TO TREATMENT/
48 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
49 (disease adj3 (duration or onset)).ti,ab.
50 or/44-49
51 19 and (23 or 29 or 34 or 43 or 50)

- 52 *HYPERTENSION/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
53 *PREHYPERTENSION/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
54 or/51-53
55 and/9,14,54
56 *DIABETIC ANGIOPATHIES/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
57 and/9,56
58 *DIABETES MELLITUS, TYPE 2/co, ep [Complications, Epidemiology]
59 *DIABETES COMPLICATIONS/ep [Epidemiology]
60 or/58-59
61 9 and (35 or 36) and 60
62 (diabet\$ adj10 (characteristic? or feature? or presentation? or complication? or comorbidit\$)).ti.
63 9 and 14 and (43 or 50) and 62
64 or/55,57,61,63

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
- 1 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,tx,kw,jw,rw.
2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,tx,kw,jw,rw.
3 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx,kw,jw,rw.
4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,tx,kw,jw,rw.
5 or/1-4
6 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw,tx,kw.
7 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw,tx,kw.
8 (NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
9 or/6-8
10 (hypertens\$ or prehypertens\$).tw,tx,kw.
11 ((high or elevat\$ or increas\$) adj3 blood pressur\$).tw,tx.
12 or/10-11
13 ((blood or systol\$ or diastol\$ or arterial) adj3 pressur\$).tw,tx,kw.
14 SEVERITY OF ILLNESS INDEX.kw.
15 (DISEASE PROGRESSION or DISEASE SEVERITY or DISEASE COURSE).kw.
16 STAGING.kw.
17 INTERNATIONAL CLASSIFICATION OF DISEASES.kw.
18 RATING SCALE.kw.
19 CLASSIFICATION.kw.
20 ((hypertens\$ or prehypertens\$) adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging or defin\$)).tw,tx.
21 or/14-20
22 RESCREENING.kw.
23 (undiagnos\$ or estimate\$).ti.
24 (screen\$ or surveill\$ or predict\$ or detect\$).ti,kw.
25 or/22-24
26 CROSS-SECTIONAL STUD\$.kw.
27 LONGITUDINAL STUD\$.kw.
28 COHORT.kw.
29 LIFE TABLE?.kw.

- 30 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti,kw.
- 31 or/26-30
- 32 AGE.kw.
- 33 TIME TO TREATMENT.kw.
- 34 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).tw,tx,kw.
- 35 (disease adj3 (duration or onset)).tw,tx,kw.
- 36 or/32-35
- 37 12 and (13 or 21 or 25 or 31 or 36)
- 38 and/5,9,37
- 39 (diabet\$ adj10 (characteristic? or feature? or presentation? or complication? or comorbidit\$)).ti.
- 40 5 and 9 and (31 or 36) and 39
- 41 or/38,40

Health Technology Assessment

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx,rw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jx,rw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 2/
- 11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw.
- 12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw.
- 13 (NIDDM or T2D or TIID or DM2 or DMII).tw.
- 14 or/10-13
- 15 HYPERTENSION/
- 16 PREHYPERTENSION/
- 17 (hypertens\$ or prehypertens\$).tw.
- 18 ((high or elevat\$ or increas\$) adj3 blood pressur\$).tw.
- 19 or/15-18
- 20 BLOOD PRESSURE/
- 21 exp BLOOD PRESSURE DETERMINATION/
- 22 ((blood or systol\$ or diastol\$ or arterial) adj3 pressur\$).tw.
- 23 or/20-22
- 24 SEVERITY OF ILLNESS INDEX/
- 25 DISEASE PROGRESSION/
- 26 INTERNATIONAL CLASSIFICATION OF DISEASES/
- 27 CLASSIFICATION/
- 28 ((hypertens\$ or prehypertens\$) adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging or defin\$)).tw.
- 29 or/24-28
- 30 MASS SCREENING/
- 31 exp POPULATION SURVEILLANCE/
- 32 (undiagnos\$ or estimate\$).ti.
- 33 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
- 34 or/30-33

- 35 PREVALENCE/
36 INCIDENCE/
37 exp COHORT STUDIES/
38 CROSS-SECTIONAL STUDIES/
39 exp MODELS, STATISTICAL/
40 LIFE TABLES/
41 exp RISK/
42 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
43 or/35-42
44 AGE FACTORS/
45 AGE DISTRIBUTION/
46 AGE OF ONSET/
47 TIME TO TREATMENT/
48 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).tw.
49 (disease adj3 (duration or onset)).tw.
50 or/44-49
51 19 and (23 or 29 or 34 or 43 or 50)
52 HYPERTENSION/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
53 PREHYPERTENSION/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
54 or/51-53
55 and/9,14,54
56 DIABETIC ANGIOPATHIES/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
57 and/9,56
58 DIABETES MELLITUS, TYPE 2/co, ep [Complications, Epidemiology]
59 DIABETES COMPLICATIONS/ep [Epidemiology]
60 or/58-59
61 9 and (35 or 36) and 60
62 (diabet\$ adj10 (characteristic? or feature? or presentation? or complication? or comorbidit\$)).ti.
63 9 and 14 and (43 or 50) and 62
64 or/55,57,61,63

Embase

- # Searches
1 exp ADOLESCENT/
2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
9 or/1-8
10 NON INSULIN DEPENDENT DIABETES MELLITUS/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14 or/10-13
15 and/9,14

16 JUVENILE DIABETES MELLITUS/
17 or/15-16
18 HYPERTENSION/
19 DIABETIC HYPERTENSION/
20 PREHYPERTENSION/
21 (hypertens\$ or prehypertens\$).ti,ab.
22 ((high or elevat\$ or increas\$) adj3 blood pressur\$).ti,ab.
23 or/18-22
24 exp BLOOD PRESSURE/
25 exp BLOOD PRESSURE MEASUREMENT/
26 ((blood or systol\$ or diastol\$ or arterial) adj3 pressur\$).ti,ab.
27 or/24-26
28 SEVERITY OF ILLNESS INDEX/
29 DISEASE SEVERITY/
30 DISEASE COURSE/
31 STAGING/
32 exp INTERNATIONAL CLASSIFICATION OF DISEASES/
33 RATING SCALE/
34 CLASSIFICATION/
35 DISEASE CLASSIFICATION/
36 ((hypertens\$ or prehypertens\$) adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging or defin\$)).ti,ab.
37 or/28-36
38 SCREENING/
39 MASS SCREENING/
40 SCREENING TEST/
41 RESCREENING/
42 exp DISEASE SURVEILLANCE/
43 (undiagnos\$ or estimate\$).ti.
44 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
45 or/38-44
46 PREVALENCE/
47 INCIDENCE/
48 CROSS-SECTIONAL STUDY/
49 LONGITUDINAL STUDY/
50 COHORT ANALYSIS/
51 STATISTICAL MODEL/
52 LIFE TABLE/
53 exp RISK/
54 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
55 or/46-54
56 AGE/
57 AGE DISTRIBUTION/
58 ONSET AGE/
59 DISEASE DURATION/
60 TIME TO TREATMENT/
61 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
62 (disease adj3 (duration or onset)).ti,ab.
63 or/56-62
64 23 and (27 or 37 or 45 or 55 or 63)
65 *HYPERTENSION/di, ep, pc [Diagnosis, Epidemiology, Prevention]
66 *PREHYPERTENSION/di, ep, pc [Diagnosis, Epidemiology, Prevention]
67 or/64-66

68 and/17,67
69 DIABETIC HYPERTENSION/di, ep, pc [Diagnosis, Epidemiology, Prevention]
70 and/9,69
71 *NON INSULIN DEPENDENT DIABETES MELLITUS/co, ep [Complication, Epidemiology]
72 9 and (46 or 47) and 71
73 (diabet\$ adj10 (characteristic? or feature? or presentation? or complication? or comorbidit\$)).ti.
74 17 and (55 or 63) and 73
75 or/68,70,72,74
76 limit 75 to english language
77 conference abstract.pt.
78 letter.pt. or LETTER/
79 note.pt.
80 editorial.pt.
81 (letter or comment* or abstracts).ti.
82 or/77-81
83 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
84 82 not 83
85 ANIMAL/ not HUMAN/
86 NONHUMAN/
87 exp ANIMAL EXPERIMENT/
88 exp EXPERIMENTAL ANIMAL/
89 ANIMAL MODEL/
90 exp RODENT/
91 (rat or rats or mouse or mice).ti.
92 or/84-91
93 76 not 92

F.25 Type 2 diabetes – dyslipidaemia

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Ovid MEDLINE(R)

Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 2/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14 or/10-13
15 exp DYSLIPIDEMIAS/

- 16 (d#slip\$ or hyp??lip\$ or hyp??alipalip\$ or hyp??betalip\$ or hyp??cholester\$ or
hyp??triglycerid\$ or hyp??triacy?glycerol\$).ti,ab.
17 or/15-16
18 LIPIDS/bl [Blood]
19 CHOLESTEROL/an, bl [Analysis, Blood]
20 CHOLESTEROL, HDL/an, bl [Analysis, Blood]
21 CHOLESTEROL, LDL/an, bl [Analysis, Blood]
22 LIPOPROTEINS/an, bl [Analysis, Blood]
23 LIPOPROTEINS, HDL/an, bl [Analysis, Blood]
24 LIPOPROTEINS, LDL/an, bl [Analysis, Blood]
25 exp TRIGLYCERIDES/an, bl [Analysis, Blood]
26 (cholester\$ or epicholester\$ or lipoprotein? or lipid?).ti,ab.
27 (alipalip\$ or alpha lipoprotein\$ or HDL cholester\$).ti,ab.
28 (betalip\$ or beta lipoprotein\$ or LDL cholester\$).ti,ab.
29 (triglyceride? or triacy?glycerol?).ti,ab.
30 ((HDL or LDL) adj3 cholester\$ adj3 ratio?).ti,ab.
31 or/18-30
32 PREVALENCE/
33 INCIDENCE/
34 exp COHORT STUDIES/
35 CROSS-SECTIONAL STUDIES/
36 exp MODELS, STATISTICAL/
37 LIFE TABLES/
38 exp RISK/
39 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
40 or/32-39
41 MASS SCREENING/
42 exp POPULATION SURVEILLANCE/
43 (undiagnos\$ or estimate\$).ti.
44 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
45 or/41-44
46 SEVERITY OF ILLNESS INDEX/
47 DISEASE PROGRESSION/
48 INTERNATIONAL CLASSIFICATION OF DISEASES/
49 CLASSIFICATION/
50 (d#slip\$ adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging or
defin\$)).ti,ab.
51 or/46-50
52 AGE FACTORS/
53 AGE DISTRIBUTION/
54 AGE OF ONSET/
55 TIME TO TREATMENT/
56 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
57 (disease adj3 (duration or onset)).ti,ab.
58 or/52-57
59 17 and (31 or 40 or 45 or 51 or 58)
60 exp *DYLIPIDEMIAS/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention &
Control]
61 or/59-60
62 and/9,14,61
63 DIABETES COMPLICATIONS/
64 and/9,14,31,63

- 65 (DIABETES MELLITUS, TYPE 2/ and COMORBIDITY/) or DIABETES MELLITUS, TYPE 2/co [Complications]
- 66 and/9,31,65
- 67 or/62,64,66
- 68 limit 67 to english language
- 69 LETTER/
- 70 EDITORIAL/
- 71 NEWS/
- 72 exp HISTORICAL ARTICLE/
- 73 ANECDOTES AS TOPIC/
- 74 COMMENT/
- 75 (letter or comment* or abstracts).ti.
- 76 or/69-75
- 77 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 78 76 not 77
- 79 ANIMALS/ not HUMANS/
- 80 exp ANIMALS, LABORATORY/
- 81 exp ANIMAL EXPERIMENTATION/
- 82 exp MODELS, ANIMAL/
- 83 exp RODENTIA/
- 84 (rat or rats or mouse or mice).ti.
- 85 or/78-84
- 86 68 not 85

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

- # Searches
- 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 5 or/1-4
- 6 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
- 7 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
- 8 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
- 9 or/6-8
- 10 (d#slip\$ or hyp??lip\$ or hyp??alphalip\$ or hyp??betalip\$ or hyp??cholester\$ or hyp??triglycerid\$ or hyp??triacy?glycerol\$).ti,ab.
- 11 (cholester\$ or epicholester\$ or lipoprotein? or lipid?).ti,ab.
- 12 (alphalip\$ or alpha lipoprotein\$ or HDL cholester\$).ti,ab.
- 13 (betalip\$ or beta lipoprotein\$ or LDL cholester\$).ti,ab.
- 14 (triglyceride? or triacy?glycerol?).ti,ab.
- 15 ((HDL or LDL) adj3 cholester\$ adj3 ratio?).ti,ab.
- 16 or/11-15
- 17 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
- 18 (undiagnos\$ or estimate\$).ti.
- 19 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
- 20 or/18-19
- 21 (d#slip\$ adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging or defin\$)).ti,ab.
- 22 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
- 23 (disease adj3 (duration or onset)).ti,ab.

- 24 or/22-23
- 25 10 and (16 or 17 or 20 or 21 or 24)
- 26 and/5,9,25

EBM Reviews - Cochrane Central Register of Controlled Trials

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 2/
- 11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
- 12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
- 13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
- 14 or/10-13
- 15 exp DYSLIPIDEMIAS/
- 16 (d#slip\$ or hyp??lip\$ or hyp??alphilip\$ or hyp??betalip\$ or hyp??cholester\$ or hyp??triglycerid\$ or hyp??triacy?glycerol\$).ti,ab.
- 17 or/15-16
- 18 LIPIDS/bl [Blood]
- 19 CHOLESTEROL/an, bl [Analysis, Blood]
- 20 CHOLESTEROL, HDL/an, bl [Analysis, Blood]
- 21 CHOLESTEROL, LDL/an, bl [Analysis, Blood]
- 22 LIPOPROTEINS/an, bl [Analysis, Blood]
- 23 LIPOPROTEINS, HDL/an, bl [Analysis, Blood]
- 24 LIPOPROTEINS, LDL/an, bl [Analysis, Blood]
- 25 exp TRIGLYCERIDES/an, bl [Analysis, Blood]
- 26 (cholester\$ or epicholester\$ or lipoprotein? or lipid?).ti,ab.
- 27 (alphalip\$ or alpha lipoprotein\$ or HDL cholester\$).ti,ab.
- 28 (betalip\$ or beta lipoprotein\$ or LDL cholester\$).ti,ab.
- 29 (triglyceride? or triacy?glycerol?).ti,ab.
- 30 ((HDL or LDL) adj3 cholester\$ adj3 ratio?).ti,ab.
- 31 or/18-30
- 32 PREVALENCE/
- 33 INCIDENCE/
- 34 exp COHORT STUDIES/
- 35 CROSS-SECTIONAL STUDIES/
- 36 exp MODELS, STATISTICAL/
- 37 LIFE TABLES/
- 38 exp RISK/
- 39 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
- 40 or/32-39
- 41 MASS SCREENING/
- 42 exp POPULATION SURVEILLANCE/
- 43 (undiagnos\$ or estimate\$).ti.
- 44 (screen\$ or surveill\$ or predict\$ or detect\$).ti.

- 45 or/41-44
 46 SEVERITY OF ILLNESS INDEX/
 47 DISEASE PROGRESSION/
 48 INTERNATIONAL CLASSIFICATION OF DISEASES/
 49 CLASSIFICATION/
 50 (d#slip\$ adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging or defin\$)).ti,ab.
 51 or/46-50
 52 AGE FACTORS/
 53 AGE DISTRIBUTION/
 54 AGE OF ONSET/
 55 TIME TO TREATMENT/
 56 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
 57 (disease adj3 (duration or onset)).ti,ab.
 58 or/52-57
 59 17 and (31 or 40 or 45 or 51 or 58)
 60 exp *DYLIPIDEMIAS/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
 61 or/59-60
 62 and/9,14,61
 63 DIABETES COMPLICATIONS/
 64 and/9,14,31,63
 65 (DIABETES MELLITUS, TYPE 2/ and COMORBIDITY/) or DIABETES MELLITUS, TYPE 2/co [Complications]
 66 and/9,31,65
 67 or/62,64,66

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects

- # Searches
 1 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,tx,kw,jw,rw.
 2 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,tx,kw,jw,rw.
 3 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx,kw,jw,rw.
 4 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,tx,kw,jw,rw.
 5 or/1-4
 6 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw,tx,kw.
 7 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw,tx,kw.
 8 (NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
 9 or/6-8
 10 (d#slip\$ or hyp??lip\$ or hyp??alphalip\$ or hyp??betalip\$ or hyp??cholester\$ or hyp??triglycerid\$ or hyp??triacy?glycerol\$).tw,tx,kw.
 11 (cholester\$ or epicholester\$ or lipoprotein? or lipid?).tw,tx,kw.
 12 (alphalip\$ or alpha lipoprotein\$ or HDL cholester\$).tw,tx,kw.
 13 (betalip\$ or beta lipoprotein\$ or LDL cholester\$).tw,tx,kw.
 14 (triglyceride? or triacy?glycerol?).tw,tx,kw.
 15 ((HDL or LDL) adj3 cholester\$ adj3 ratio?).tw,tx.
 16 or/11-15
 17 LIFE TABLE\$.kw.
 18 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti,kw.
 19 or/17-18
 20 RESCREENING.kw.

- 21 (undiagnos\$ or estimate\$).ti.
- 22 (screen\$ or surveill\$ or predict\$ or detect\$).ti,kw.
- 23 or/20-22
- 24 SEVERITY OF ILLNESS INDEX.kw.
- 25 (DISEASE PROGRESSION or DISEASE COURSE or DISEASE SEVERITY).kw.
- 26 STAGING.kw.
- 27 INTERNATIONAL CLASSIFICATION OF DISEASES.kw.
- 28 RATING SCALE.kw.
- 29 CLASSIFICATION.kw.
- 30 (d#slip\$ adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging or defin\$)).tw,tx.
- 31 or/24-30
- 32 AGE.kw.
- 33 TIME TO TREATMENT.kw.
- 34 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).tw,tx,kw.
- 35 (disease adj3 (duration or onset)).tw,tx,kw.
- 36 or/32-35
- 37 10 and (16 or 19 or 23 or 31 or 36)
- 38 DIABETES COMPLICATIONS.kw.
- 39 and/16,38
- 40 or/37,39
- 41 and/5,9,40
- 42 (COMORBIDITY and (DIABETES MELLITUS, TYPE 2 or NON INSULIN DEPENDENT DIABETES MELLITUS)).kw.
- 43 and/5,16,42
- 44 or/41,43

Health Technology Assessment

- # Searches
- 1 ADOLESCENT/ or MINORS/
- 2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw,jx,rw.
- 3 exp CHILD/
- 4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw,jx,rw.
- 5 exp INFANT/
- 6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw,jx,rw.
- 7 exp PEDIATRICS/ or exp PUBERTY/
- 8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw,jx,rw.
- 9 or/1-8
- 10 exp DIABETES MELLITUS, TYPE 2/
- 11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw.
- 12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw.
- 13 (NIDDM or T2D or TIID or DM2 or DMII).tw.
- 14 or/10-13
- 15 exp DYSLIPIDEMIAS/
- 16 (d#slip\$ or hyp??lip\$ or hyp??alphalip\$ or hyp??betalip\$ or hyp??cholester\$ or hyp??triglycerid\$ or hyp??triacy?glycerol\$).tw.
- 17 or/15-16
- 18 LIPIDS/
- 19 CHOLESTEROL/
- 20 CHOLESTEROL, HDL/
- 21 CHOLESTEROL, LDL/

- 22 LIPOPROTEINS/
- 23 LIPOPROTEINS, HDL/
- 24 LIPOPROTEINS, LDL/
- 25 exp TRIGLYCERIDES/
- 26 (cholester\$ or epicholester\$ or lipoprotein? or lipid?).tw.
- 27 (alphalip\$ or alpha lipoprotein\$ or HDL cholester\$).tw.
- 28 (betalip\$ or beta lipoprotein\$ or LDL cholester\$).tw.
- 29 (triglyceride? or triacy?glycerol?).tw.
- 30 ((HDL or LDL) adj3 cholester\$ adj3 ratio?).tw.
- 31 or/18-30
- 32 PREVALENCE/
- 33 INCIDENCE/
- 34 exp COHORT STUDIES/
- 35 CROSS-SECTIONAL STUDIES/
- 36 exp MODELS, STATISTICAL/
- 37 LIFE TABLES/
- 38 exp RISK/
- 39 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
- 40 or/32-39
- 41 MASS SCREENING/
- 42 exp POPULATION SURVEILLANCE/
- 43 (undiagnos\$ or estimate\$).ti.
- 44 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
- 45 or/41-44
- 46 SEVERITY OF ILLNESS INDEX/
- 47 DISEASE PROGRESSION/
- 48 INTERNATIONAL CLASSIFICATION OF DISEASES/
- 49 CLASSIFICATION/
- 50 (d#slip\$ adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging or defin\$)).tw.
- 51 or/46-50
- 52 AGE FACTORS/
- 53 AGE DISTRIBUTION/
- 54 AGE OF ONSET/
- 55 TIME TO TREATMENT/
- 56 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).tw.
- 57 (disease adj3 (duration or onset)).tw.
- 58 or/52-57
- 59 17 and (31 or 40 or 45 or 51 or 58)
- 60 DIABETES COMPLICATIONS/
- 61 and/31,60
- 62 or/59,61
- 63 and/9,14,62
- 64 DIABETES MELLITUS, TYPE 2/ and COMORBIDITY/
- 65 and/9,31,64
- 66 or/63,65

Embase

- # Searches
- 1 exp ADOLESCENT/
- 2 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
- 3 exp CHILD/

4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or
kindergar\$ or boy? or girl?).ti,ab,jx.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jx.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jx,ec.
9 or/1-8
10 NON INSULIN DEPENDENT DIABETES MELLITUS/
11 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late
or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
12 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
13 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
14 or/10-13
15 JUVENILE DIABETES MELLITUS/
16 and/9,14
17 or/15-16
18 exp "DISORDERS OF CHOLESTEROL METABOLISM"/
19 "DISORDERS OF LIPID METABOLISM"/
20 exp "DISORDERS OF LIPOPROTEIN METABOLISM"/
21 DYSLIPIDEMIA/
22 exp HYPERLIPIDEMIA/
23 HYPOLIPEMIA/
24 (d#slip\$ or hyp??lip\$ or hyp??alphalip\$ or hyp??betalip\$ or hyp??cholester\$ or
hyp??triglycerid\$ or hyp??triacy?glycerol\$).ti,ab.
25 or/18-24
26 exp LIPID BLOOD LEVEL/ or LIPID/ec [Endogenous Compound]
27 CHOLESTEROL/an, ec [Drug Analysis, Endogenous Compound]
28 HIGH DENSITY LIPOPROTEIN CHOLESTEROL/an, ec [Drug Analysis, Endogenous
Compound]
29 LOW DENSITY LIPOPROTEIN CHOLESTEROL/an, ec [Drug Analysis, Endogenous
Compound]
30 LIPOPROTEIN/an, ec [Drug Analysis, Endogenous Compound]
31 HIGH DENSITY LIPOPROTEIN/an, ec [Drug Analysis, Endogenous Compound]
32 LOW DENSITY LIPOPROTEIN/an, ec [Drug Analysis, Endogenous Compound]
33 TRIACYLGLYCEROL/an, ec [Drug Analysis, Endogenous Compound]
34 (cholester\$ or epicholester\$ or lipoprotein? or lipid?).ti,ab.
35 (alphalip\$ or alpha lipoprotein\$ or HDL cholester\$).ti,ab.
36 (betalip\$ or beta lipoprotein\$ or LDL cholester\$).ti,ab.
37 (triglyceride? or triacy?glycerol?).ti,ab.
38 ((HDL or LDL) adj3 cholester\$ adj3 ratio?).ti,ab.
39 or/26-38
40 PREVALENCE/
41 INCIDENCE/
42 STATISTICAL MODEL/
43 LIFE TABLE/
44 exp RISK/
45 (prevalen\$ or incidence? or model\$ or risk\$ or rate?).ti.
46 or/40-45
47 SCREENING/
48 MASS SCREENING/
49 SCREENING TEST/
50 RESCREENING/
51 exp DISEASE SURVEILLANCE/

52 (undiagnos\$ or estimate\$).ti.
53 (screen\$ or surveill\$ or predict\$ or detect\$).ti.
54 or/47-53
55 SEVERITY OF ILLNESS INDEX/
56 DISEASE SEVERITY/
57 DISEASE COURSE/
58 STAGING/
59 exp INTERNATIONAL CLASSIFICATION OF DISEASES/
60 RATING SCALE/
61 CLASSIFICATION/
62 DISEASE CLASSIFICATION/
63 (d#slip\$ adj3 (grad\$ or sever\$ or classif\$ or index\$ or indice? or stage\$ or staging or
defin\$)).ti,ab.
64 or/55-63
65 AGE/
66 AGE DISTRIBUTION/
67 ONSET AGE/
68 DISEASE DURATION/
69 TIME TO TREATMENT/
70 (age\$ adj4 (factor\$ or onset or diagnos\$ or treatment\$)).ti,ab.
71 (disease adj3 (duration or onset)).ti,ab.
72 or/65-71
73 25 and (39 or 46 or 54 or 64 or 72)
74 exp *"DISORDERS OF CHOLESTEROL METABOLISM"/di, ep, pc [Diagnosis, Epidemiology,
Prevention]
75 *"DISORDERS OF LIPID METABOLISM"/di, ep, pc [Diagnosis, Epidemiology, Prevention]
76 exp *"DISORDERS OF LIPOPROTEIN METABOLISM"/di, ep, pc [Diagnosis, Epidemiology,
Prevention]
77 *DYSLIPIDEMIA/di, ep, pc [Diagnosis, Epidemiology, Prevention]
78 exp *HYPERLIPIDEMIA/di, ep, pc [Diagnosis, Epidemiology, Prevention]
79 *HYPOLIPEMIA/di, ep, pc [Diagnosis, Epidemiology, Prevention]
80 or/73-79
81 and/17,80
82 (NON INSULIN DEPENDENT DIABETES MELLITUS/ and COMORBIDITY/) or NON INSULIN
DEPENDENT DIABETES MELLITUS/co [Complication]
83 and/9,39,82
84 or/81,83
85 limit 84 to english language
86 conference abstract.pt.
87 letter.pt. or LETTER/
88 note.pt.
89 editorial.pt.
90 (letter or comment* or abstracts).ti.
91 or/86-90
92 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
93 91 not 92
94 ANIMAL/ not HUMAN/
95 NONHUMAN/
96 exp ANIMAL EXPERIMENT/
97 exp EXPERIMENTAL ANIMAL/
98 ANIMAL MODEL/
99 exp RODENT/
100 (rat or rats or mouse or mice).ti.

101 or/93-100
102 85 not 101

F.26 Health economics

Ovid MEDLINE(R)

Searches
1 ECONOMICS/
2 VALUE OF LIFE/
3 exp "COSTS AND COST ANALYSIS"/
4 exp ECONOMICS, HOSPITAL/
5 exp ECONOMICS, MEDICAL/
6 exp RESOURCE ALLOCATION/
7 ECONOMICS, NURSING/
8 ECONOMICS, PHARMACEUTICAL/
9 exp "FEES AND CHARGES"/
10 exp BUDGETS/
11 budget*.ti,ab.
12 cost*.ti,ab.
13 (economic* or pharmaco?economic*).ti,ab.
14 (price* or pricing*).ti,ab.
15 (financ* or fee or fees or expenditure* or saving*).ti,ab.
16 (value adj2 (money or monetary)).ti,ab.
17 resourc* allocat*.ti,ab.
18 (fund or funds or funding* or funded).ti,ab.
19 (ration or rations or rationing* or rationed).ti,ab.
20 ec.fs.
21 or/1-20
22 ADOLESCENT/ or MINORS/
23 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jw.
24 exp CHILD/
25 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jw.
26 exp INFANT/
27 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab,jw.
28 exp PEDIATRICS/ or exp PUBERTY/
29 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,jw.
30 or/22-29
31 exp DIABETES MELLITUS, TYPE 1/
32 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
33 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
34 or/31-33
35 exp DIABETES MELLITUS, TYPE 2/
36 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
37 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
38 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
39 or/35-38
40 or/34,39
41 and/30,40
42 limit 41 to english language

43 LETTER/
44 EDITORIAL/
45 NEWS/
46 exp HISTORICAL ARTICLE/
47 ANECDOTES AS TOPIC/
48 COMMENT/
49 CASE REPORT/
50 (letter or comment* or abstracts).ti.
51 or/43-50
52 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
53 51 not 52
54 ANIMALS/ not HUMANS/
55 exp ANIMALS, LABORATORY/
56 exp ANIMAL EXPERIMENTATION/
57 exp MODELS, ANIMAL/
58 exp RODENTIA/
59 (rat or rats or mouse or mice).ti.
60 or/53-59
61 42 not 60
62 and/21,61

Cochrane Central Register of Controlled Trials

Searches
1 ECONOMICS/
2 VALUE OF LIFE/
3 exp "COSTS AND COST ANALYSIS"/
4 exp ECONOMICS, HOSPITAL/
5 exp ECONOMICS, MEDICAL/
6 exp RESOURCE ALLOCATION/
7 ECONOMICS, NURSING/
8 ECONOMICS, PHARMACEUTICAL/
9 exp "FEES AND CHARGES"/
10 exp BUDGETS/
11 budget*.ti,ab.
12 cost*.ti,ab.
13 (economic* or pharmaco?economic*).ti,ab.
14 (price* or pricing*).ti,ab.
15 (financ* or fee or fees or expenditure* or saving*).ti,ab.
16 (value adj2 (money or monetary)).ti,ab.
17 resourc* allocat*.ti,ab.
18 (fund or funds or funding* or funded).ti,ab.
19 (ration or rations or rationing* or rationed).ti,ab.
20 ec.fs.
21 or/1-20
22 ADOLESCENT/ or MINORS/
23 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab.
24 exp CHILD/
25 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab.
26 exp INFANT/
27 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
28 exp PEDIATRICS/ or exp PUBERTY/
29 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab.

- 30 or/22-29
31 exp DIABETES MELLITUS, TYPE 1/
32 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
33 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
34 or/31-33
35 exp DIABETES MELLITUS, TYPE 2/
36 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
37 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
38 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
39 or/35-38
40 or/34,39
41 and/30,40

Health Technology Assessment, EBM Reviews - NHS Economic Evaluation Database

- # Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).tw.
3 exp CHILD/
4 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).tw.
5 exp INFANT/
6 (infan\$ or neonat\$ or newborn\$ or baby or babies).tw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).tw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/
11 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).tw.
12 (IDDM or T1D or TID or DM1 or DMI).tw.
13 or/10-12
14 exp DIABETES MELLITUS, TYPE 2/
15 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).tw.
16 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).tw.
17 (NIDDM or T2D or TIID or DM2 or DMII).tw.
18 or/14-17
19 or/13,18
20 and/9,19

Embase

- # Searches
1 HEALTH ECONOMICS/
2 exp ECONOMIC EVALUATION/
3 exp HEALTH CARE COST/
4 exp FEE/
5 BUDGET/
6 FUNDING/
7 RESOURCE ALLOCATION/
8 budget*.ti,ab.
9 cost*.ti,ab.
10 (economic* or pharmaco?economic*).ti,ab.

- 11 (price* or pricing*).ti,ab.
- 12 (financ* or fee or fees or expenditure* or saving*).ti,ab.
- 13 (value adj2 (money or monetary)).ti,ab.
- 14 resourc* allocat*.ti,ab.
- 15 (fund or funds or funding* or funded).ti,ab.
- 16 (ration or rations or rationing* or rationed).ti,ab.
- 17 or/1-16
- 18 exp ADOLESCENT/
19 (adolescens\$ or teen\$ or youth\$ or young or juvenile? or minors or highschool\$).ti,ab,jx.
- 20 exp CHILD/
21 (child\$ or schoolchild\$ or "school age" or "school aged" or preschool\$ or toddler\$ or kid? or kindergar\$ or boy? or girl?).ti,ab,jx.
- 22 exp NEWBORN/
23 (infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
- 24 exp PEDIATRICS/ or exp PUBERTY/
25 (p?ediatric\$ or pubert\$ or prepubert\$ or pubescen\$ or prepubescen\$).ti,ab,ec.
- 26 or/18-25
- 27 INSULIN DEPENDENT DIABETES MELLITUS/
28 (diabet\$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend\$ or juvenile or child\$ or earl\$ or labile or brittle or sudden onset or auto immun\$ or auto?immun\$)).ti,ab.
- 29 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
- 30 or/27-29
- 31 NON INSULIN DEPENDENT DIABETES MELLITUS/
32 (diabet\$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur\$ or adult\$ or slow or late or stable or ketosis resistant or keto resist\$ or keto?resist\$ or non keto\$ or non?keto\$)).ti,ab.
- 33 (diabet\$ adj5 ((non insulin or non?insulin) adj2 depend\$)).ti,ab.
- 34 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
- 35 or/31-34
- 36 or/30,35
- 37 JUVENILE DIABETES MELLITUS/
38 and/26,36
- 39 or/37-38
- 40 limit 39 to english language
- 41 conference abstract.pt.
- 42 letter.pt. or LETTER/
43 note.pt.
- 44 editorial.pt.
- 45 CASE REPORT/ or CASE STUDY/
46 (letter or comment* or abstracts).ti.
- 47 or/41-46
- 48 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 49 47 not 48
- 50 ANIMAL/ not HUMAN/
51 NONHUMAN/
52 exp ANIMAL EXPERIMENT/
53 exp EXPERIMENTAL ANIMAL/
54 ANIMAL MODEL/
55 exp RODENT/
56 (rat or rats or mouse or mice).ti.
- 57 or/49-56
- 58 40 not 57
- 59 and/17,58

Appendix G: Summary of identified studies

G.1 Diagnosis

Review question: What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?

The systematic review for this question was conducted by the guidance-producing centre for the guideline 'Type 1 diabetes in adults'.

Number of papers identified, 2536

Number of papers weeded out, 2216

Number of papers excluded, 298

Number of papers included, 22

G.2 Type 1 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

Number of papers identified, 1280

Number of papers weeded out, 1204

Number of papers excluded, 68

Number of papers included, 8

G.3 Type 1 diabetes – behavioural interventions

Review question: What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 1 diabetes?

Number of papers identified, 771

Number of papers weeded out, 656

Number of papers excluded, 100

Number of papers included, 15

G.4 Type 1 diabetes – multiple daily injections

Review question: What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

Number of papers identified, 3775

Number of papers weeded out, 3588

Number of papers excluded, 174

Number of papers included, 13

G.5 Type 1 diabetes – HbA1c targets

Review question: What is the optimal haemoglobin A1c (HbA1c) target for children and young people with type 1 diabetes?

Number of papers identified, 293

Number of papers weeded out, 291

Number of papers excluded, 2

Number of papers included, 0

G.6 Type 1 diabetes – blood glucose targets

Review question: What are the optimal blood glucose targets for children and young people with type 1 diabetes?

Number of papers identified, 1303

Number of papers weeded out, 1292

Number of papers excluded, 11

Number of papers included, 0

G.7 Type 1 diabetes – blood glucose monitoring

Review questions:

How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?

Number of papers identified, 2060

Number of papers weeded out, 2011

Number of papers excluded, 36

Number of papers included, 13

What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?

Number of papers identified, 867

Number of papers weeded out, 821

Number of papers excluded, 42

Number of papers included, 4

What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?

Number of papers identified, 1302

Number of papers weeded out, 1266

Number of papers excluded, 35

Number of papers included, 1

G.8 Type 1 diabetes – blood ketone monitoring

Review question: What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis?

Number of papers identified, 435

Number of papers weeded out, 419

Number of papers excluded, 15

Number of papers included, 1

G.9 Type 1 diabetes – dietary advice

Review questions:

What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?

Number of papers identified, 729

Number of papers weeded out, 704

Number of papers excluded, 23

Number of papers included, 2

What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?

Number of papers identified, 712

Number of papers weeded out, 699

Number of papers excluded, 11

Number of papers included, 2

G.10 Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

Review question: What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?

Number of papers identified, 1289

Number of papers weeded out, 1274

Number of papers excluded, 11

Number of papers included, 4

G.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions:

What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?

Number of papers identified, 1576

Number of papers weeded out, 1576

Number of papers excluded, 0

Number of papers included, 0

Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:

- general observations (for example, heart and respiratory rate and blood pressure)
- body weight
- hydration status
- fluid balance
- neurological observations
- electrocardiographic (ECG) monitoring?

Number of papers identified, 1576

Number of papers weeded out, 1561

Number of papers excluded, 15

Number of papers included, 0

Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:

- blood glucose
- blood or urine ketones
- serum urea or electrolytes
- acid/base status?

Number of papers identified, 1576

Number of papers weeded out, 1572

Number of papers excluded, 1

Number of papers included, 3

G.12 Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

Review questions:

What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?

Number of papers identified, 1108

Number of papers weeded out, 1108

Number of papers excluded, 0

Number of papers included, 0

At what rate should children and young people with diabetic ketoacidosis be rehydrated?

Number of papers identified, 1108

Number of papers weeded out, 1098

Number of papers excluded, 4

Number of papers included, 6

What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

Number of papers identified, 1108

Number of papers weeded out, 1090

Number of papers excluded, 11

Number of papers included, 7

G.13 Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents

Review question: What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?

Number of papers identified, 88

Number of papers weeded out, 80

Number of papers excluded, 7

Number of papers included, 1

G.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

Review questions:

When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?

Number of papers identified, 389

Number of papers weeded out, 388

Number of papers excluded, 0

Number of papers included, 1

How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

Number of papers identified, 389

Number of papers weeded out, 386

Number of papers excluded, 0

Number of papers included, 3

G.15 Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis

Review question: What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?

Number of papers identified, 24

Number of papers weeded out, 24

Number of papers excluded, 0

Number of papers included, 0

G.16 Type 1 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?

Number of papers identified, 5684

Number of papers weeded out, 5382

Number of papers excluded, 69

Number of papers included, 18

G.17 Type 1 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?

Number of papers identified, 2924

Number of papers weeded out, 2819

Number of papers excluded, 91

Number of papers included, 14

G.18 Type 2 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?

Number of papers identified, 1435

Number of papers weeded out, 1402

Number of papers excluded, 33

Number of papers included, 0

G.19 Type 2 diabetes – behavioural interventions

Review questions:

What is the effectiveness of behavioural interventions to promote engagement with clinical services in children and young people with type 2 diabetes?

Number of papers identified, 1637

Number of papers weeded out, 1624

Number of papers excluded, 13

Number of papers included, 0

What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 2 diabetes?

Number of papers identified, 1637

Number of papers weeded out, 1617

Number of papers excluded, 20

Number of papers included, 0

G.20 Type 2 diabetes – dietary advice

Review question: What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?

Number of papers identified, 2605

Number of papers weeded out, 2588

Number of papers excluded, 16

Number of papers included, 1

G.21 Type 2 diabetes – weight loss

Review question: Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?

Number of papers identified, 697

Number of papers weeded out, 624

Number of papers excluded, 27

Number of papers included, 1

G.22 Type 2 diabetes – metformin

Review question: What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?

Number of papers identified, 604

Number of papers weeded out, 581

Number of papers excluded, 22

Number of papers included, 1

G.23 Type 2 diabetes – HbA1c targets

Review question: what is the optimal HbA1c target for children and young people with type 2 diabetes?

Number of papers identified, 716

Number of papers weeded out, 706

Number of papers excluded, 10

Number of papers included, 0

G.24 Type 2 diabetes – hypertension

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Number of papers identified, 3205

Number of papers weeded out, 3190

Number of papers excluded, 7

Number of papers included, 8

G.25 Type 2 diabetes – dyslipidaemia

Review question: What is the optimal monitoring strategy for identifying dyslipidaemia in children and young people with type 2 diabetes?

Number of papers identified, 1613

Number of papers weeded out, 1595

Number of papers excluded, 11

Number of papers included, 7

G.26 Type 2 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?

Number of papers identified, 2594

Number of papers weeded out, 2575

Number of papers excluded, 17

Number of papers included, 2

G.27 Type 2 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

Number of papers identified, 2923

Number of papers weeded out, 2913

Number of papers excluded, 7

Number of papers included, 3

G.28 Health economics

Number of papers identified, 2754

Number of papers weeded out, 2731

Number of papers excluded, 19

Number of papers included, 2

Appendix H: Excluded studies

H.1 Diagnosis

Review question

What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?

The systematic review for this question was conducted by the guidance-producing centre for the guideline 'Type 1 diabetes in adults'.

Study	Reason for exclusion
J. M. Wenzlau, O. Moua, S. A. Sarkar, L. Yu, M. Rewers, G. S. Eisenbarth, H. W. Davidson, and J. C. Hutton. SIC30A8 is a major target of humoral autoimmunity in type 1 diabetes and a predictive marker in prediabetes. <i>Ann N Y Acad Sci</i> 1150:256-259, 2008.	Age of population not reported
A. Zmyslowska, A. Szadkowska, B. Mianowska, I. Pietrzak, and W. Mlynarski. Association between adiponectin level and residual insulin secretion in type 1 diabetes in children. <i>Prz.Pediatr.</i> 41 (2):69-73, 2011.	Not in English
J. Dretzke, C. Cummins, J. Sandercock, A. Fry-Smith, T. Barrett, and A. Burls. Autoantibody testing in children with newly diagnosed type 1 diabetes mellitus. <i>Health Technol.Assess.</i> 8 (22):1-196, 2004.	HTA 2004 in T1D children. Wrong markers being assessed: auto-antibodies for celiac and thyroid disease
M. Galgani, R. Nugnes, M. Santopaolo, A. Franzese, S. Formisano, and G. Matarese. Meta-immunological profile of children with type 1 diabetes: Toward the possibility to predict progression of autoimmune diabetes. <i>Am.J.Pathol.</i> 181 (3 SUPPL. 1):S11, 2012.	Conference abstract
H. Takeda, E. Kawasaki, I. Shimizu, E. Konoue, M. Fujiyama, S. Muraio, K. Tanaka, K. Mori, Y. Tarumi, I. Seto, Y. Fujii, et al. Clinical, autoimmune, and genetic characteristics of adult-onset diabetic patients with GAD autoantibodies in Japan (Ehime Study). <i>Diabetes Care</i> 25 (6):995-1001, 2002.	Wrong population: has not categorised diabetics into the standard different types (T1D, T2D etc) but insulin-deficient and non-insulin deficient
A Balasubramanyam, G Garza, L Rodriguez, CS. Hampe, L Gaur, A Lernmark, and MR. Maldonado. Accuracy and predictive value of classification schemes for ketosis-prone diabetes. <i>Diabetes Care</i> 29 (12):2575-2579, 2006.	Wrong population: has not categorised diabetics into the standard different types (T1D, T2D etc) but KPD (ketone-prone diabetes) subtypes. Wrong study design: sensitivity and specificity of classification schemes to determine KPD subtypes
JM. Barker, SH. Goehrig, K Barriga, M Hoffman, R Slover, GS. Eisenbarth, JM. Norris, G Klingensmith, M Rewers, and study DAISY. Clinical characteristics of children diagnosed with type 1 diabetes through intensive screening and follow-up. <i>Diabetes Care</i> 27 (6):1399-1404, 2004.	Wrong intervention and outcomes: does not look at any of our specified markers
D. Dabelea, C. Pihoker, J. W. Talton, Jr D'Agostino, W. Fujimoto, G. J. Klingensmith, J. M. Lawrence, B. Linder, S. M. Marcovina, E. J. Mayer-Davis, G. Imperatore, and L. M. Dolan. Etiological approach to characterization of diabetes type: The SEARCH for diabetes in youth study. <i>Diabetes Care</i> 34 (7):1628-1633, 2011.	Wrong population: has not categorised diabetics into the standard different types (T1D, T2D etc)
E. Lindholm, E. Agardh, T. Tuomi, L. Groop, and C. D. Agardh. Classifying diabetes according to the new WHO clinical stages. <i>Eur.J.Epidemiol.</i> 17 (11):983-989, 2001.	Wrong population: has not categorised diabetics into the standard different types (T1D, T2D etc) but insulin-requiring for control (IRC) and non-insulin requiring (NIR)
J. S. Sorensen, F. Vaziri-Sani, F. Pociot, K. Kristensen, C. Brorsson, L. Lyngsoe, B. Dolmer, and N. H. Birkebaek. ZnT8 autoantibody specificities at, and 3-5 years after clinical onset, associates with the age at diagnosis and the SLC30A8 gene polymorphism in Danish children with type 1 diabetes. <i>Pediatr Diabetes</i> 11:24, 2010.	Conference abstract
M. J. Redondo, L. M. Rodriguez, M. Escalante, A. Balasubramanyam, and M. Haymond. Forms of pediatric diabetes mellitus defined by antiislet autoimmunity and beta-cell function at diagnosis. <i>Pediatr Diabetes</i> 12:98, 2011.	Conference abstract
K. Seifert, K. Tornow, U. Walschus, H. Kenk, and M. Schlosser. Examination of GAD65 in human serum as a possible marker of ongoing beta cell destruction in autoimmune diabetes. <i>Diabetologia</i> 54:S74, 2011.	Conference abstract
Z. Huang, Y. Chen, F. Li, and Y. Li. Clinical heterogeneity of type 1 diabetes mellitus at onset. <i>Diabetologia</i> 53:S396, 2010.	Conference abstract
A Soderbergh, A Grethe Myhre, O Ekwall, G Gebre-Medhin, H Hedstrand, E Landgren, A Miettinen, P Eskelin, M Halonen et al. Prevalence and clinical associations of 10 defined autoantibodies in autoimmune polyendocrine syndrome type I. <i>J.Clin.Endocrinol.Metab.</i> 89 (2):557-562, 2004.	Wrong population: T1D with APECED (autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy)
S Oak, L K. Gilliam, M Landin-Olsson, C Torn, I Kockum, CR. Pennington, M J.	Wrong outcomes: not the presence of

Study	Reason for exclusion
Rowley, MR, Christie, JP, Banga, and CS. Hampe. The lack of anti-idiotypic antibodies, not the presence of the corresponding autoantibodies to glutamate decarboxylase, defines type 1 diabetes. <i>Proc.Natl.Acad.Sci.U.S.A.</i> 105 (14):5471-5476, 2008.	markers in T1D, as recruited pts who were already GAD65+
L. C. G. de Graaff, J. W. A. Smit, and J. K. Radder. Prevalence and clinical significance of organ-specific autoantibodies in type 1 diabetes mellitus. <i>Neth.J.Med.</i> 65 (7):235-247, 2007.	Wrong intervention and outcomes: does not look at any of our specified markers
EH. Hathout, N Hartwick, OR. Fagoaga, AR Colacino, J Sharkey, M Racine, S Nelsen-Cannarella, and JW. Mace. Clinical, autoimmune, and HLA characteristics of children diagnosed with type 1 diabetes before 5 years of age. <i>Pediatrics</i> 111 (4 Pt 1):860-863, 2003.	Wrong population: children <12 years old (both early and later childhood onset)
L Thumer, K Adler, E Bonifacio, F Hofmann, M Keller, C Milz, A Munte, and A Gabriele Ziegler. German new onset diabetes in the young incident cohort study: DiMelli study design and first-year results. <i>Rev.diabet.stud.</i> 7 (3):202-208, 2010.	Wrong population: children and young people
A. J. Al Abbasi and F. A. Al Jenaidi. Frequency of auto-antibodies in newly diagnosed Bahraini type I diabetes mellitus children and their healthy siblings. <i>J.Bahrain Med.Soc.</i> 15 (1):9-12, 2003.	Wrong population: children 1-13 years old
M. Desai and A. Clark. Autoimmune diabetes in adults: lessons from the UKPDS. <i>Diabet.Med.</i> 25 Suppl 2:30-34, 2008.	Literature review
A. W. van Deutekom, R. J. Heine, and S. Simsek. The islet autoantibody titres: their clinical relevance in latent autoimmune diabetes in adults (LADA) and the classification of diabetes mellitus. <i>Diabet.Med.</i> 25 (2):117-125, 2008.	Literature review
R. Jensen, L. Gilliam, C. Torn, M. Landin-Olsson, J. Palmer, K. Akesson, I. Kockum, B. Lernmark, A. F. Karlsson, K. F. Lynch, N. Breslow, A. Lernmark, G. Sundkvist, and Diabetes Incidence Study in Sweden group. Islet cell autoantibody levels after the diagnosis of young adult diabetic patients. <i>Diabet.Med.</i> 24 (11):1221-1228, 2007.	Wrong population: shows changes in markers over time but does not categorise the diabetes population into different types of diabetes
S. Allen, J. Huber, and D. Devendra. Prevalence of organ-specific autoantibodies in childhood- and adult-onset type 1 diabetes. <i>Ann.N.Y.Acad.Sci.</i> 1150:260-262, 2008.	Wrong markers being assessed
T. Kobayashi, S. Tanaka, N. Harii, K. Aida, H. Shimura, M. Ohmori, M. Kanesige, A. Shimada, and T. Maruyama. Immunopathological and genetic features in slowly progressive insulin-dependent diabetes mellitus and latent autoimmune diabetes in adults. <i>Ann.N.Y.Acad.Sci.</i> 1079:60-66, 2006.	Literature review
JC. Low, EI. Felner, AB. Muir, M Brown, M Dorcelet, L Peng, and G E. Umpierrez. Do obese children with diabetic ketoacidosis have type 1 or type 2 diabetes? <i>Prim Care Diabetes</i> 6 (1):61-65, 2012.	Wrong outcomes: pools together results for Islet cell Abs and GAD Abs so can't separate the two
BW Lee, SY Kim, JY Kim, KY Cho, YJ Chung, YK Min, JH Chung, MK Lee, MS Lee, and KW Kim. Heterogeneity of early-onset and ketosis-resistant diabetes in Korean subjects--is it possible to determine cut-off age of early-onset type 2 diabetes? <i>Diabetes Res.Clin.Pract.</i> 70 (1):38-45, 2005.	Wrong population: unclear – just says 'early onset diabetes'
JL. Mahon, JM. Sosenko, L Rafkin-Mervis, H Krause-Steinrauf, JM. Lachin, C Thompson, PJ. Bingley, E Bonifacio, JP. Palmer, GS. Eisenbarth, J Wolfsdorf, JS. Skyler, TrialNet Natural History Committee, and Diabetes TrialNet Study Group. The TrialNet Natural History Study of the Development of Type 1 Diabetes: objectives, design, and initial results. <i>Pediatr Diabetes</i> 10 (2):97-104, 2009.	Wrong outcomes: does not give Ab results for the T1D pts; this is just the screening and baseline risk assessment paper. Wrong study population and design – presence of Abs in relatives and see if predicts development of diabetes
X Li, Z Zhou, G Huang, H Su, X Yan, and L Yang. Metabolic syndrome in adult-onset latent autoimmune diabetes. <i>Metab.syndr.relat.disord.</i> 3 (2):174-180, 2005.	Wrong outcomes: prevalence of metabolic syndrome (pts already divided into GAD+ and GAD-
FJ. Quintana, G Getz, G Hed, E Domany, and IR. Cohen. Cluster analysis of human autoantibody reactivities in health and in type 1 diabetes mellitus: a bioinformatic approach to immune complexity. <i>J.Autoimmun.</i> 21 (1):65-75, 2003.	Wrong interventions and outcomes: different assays / quantification of various markers in antigen clusters
M Nagata, R Kotani, H Moriyama, K Yokono, BO. Roep, and M Peakman. Detection of autoreactive T cells in type 1 diabetes using coded autoantigens and an immunoglobulin-free cytokine ELISPOT assay: report from the fourth immunology of diabetes society T cell workshop. <i>Ann.N.Y.Acad.Sci.</i> 1037:10-15, 2004.	Wrong interventions and outcomes: testing different assays and antibody types for GAD65
S. Brophy, H. Davies, G. Dunseath, J. W. Stephens, J. Platts, H. Lane, C. Beaverstock, L. Wakeman, I. Russell, M. Williams, and D. R. Williams. Experience of the introduction of routine antibody testing in primary care and of running a trial for latent autoimmune diabetes in adults (LADA). <i>Diabetes Res.Clin.Pract.</i> 93 (1):e49-e52, 2011.	Age of population not given for the main group recruited
E. Ortqvist, B. Brooks-Worrell, K. Lynch, J. Radtke, L. M. Bekris, I. Kockum, C. D. Agardh, C. M. Cilio, A. L. Lethagen, B. Persson, A. Lernmark, J. Reichow, S. Oak, J. P. Palmer, and C. S. Hampe. Changes in GAD65Ab-specific antiidiotypic antibody levels correlate with changes in C-peptide levels and progression to islet cell autoimmunity. <i>J.Clin.Endocrinol.Metab.</i> 95 (11):E310-E318, 2010.	Adult patients were treated with anti-GADA and so this study is about treatment effect
F Mauvais-Jarvis, E Sobngwi, R Porcher, JP Riveline, JP Kevorkian, C Vaisse, G Charpentier, PJ Guillausseau, P Vexiau, and JF Gautier. Ketosis-prone type 2 diabetes in patients of sub-Saharan African origin: clinical pathophysiology and natural history of beta-cell dysfunction and insulin resistance. <i>Diabetes</i> 53	Adult patients but results divided into ketosis-prone and non-ketosis prone pts

Diagnosis and management of type 1 diabetes in children and young people
Excluded studies

Study	Reason for exclusion
(3):645-653, 2004.	
A. Rogowicz-Frontczak, D. Zozulinska-Ziolkiewicz, P. Niedzwiecki, M. Litwinowicz, and B. Wierusz-Wysocka. Does glucagon stimulation test help to predict autoimmunity in newly diagnosed non obese adults with diabetes? <i>Exp.Clin.Endocrinol.Diabetes</i> 120 (7):428-434, 2012.	Type of diabetes population unspecified
B. Littorin, L. Nystrom, B. Gullberg, L. Rastam, J. Ostman, H. J. Arnqvist, E. Bjork, G. Blohme, J. Bolinder, J. W. Eriksson, B. Schersten, and G. Sundkvist. Increasing body mass index at diagnosis of diabetes in young adult people during 1983-1999 in the Diabetes Incidence Study in Sweden (DISS). <i>J.Intern.Med.</i> 254 (3):251-256, 2003.	Does not give the % of marker in each type of diabetes
S Porksen, LB Laborie, L Nielsen, MLM Andersen, T Sandal, H de Wet, E Schwarcz, J Aman, P Swift, M Kocova, EJ. Schonle, C de Beaufort, P Hougaard, F Ashcroft, A Molven, MI Knip, HB. Mortensen, L Hansen, PR. Njolstad, and Hydore Study Group on Childhood Diabetes. Disease progression and search for monogenic diabetes among children with new onset type 1 diabetes negative for ICA, GAD- and IA-2 Antibodies. <i>BMC Endocrine Disorders</i> 10:16, 2010.	Does not give results for each of the markers separately
S. Bilgic, E. Aktas, F. Salman, G. Ersahin, G. Erten, M. T. Yilmaz, and G. Deniz. Intracytoplasmic cytokine levels and neutrophil functions in early clinical stage of type 1 diabetes. <i>Diabetes Res.Clin.Pract.</i> 79 (1):31-36, 2008.	Wrong markers
M. Khalangot, V. Kravchenko, M. Tronko, and V. Gur'ianov. Correlation between the prevalence of type 1 diabetes with the daily insulin dose and the autoimmune process against glutamic acid decarboxylase in adults. <i>EUR.J.INTERN.MED.</i> 20 (6):611-615, 2009.	Wrong markers
MWMD. Lutgens, M Meijer, B Peeters, ML Poulsen, MJ. Rutten, ML. Bots, GJMG. van der Heijden, and SS. Soedamah-Muthu. Easily obtainable clinical features increase the diagnostic accuracy for latent autoimmune diabetes in adults: an evidence-based report. <i>Prim Care Diabetes</i> 2 (4):207-211, 2008.	Clinical screening tool for LADA but does not use our pre-specified markers
O. Rubio-Cabezas, E. L. Edghill, J. Argente, and A. T. Hattersley. Testing for monogenic diabetes among children and adolescents with antibody-negative clinically defined Type 1 diabetes. <i>Diabet.Med.</i> 26 (10):1070-1074, 2009.	Results are split into different genotypes of T1D, but not show the markers in each genotype
K. Zorena, J. Mysliwska, M. Mysliwiec, and A. Balcerska. Analysis of levels of angiogenin in children and adolescents with type 1 diabetes mellitus in relation to the duration of the disease. <i>Int.Rev.Allergol.Clin.Immunol.</i> 14 (3-4):98-100, 2008.	Wrong markers
A Makinen, T Harkonen, J Ilonen, M Knip, and Diabetes Register Finnish Pediatric. Characterization of the humoral immune response to islet antigen 2 in children with newly diagnosed type 1 diabetes. <i>European journal of endocrinology</i> 159 (1):19-26, 2008.	Results of patients categorised into responders and non-responders to single of combination of markers. And specifically recruited pts of IA-2A negative T1D
BM. Brooks-Worrell, JL. Reichow, A Goel, H Ismail, and JP. Palmer. Identification of autoantibody-negative autoimmune type 2 diabetic patients. <i>Diabetes Care</i> 34 (1):168-173, 2011.	Results of pts categorised into T-cell + and - and combination of all 5 markers, rather than each marker separately
KATULANDA 2008 P. Katulanda, B. Shine, G. W. Katulanda, A. Silva, E. L. Asfir, R. Sheriff, N. Somasundaram, A. E. Long, P. J. Bingley, M. I. McCarthy, A. Clark, and D. R. Matthews. Diabetes mellitus among young adults in Sri Lanka--role of GAD antibodies in classification and treatment: the Sri Lanka Young Diabetes study. <i>Diabetologia</i> 51 (8):1368-1374, 2008.	Wrong population: mixture of T1D, T2D and LADA with no subgroup analyses for each of these. And further divided into GAD- and GAD+
S Furlanos, C Perry, MS. Stein, J Stankovich, LC. Harrison, and PG. Colman. A clinical screening tool identifies autoimmune diabetes in adults. <i>Diabetes Care</i> 29 (5):970-975, 2006.	Risk scores which do not include our pre-specified markers
J. Bolinder, P. Fernlund, H. Borg, H. J. Arnqvist, E. Bjork, G. Blohme, J. W. Eriksson, L. Nystrom, J. Ostman, and G. Sundkvist. Hyperproinsulinemia segregates young adult patients with newly diagnosed autoimmune (type 1) and non-autoimmune (type 2) diabetes. <i>Scand.J.Clin.Lab.Invest.</i> 65 (7):585-594, 2005.	Wrong markers
C. Steele, W. A. Hagopian, S. Gitelman, U. Masharani, M. Cavaghan, K. I. Rother, D. Donaldson, D. M. Harlan, J. Bluestone, and K. C. Herold. Insulin secretion in type 1 diabetes. <i>Diabetes</i> 53 (2):426-433, 2004.	
M. Andrade Lima Gabbay, M. N. Sato, A. J. S. Duarte, and S. A. Dib. Serum titres of anti-glutamic acid decarboxylase-65 and anti-IA-2 autoantibodies are associated with different immunoregulatory milieu in newly diagnosed type 1 diabetes patients. <i>Clin.Exp.Immunol.</i> 168 (1):60-67, 2012.	
C.J. Greenbaum, CA. Beam, D Boulware, SE. Gitelman, PA. Gottlieb, KC. Herold, JM. Lachin, P McGee et al., and Diabetes TrialNet Study Group. Fall in C-peptide during first 2 years from diagnosis: evidence of at least two distinct phases from composite Type 1 Diabetes TrialNet data. <i>Diabetes</i> 61 (8):2066-2073, 2012.	
JM. Sosenko, JP. Palmer, L Rafkin-Mervis, JP. Krischer, D Cuthbertson, D Matheson, and JS. Skyler. Glucose and C-peptide changes in the perionset period of type 1 diabetes in the Diabetes Prevention Trial-Type 1. <i>Diabetes Care</i> 31 (11):2188-2192, 2008.	
A. G. Unnikrishnan, E. Bhatia, V. Bhatia, S. K. Bhadada, R. K. Sahay, A. Kannan, V. Kumaravel, D. Sarma, B. Ganapathy, N. Thomas, M. John, R. V.	

Study	Reason for exclusion
Jayakumar, H. Kumar, V. Nair, and C. B. Sanjeevi. Type 1 diabetes versus type 2 diabetes with onset in persons younger than 20 years of age: Results from an Indian multicenter study. <i>Ann.N.Y.Acad.Sci.</i> 1150:239-244, 2008.	
E Aguilera, R Casamitjana, G Ercilla, J Oriola, R Gomis, and I Conget. Adult-onset atypical (type 1) diabetes: additional insights and differences with type 1A diabetes in a European Mediterranean population. <i>Diabetes Care</i> 27 (5):1108-1114, 2004.	
O. Raha, B. N. Sarkar, L. V. K. S. Bhaskar, P. Veeraj, S. Chowdhury, S. Mukhopadhyay, T. K. Biswas, and V. R. Rao. Insulin (INS) promoter vnr polymorphisms: Interactions and association with type 1 diabetes mellitus in bengali speaking patients of Eastern India. <i>Diabetol.Croat.</i> 40 (4):99-106, 2011.	
V. Serban, A. Enache, A. Vlad, Alexandra Sima, Mihaela Rosu, Adriana Rosca, and Carmina Draghici. GADA and islet cell antibodies in Romanian children and adolescents with diabetes mellitus. <i>Rom.J.Intern.Med.</i> 42 (2):325-332, 2004.	
S Tanaka, T Endo, K Aida, H Shimura, N Yokomori, M Kaneshige, F Furuya, S Amemiya, M Mochizuki, K Nakanishi, and T Kobayashi. Distinct diagnostic criteria of fulminant type 1 diabetes based on serum C-peptide response and HbA1c levels at onset. <i>Diabetes Care</i> 27 (8):1936-1941, 2004.	
L Yang, S Luo, G Huang, J Peng, X Li, X Yan, J Lin, JM. Wenzlau, HW. Davidson, JC. Hutton, and Z Zhou. The diagnostic value of zinc transporter 8 autoantibody (ZnT8A) for type 1 diabetes in Chinese. <i>Diabetes.Metab.Res.Rev.</i> 26 (7):579-584, 2010.	
E. S. Siraj, D. G. Rogers, M. K. Gupta, and S. S. K. Reddy. A Simple Screening Method for Individuals at Risk of Developing Type 1 Diabetes: Measurement of Islet Cell Autoantibodies (GADA, IA-2A, and IAA) on Dried Capillary Blood Spots Collected on Filter Paper. <i>Horm.Metab.Res.</i> 44 (11):855-860, 2012.	
T Maruyama, S Oak, A Shimada, and CS. Hampe. GAD65 autoantibody responses in Japanese latent autoimmune diabetes in adult patients. <i>Diabetes Care</i> 31 (8):1602-1607, 2008.	
S. Dagdelen, G. Hascelik, and M. Bayraktar. Simultaneous triple organ specific autoantibody profiling in adult patients with type 1 diabetes mellitus and their first-degree relatives. <i>Int.J.Clin.Pract.</i> 63 (3):449-456, 2009.	
D Hickey, G Joshy, P Dunn, D Simmons, and R Lawrenson. Glycaemic control and antibody status among patients with newly diagnosed Type 1 diabetes. <i>N.Z.Med.J.</i> 120 (1262):U2732, 2007.	
N. C. Schloot, P. Hanifi-Moghaddam, N. Aabenhus-Andersen, B. Z. Alizadeh, M. T. Saha, M. Knip, D. Devendra, T. Wilkin, E. Bonifacio, B. O. Roep, H. Kolb, and T. Mandrup-Poulsen. Association of immune mediators at diagnosis of Type 1 diabetes with later clinical remission. <i>Diabet.Med.</i> 24 (5):512-520, 2007.	
R. C. Silva, C. Sallorenzo, C. E. Kater, S. A. Dib, and A. Falorni. Autoantibodies against glutamic acid decarboxylase and 21-hydroxylase in Brazilian patients with type 1 diabetes or autoimmune thyroid diseases. <i>Diabetes Nutr Metab</i> 16 (3):160-168, 2003.	
W. Y. Ng, Y. S. Lee, A. L. Todd, K. F. Lui, K. Y. Loke, and A. C. Thai. Tyrosine phosphatase-like protein (IA-2) and glutamic acid decarboxylase (GAD65) autoantibodies: a study of Chinese patients with diabetes mellitus. <i>Autoimmunity</i> 35 (2):119-124, 2002.	
E Kawasaki, K Nakamura, G Kuriya, T Satoh, M Kobayashi, H Kuwahara, N Abiru, H Yamasaki, N Matsuura, J Miura, Y Uchigata, and K Eguchi. Differences in the humoral autoreactivity to zinc transporter 8 between childhood- and adult-onset type 1 diabetes in Japanese patients. <i>Clin.Immunol.</i> 138 (2):146-153, 2011.	
E Kawasaki, K Nakamura, G Kuriya, T Satoh, M Kobayashi, H Kuwahara, N Abiru, H Yamasaki, N Matsuura, J Miura, Y Uchigata, and K Eguchi. Zinc transporter 8 autoantibodies in fulminant, acute-onset, and slow-onset patients with type 1 diabetes. <i>Diabetes.Metab.Res.Rev.</i> 27 (8):895-898, 2011.	
T Maruyama, T Nakagawa, A Kasuga, and M Murata. Heterogeneity among patients with latent autoimmune diabetes in adults. <i>Diabetes.Metab.Res.Rev.</i> 27 (8):971-974, 2011.	
J. F. Louet, S. B. Smith, J. F. Gautier, M. Molokhia, M. L. Virally, J. P. Kevorkian, P. J. Guillausseau, P. Vexiau, G. Charpentier, M. S. German, C. Vaisse, M. Urbanek, and F. Mauvais-Jarvis. Gender and neurogenin3 influence the pathogenesis of ketosis-prone diabetes. <i>Diabetes Obes Metab</i> 10 (10):912-920, 2008.	
R Buzzetti, S Di Pietro, A Giaccari, A Petrone, M Locatelli, C Suraci, M Capizzi, M L Arpi, E Bazzigaluppi, F Dotta, E Bosi, and Non Insulin Requiring Autoimmune Diabetes Study Group. High titer of autoantibodies to GAD identifies a specific phenotype of adult-onset autoimmune diabetes. <i>Diabetes Care</i> 30 (4):932-938, 2007.	Wrong population: age groups not specified
V Tica, MW Hanif, A Andersson, G. Valsamakis, A. H. Barnett, S Kumar, and C. B. Sanjeevi. Frequency of latent autoimmune diabetes in adults in Asian patients diagnosed as type 2 diabetes in Birmingham, United Kingdom. <i>Ann.N.Y.Acad.Sci.</i> 1005:356-358, 2003.	

Study	Reason for exclusion
J. Skupien, S. Gorczynska-Kosiorz, T. Klupa, K. Cyganek, K. Wanic, M. Borowiec, J. Sieradzki, and M. T. Malecki. Molecular background and clinical characteristics of HNF1A MODY in a Polish population. <i>Diabetes Metab.</i> 34 (5):524-528, 2008.	
MC Moreira, GM Lara, R Linden, LR Feksa, R G Tavares, SE de Matos Almeida, and DB Berlese. Frequency of the anti-glutamic acid decarboxylase immunological marker in patients with diabetes duration longer than three years in southern Brazil. <i>Sao Paulo Med J</i> 129 (3):130-133, 2011.	Age range of population not specified
M. Prazny, J. Skrha, Z. Limanova, Z. Vanickova, J. Hilgertova, J. Prazna, M. Jaresova, and I. Striz. Screening for associated autoimmunity in type 1 diabetes mellitus with respect to diabetes control. <i>Physiol.Res.</i> 54 (1):41-48, 2005.	Age range of population not specified
Ju Xu, QH Dan, V Chan, NMS. Wat, S Tam, SC Tiu, KF Lee, SC Siu, MW Tsang, L M Fung, KW Chan, and KSL. Lam. Genetic and clinical characteristics of maturity-onset diabetes of the young in Chinese patients. <i>Eur.J.Hum.Genet.</i> 13 (4):422-427, 2005.	Age range of population not specified
AJ. Delli, Fariba Vaziri-Sani, Bengt Lindblad, Helena Elding-Larsson, Annelie Carlsson, Gun Forsander, Sten A. Ivarsson, et al. and Better Diabetes Diagnosis study group. Zinc transporter 8 autoantibodies and their association with SLC30A8 and HLA-DQ genes differ between immigrant and Swedish patients with newly diagnosed type 1 diabetes in the Better Diabetes Diagnosis study. <i>Diabetes</i> 61 (10):2556-2564, 2012.	Excluded even for children/young pple GL, because doesn't give the actual % of pple (or the titre) who are Ab+ for the young pple or children's subgroup
N. A. Ali, E. Swelam, E. A. Al Banna, and A. Showkry. Role of beta-cell autoantibodies as a predictor marker in diabetic patients and their relationship to glycemic control. <i>Egyptian journal of immunology / Egyptian Association of Immunologists</i> 19 (1):39-49, 2012.	Adults and children mixed population – but adult subgroup analysis. Adult subgroup N<50. Children = mix of children and young pple, also N<50
MH Black, Jean M. Lawrence, Catherine Pihoker, Lawrence M. Dolan, Andrea Anderson, Beatriz Rodriguez, Santica M. Marcovina, Elizabeth J. Mayer-Davis, Giuseppina Imperatore, Dana Dabelea, and SEARCH for Diabetes in Youth Study Group. HLA-associated phenotypes in youth with autoimmune diabetes. <i>Pediatr.Diabetes</i> 14 (2):121-128, 2013.	Mixed population of all ages, with no age subgroup analyses
M. Borowiec, W. Fendler, P. Dusatkova, K. Antosik, S. Pruhova, O. Cinek, M. Mysliwiec, P. Jarosz-Chobot, M. T. Malecki, and W. Mlynarski. HbA1c-based diabetes diagnosis among patients with glucokinase mutation (GCK-MODY) is affected by a genetic variant of glucose-6-phosphatase (G6PC2). <i>Diabet.Med.</i> 29 (11):1465-1469, 2012.	Does not give % of patients with the markers pre-specified in our protocol
C Chao, Gan Huang, Xia Li, Lin Yang, Jian Lin, Ping Jin, Shuo Ming Luo, Yi Yu Zhang, Ling Ling Pan, and Zhi Guang Zhou. Change of glutamic acid decarboxylase antibody and protein tyrosine phosphatase antibody in Chinese patients with acute-onset type 1 diabetes mellitus. <i>Chin.Med.J.(Engl).</i> 126 (21):4006-4012, 2013.	Wrong population: mixed population of all ages, with no age sub-group analysis
C. O. Ekpebegh and B. Longo-Mbenza. Clinical, immunologic and insulin secretory characteristics of young black South African patients with diabetes: Hospital based single centre study. <i>Diabetes Res.Clin.Pract.</i> 99 (3):380-384, 2013.	Wrong population: mixed population of all ages, with no age sub-group analysis
T. Eto, S. Inoue, and T. Kadowaki. Effects of once-daily teneligliptin on 24-h blood glucose control and safety in Japanese patients with type 2 diabetes mellitus: A 4-week, randomized, double-blind, placebo-controlled trial. <i>Diabetes Obes.Metab.</i> 14 (11):1040-1046, 2012.	Tx study
R Fernandez, Ranjita Misra, Ramaswami Nalini, Christiane S. Hampe, Kerem Ozer, and Ashok Balasubramanyam. Characteristics of patients with ketosis-prone diabetes (KPD) presenting with acute pancreatitis: implications for the natural history and etiology of a KPD subgroup. <i>Endocr Pract</i> 19 (2):243-251, 2013.	Unclear if T1D or T2D – just says ketosis-prone diabetics
BN. Frederiksen, Miranda Kroehl, Tasha E. Fingerlin, Randall Wong, Andrea K. Steck, Marian Rewers, and Jill M. Norris. Association between vitamin D metabolism gene polymorphisms and risk of islet autoimmunity and progression to type 1 diabetes: the diabetes autoimmunity study in the young (DAISY). <i>J.Clin.Endocrinol.Metab.</i> 98 (11):E1845-E1851, 2013.	Does not answer question: markers as predictors of future development of T1D
I Hojsak, Noam Zevit, Orith Waisbourd-Zinman, Yoram Rosenbach, Yael Mozer-Glassberg, Shlomit Shalitin, Moshe Phillip, and Raanan Shamir. Concomitant autoantibodies in newly diagnosed diabetic children with transient celiac serology or proven celiac disease. <i>J.Pediatr.Endocrinol.Metab.</i> 26 (11-12):1099-1104, 2013.	Wrong population: mixed population of children and young pple, with no age sub-group analysis
H. U. Irgens, J. Molnes, B. B. Johansson, M. Ringdal, T. Skrivarhaug, D. E. Undlien, O. Sovik, G. Joner, A. Molven, and P. R. Njolstad. Prevalence of monogenic diabetes in the population-based Norwegian Childhood Diabetes Registry. <i>Diabetologia</i> 56 (7):1512-1519, 2013.	Mixed population of children and young people; can get data for young people but this is incomplete (some is missing or not available)
K Johnson, Randall Wong, Katherine J. Barriga, Georgeanna Klingensmith, Anette G. Ziegler, Marian J. Rewers, and Andrea K. Steck. rs11203203 is associated with type 1 diabetes risk in population pre-screened for high-risk HLA-DR,DQ genotypes. <i>Pediatr.Diabetes</i> 13 (8):611-615, 2012.	Wrong population: children only
B. S. Karagun, F. Temiz, G. Ozer, B. Yuksel, A. K. Topaloglu, N. O. Mungan, M. Mazman, and G. M. Karagun. Chromium levels in healthy and newly diagnosed type 1 diabetic children. <i>Pediatr Int</i> 54 (6):780-785, 2012.	Wrong population: children only

Study	Reason for exclusion
S Krause, Ruth Chmiel, Ezio Bonifacio, Marlon Scholz, Michael Powell, Jadwiga Furmaniak, Bernard Rees Smith, Anette G. Ziegler, and Peter Achenbach. IA-2 autoantibody affinity in children at risk for type 1 diabetes. <i>Clin.Immunol.</i> 145 (3):224-229, 2012.	Wrong population: children only. Risk of future development of T1D
TH Lee, Ah Reum Kwon, Ye Jin Kim, Hyun Wook Chae, Ho Seong Kim, and Duk Hee Kim. The clinical measures associated with C-peptide decline in patients with type 1 diabetes over 15 years. <i>J Korean Med Sci</i> 28 (9):1340-1344, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
J. Lempainen, T. Harkonen, Ap Laine, M. Knip, J. Ilonen, and Diabetes Register Finnish Pediatric. Associations of polymorphisms in non-HLA loci with autoantibodies at the diagnosis of type 1 diabetes: INS and IKZF4 associate with insulin autoantibodies. <i>Pediatr.Diabetes</i> 14 (7):490-496, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
J Ludvigsson, Annelie Carlsson, Ahmed Deli, Gun Forsander, Sten A. Ivarsson, Ingrid Kockum, Bengt Lindblad, Claude Marcus, Ake Lenmark, and Ulf Samuelsson. Decline of C-peptide during the first year after diagnosis of Type 1 diabetes in children and adolescents. <i>Diabetes Res.Clin.Pract.</i> 100 (2):203-209, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
D Miao, K. Michelle Guyer, Fran Dong, Ling Jiang, Andrea K. Steck, Marian Rewers, George S. Eisenbarth, and Liping Yu. GAD65 autoantibodies detected by electrochemiluminescence assay identify high risk for type 1 diabetes. <i>Diabetes</i> 62 (12):4174-4178, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
S Miersch, Xiaofang Bian, Garrick Wallstrom, Sahar Sibani, Tanya Logvinenko, Clive H. Wasserfall, Desmond Schatz, Mark Atkinson, Ji Qiu, and Joshua LaBaer. Serological autoantibody profiling of type 1 diabetes by protein arrays. <i>J Proteomics</i> 94:486-496, 2013.	Doesn't give % of pple with Abs or the titre
M. Moritani, I. Yokota, K. Tsubouchi, R. Takaya, K. Takemoto, K. Minamitani, T. Urakami, T. Kawamura, N. Kikuchi, M. Itakura, T. Ogata, S. Sugihara, and S. Amemiya. Identification of INS and KCNJ11 gene mutations in type 1B diabetes in Japanese children with onset of diabetes before 5 yr of age. <i>Pediatr.Diabetes</i> 14 (2):112-120, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis. Doesn't give results for our pre-specified markers
S. A. Mughal, R. Park, N. Nowak, A. L. Gloyn, F. Karpe, H. Matile, M. T. Malecki, M. I. McCarthy, M. Stoffel, and K. R. Owen. Apolipoprotein M can discriminate HNF1A-MODY from Type 1 diabetes. <i>Diabet.Med.</i> 30 (2):246-250, 2013.	Doesn't look at the markers pre-specified in our protocol
L. Petruzelkova, R. Ananieva-Jordanova, J. Vcelakova, Z. Vesely, K. Stechova, J. Lebl, P. Dusatkova, Z. Sumnik, R. Coles, M. Powell, J. Furmaniak, Smith B. Rees, and S. Kolouskova. The dynamic changes of zinc transporter 8 autoantibodies in Czech children from the onset of Type 1 diabetes mellitus. <i>Diabet.Med.</i> 31 (2):165-171, 2014.	Wrong population: mix of children and young people, with no age subgroup analysis
MN Pham, Hubert Kolb, Thomas Mandrup-Poulsen, Tadej Battelino, Johnny Ludvigsson, Paolo Pozzilli, Michael Roden, Nanette C. Schloot, and C. P. European. Serum adipokines as biomarkers of beta-cell function in patients with type 1 diabetes: positive association with leptin and resistin and negative association with adiponectin. <i>Diabetes.Metab.Res.Rev.</i> 29 (2):166-170, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
C Pihoker, Lisa K. Gilliam, Sian Ellard, Dana Dabelea, Cralen Davis, et al and SEARCH for Diabetes in Youth Study Group. Prevalence, characteristics and clinical diagnosis of maturity onset diabetes of the young due to mutations in HNF1A, HNF4A, and glucokinase: results from the SEARCH for Diabetes in Youth. <i>J.Clin.Endocrinol.Metab.</i> 98 (10):4055-4062, 2013.	Wrong population: mix of all ages, with no age subgroup analysis
M.J. Redondo, Luisa M. Rodriguez, Mirna Escalante, E. O'Brian Smith, Ashok Balasubramanyam, and Morey W. Haymond. Beta cell function and BMI in ethnically diverse children with newly diagnosed autoimmune type 1 diabetes. <i>Pediatr.Diabetes</i> 13 (7):564-571, 2012.	Wrong population: mix of children and young people, with no age subgroup analysis
M. J. Redondo, L. M. Rodriguez, M. Escalante, E. O. Smith, A. Balasubramanyam, and M. W. Haymond. Types of pediatric diabetes mellitus defined by anti-islet autoimmunity and random C-peptide at diagnosis. <i>Pediatr.Diabetes</i> 14 (5):333-340, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
JL. Sherr, Tara Ghazi, Anna Wurtz, Linda Rink, and Kevan C. Herold. Characterization of residual beta cell function in long-standing type 1 diabetes. <i>Diabetes.Metab.Res.Rev.</i> 30 (2):154-162, 2014.	Wrong population: mix of all ages, with no age subgroup analysis
E Pettersen Sorgjer, Frank Skorpen, Kirsti Kvaloy, Kristian Midthjell, and Valdemar Grill. Prevalence of ZnT8 antibody in relation to phenotype and SLC30A8 polymorphism in adult autoimmune diabetes: results from the HUNT study, Norway. <i>Autoimmunity</i> 46 (1):74-79, 2013.	Wrong population: mix of all ages, with no age subgroup analysis
JM. Sosenko, Jay S. Skyler, Jerry P. Palmer, Jeffrey P. Krischer, et al Diabetes TrialNet Study Group, and Prevention Trial-Type Diabetes. The prediction of type 1 diabetes by multiple autoantibody levels and their incorporation into an autoantibody risk score in relatives of type 1 diabetic patients. <i>Diabetes Care</i> 36 (9):2615-2620, 2013.	Does not answer the question: uses markers as predictors of future development of T1D
P Xu, Craig A. Beam, David Cuthbertson, Jay M. Sosenko, Jay S. Skyler, Jeffrey P. Krischer, and Study Group. Prognostic accuracy of immunologic and metabolic markers for type 1 diabetes in a high-risk population: receiver operating characteristic analysis. <i>Diabetes Care</i> 35 (10):1975-1980, 2012.	Does not answer the question: uses markers as predictors of future development of T1D
L Yu, Fran Dong, Dongmei Miao, Alexandra R. Fouts, Janet M. Wenzlau, and Andrea K. Steck. Proinsulin/Insulin autoantibodies measured with	Wrong population: mix of children and young people, with no age subgroup

Study	Reason for exclusion
electrochemiluminescent assay are the earliest indicator of prediabetic islet autoimmunity. <i>Diabetes Care</i> 36 (8):2266-2270, 2013.	analysis
SY Chai, Xiao Yu Pan, Ke Xiu Song, Yue Ye Huang, Fei Li, Xiao Yun Cheng, and Shen Qu. Differential patterns of insulin secretion and sensitivity in patients with type 2 diabetes mellitus and nonalcoholic fatty liver disease versus patients with type 2 diabetes mellitus alone. <i>Lipids health dis.</i> 13:7, 2014.	Adults but N<50
H. Demirbilek, Ozbek M. Nuri, and Baran R. Taner. Incidence of type 1 diabetes mellitus in Turkish children from the Southeastern region of the country: A regional report. <i>JCRPE J.Clin.Res.Pediatr.Endocrinol.</i> 5 (2):98-103, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
W Donelan, Hai Wang, Shi Wu Li, David Pittman, Yi Li, Shuhong Han, Yu Sun, Christopher Carter, Mark Atkinson, Westley Reeves, William E. Winter, and Li Jun Yang. Novel detection of pancreatic and duodenal homeobox 1 autoantibodies (PAA) in human sera using luciferase immunoprecipitation systems (LIPS) assay. <i>Int J Clin Exp Pathol</i> 6 (6):1202-1210, 2013.	Validation study of new methods for Ab detection
E. Ekholm, N. Shaat, and J. J. Holst. Characterization of beta cell and incretin function in patients with MODY1 (HNF4A MODY) and MODY3 (HNF1A MODY) in a Swedish patient collection. <i>Acta Diabetol.</i> 49 (5):349-354, 2012.	Adults but N<50
C Ekpebegh, Benjamin Longo-Mbenza, and Ernesto Blanco-Blanco. Islet immunity and beta cell reserve of indigenous Black South Africans with ketoacidosis at initial diagnosis of diabetes. <i>Ethn Dis</i> 23 (2):196-201, 2013.	Unclear population: just says DKA. Most were later recognised as T2D (in the discussion section), but no analysis done by type of diabetes
G Huang, Xuxu Mo, Muwen Li, Yufei Xiang, Xia Li, Shuoming Luo, and Zhiguang Zhou. Autoantibodies to CCL3 are of low sensitivity and specificity for the diagnosis of type 1 diabetes. <i>Acta Diabetol.</i> 49 (5):395-399, 2012.	Wrong population: mix of all ages, with no age subgroup analysis
N. M. Kamal Alanani and A. A. Alsulaimani. Epidemiological pattern of newly diagnosed children with type 1 diabetes mellitus, Taif, Saudi Arabia. <i>Sci.World J.</i> 2013, 2013.	Wrong population: children
I Kikkas, Roberto Mallone, Nadia Tubiana-Rufi, Didier Chevenne, Jean Claude Carel, Christophe Creminon, Herve Volland, Christian Boitard, and Nathalie Morel. A simple and fast non-radioactive bridging immunoassay for insulin autoantibodies. <i>PLoS one</i> 8 (7):e69021, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
H Kolb, Kathrin Luckemeyer, Tim Heise, Christian Herder, Nanette C. Schloot, Wolfgang Koenig, Lutz Heinemann, Stephan Martin, and DIATOR Study Group. The systemic immune network in recent onset type 1 diabetes: central role of interleukin-1 receptor antagonist (DIATOR Trial). <i>PLoS one</i> 8 (8):e72440, 2013.	Does not give levels or % of pts with markers; just correlations with other markers
S Masala, Maria Antonietta Zedda, Davide Cossu, Carlo Ripoli, Mario Palermo, and Leonardo A. Sechi. Zinc transporter 8 and MAP3865c homologous epitopes are recognized at T1D onset in Sardinian children. <i>PLoS one</i> 8 (5):e63371, 2013.	Wrong population: children
RH. Muni, Radha P. Kohly, Eudocia Q. Lee, JoAnn E. Manson, Richard D. Semba, and Debra A. Schaumberg. Prospective study of inflammatory biomarkers and risk of diabetic retinopathy in the diabetes control and complications trial. <i>JAMA Ophthalmol</i> 131 (4):514-521, 2013.	Wrong markers: not those pre-specified in our protocol
A Parkkola, Taina Harkonen, Samppa J. Ryhanen, Jorma Ilonen, Mikael Knip, and Diabetes Register Finnish Pediatric. Extended family history of type 1 diabetes and phenotype and genotype of newly diagnosed children. <i>Diabetes Care</i> 36 (2):348-354, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
A Ryden and Maria Faresjo. Altered immune profile from pre-diabetes to manifestation of type 1 diabetes. <i>Diabetes Res.Clin.Pract.</i> 100 (1):74-84, 2013.	Wrong population: mix of children and young people, with no age subgroup analysis
H Skarstrand, L. B. Dahlin, A. Lernmark, and F. Vaziri-Sani. Neuropeptide Y autoantibodies in patients with long-term type 1 and type 2 diabetes and neuropathy. <i>J.Diabetes Complications</i> 27 (6):609-617, 2013.	Wrong population: mix of all ages, with no age subgroup analysis
P Varadarajan, Thangavelu Sangaralingam, Senthil Senniappan, Suresh Jahnavi, Venkatesan Radha, and Viswanathan Mohan. Clinical profile and outcome of infantile onset diabetes mellitus in southern India. <i>Indian Pediatr</i> 50 (8):759-763, 2013.	Wrong population: children
J Vcelakova, Radek Blatny, Zbynek Halhuber, Michal Kolar, Ales Neuwirth, et al. The effect of diabetes-associated autoantigens on cell processes in human PBMCs and their relevance to autoimmune diabetes development. <i>J Diabetes Res</i> 2013:589451, 2013.	Wrong population: mix of all ages, with no age subgroup analysis
K Warncke, M Krasmann, R Puff, D Dunstheimer, AG Ziegler, and A Beyerlein. Does diabetes appear in distinct phenotypes in young people? Results of the diabetes mellitus incidence Cohort Registry (DiMelli). <i>PLoS one</i> 8 (9):e74339, 2013.	Wrong population: mix of all ages, with no age subgroup analysis
AJ. K. Williams, SL. Thrower, IM. Sequeiros, A Ward, AS. Bickerton, JM. Triay, MP. Callaway, and CM. Dayan. Pancreatic volume is reduced in adult patients with recently diagnosed type 1 diabetes. <i>J.Clin.Endocrinol.Metab.</i> 97 (11):E2109-E2113, 2012.	Adults, but N<50
A M Zahran, KI Elsayh, and K A Metwalley. Regulatory T cells in children with recently diagnosed type 1 diabetes. <i>Indian J Endocrinol Metab</i> 16 (6):952-957, 2012.	Wrong population: children

Study	Reason for exclusion
AG. Ziegler, M Rewers, O Simell, T Simell, J Lempainen, A Steck, C Winkler, J Ilonen, R Veijola, M Knip, E Bonifacio, and GS. Eisenbarth. Seroconversion to multiple islet autoantibodies and risk of progression to diabetes in children. <i>JAMA</i> 309 (23):2473-2479, 2013.	Does not answer the question: uses markers as predictors of future development of T1D
Hartemann A, Bensimon G, Payan CA, Jacqueminet S, Bourron O, Nicolas N et al. Low-dose interleukin 2 in patients with type 1 diabetes: A phase 1/2 randomised, double-blind, placebo-controlled trial. <i>Lancet Diabetes and Endocrinology</i> . 2013; 1(4):295-305	Treatment study. Article currently unavailable
DT. Papadimitriou, C Marakaki, A Fretzayas, P Nicolaidou, and A Papadimitriou. Negativation of type 1 diabetes-associated autoantibodies to glutamic acid decarboxylase and insulin in children treated with oral calcitriol. <i>J Diabetes</i> 5 (3):344-348, 2013.	Article currently unavailable
R. J. Aitken, I. V. Wilson, A. E. Long, A. J. K. Williams, T. J. McDonald, K. M. Gillespie, F. S. Wong, A. T. Hattersley, and P. J. Bingley. Residual beta cell function in long-standing childhood onset Type 1 diabetes. <i>Diabet Med</i> 31:19-20, 2014.	Conference abstract
A. Al-Farwi. The prevalence, autoimmune and genetic markers of latent autoimmune diabetes of adults in the coastal area/Syria. <i>Diabetes Technol. Ther.</i> 16:A135, 2014.	Conference abstract
C Andersson, M Kolmodin, S A Ivarsson, A Carlsson, G Forsander, B Lindblad, J Ludvigsson, I Kockum, C Marcus et al and Better Diabetes Diagnosis Study Group. Islet cell antibodies (ICA) identify autoimmunity in children with new onset diabetes mellitus negative for other islet cell antibodies. <i>Pediatr Diabetes</i> 15 (5):336-344, 2014	Unable to acquire article. Also in children
S. Axelsson, M. Hjorth, J. Ludvigsson, and R. Casas. Decreased GAD(65)-specific Th1/Tc1 phenotype in children with Type 1 diabetes treated with GAD-alum. <i>Diabet Med</i> 29 (10):1272-1278, 2012.	Does not give the results for our pre-specified markers of interest
A. Bossowski, J. Furmaniak, J. Michalak, T. Diana, B. Glowin'ska-Olszewska, and G. Kahaly. Assessment of the occurrence of the autoantibodies in children with diabetes type 1. <i>Pediatr Diabetes</i> 14:125, 2013.	Conference abstract
R. Braham, A. A. Zaid, R. Ahmed, M. Zitouni, S. Sobki, and F. A. Sabaan. Double diabetes in Saudi Arabia: A new entity or an underestimated condition? <i>Diabetes</i> 63:A402, 2014.	Conference abstract
V. Bravis, A. Kaur, H. Walkey, I. Godsland, C. Dayan, M. Peakman, P. Bingley, and D. G. Johnston. An incident and high-risk type 1 diabetes cohort-after diagnosis diabetes research support system-2 (address-2): Key initial findings. <i>Diabetes</i> 63:A645, 2014.	Conference abstract
B. A. Buckingham, P. Cheng, R. W. Beck, C. Kollman, K. Ruedy, S. A. Weinzimer, R. Slover, A. A. Bremer, W. V. Tamborlane, and J. Fuqua. Relationship of glycemic control and c-peptide levels 2 years following diagnosis of T1D. <i>Diabetes</i> 63:A392, 2014.	Conference abstract
L. E. Calliari, B. L. Barbosa, D. C. F. Lago, R. M. Noronha, and A. F. Reis. Maturity-onset diabetes of the young (MODY) type 2 in infancy and adolescence: Description of three families. <i>Pediatr Diabetes</i> 14:133, 2013.	Conference abstract
H. A. Castleden, A. E. Long, I. V. Wilson, R. J. Aitken, A. J. Williams, P. J. Bingley, and K. M. Gillespie. The characteristics of slow progression to Type 1 diabetes. <i>Diabet Med</i> 31:19, 2014.	Conference abstract
BM. Cerqueiro, L. Grahnquist, E. Orqvist, A. Carlsson, and S. Ivarsson. Transglutaminas antibodies in Swedish children with type 1 diabetes in relation to HLA types and islet autoantibodies. <i>Pediatr Diabetes</i> 14:128-129, 2013.	Conference abstract
C. M. Chambers, A. R. Fouts, R. M. Sippl, K. Colclough, Z. X. Wang, Batish S. Dev, M. Jaremko, S. Ellard, A. T. Hattersley, G. J. Klingensmith, and A. K. Steck. Characteristics of maturity onset diabetes of the young in a large diabetes center. <i>Diabetes</i> 63:A363, 2014.	Conference abstract
K. K. Danielson, R. S. Monson, and T. J. Lecaie. Lower residual c-peptide at type 1 diabetes diagnosis and poor 10-year glycemic control independently predict higher pro-inflam matory tumor necrosis factor-alpha at 13-18 years diabetes duration. <i>Diabetes</i> 63:A409, 2014.	Conference abstract
L. A. Dimeglio, P. Cheng, R. W. Beck, C. Kollman, K. Ruedy, B. A. Buckingham, S. A. Weinzimer, R. Slover, A. A. Bremer, and T. Aye. Early predictors of stimulated C-peptide in persons with type 1 diabetes (T1D). <i>Diabetes</i> 63:A392, 2014.	Conference abstract
LH. Elding, K. Vehik, P. Gesualdo, B. Akolkar, W. Hagopian, J. Krischer, A. Lernmark, M. Rewers, O. Simell, J.-X. She, A. Ziegler, and M. J. Haller. Children followed in the TEDDY study are diagnosed with type 1 diabetes at an early stage of disease. <i>Pediatr Diabetes</i> 15 (2):118-126, 2014.	Does not answer question: presence of Abs BEFORE diagnosis
H Fan, QingRong Pan, Pengrui Zhang, Jia Liu, Yuan Xu, and Xinchun Yang. Influence of islet function on typing and prognosis of new-onset diabetes after intensive insulin therapy. <i>Med Sci Monit</i> 19:787-793, 2013.	Already found this study in first set of reruns. Has been included in review
LA. Fernandez, Moreira Garcia, V, Gonzalez B. Laborda, Corona L. Marcos, N. Beridze, and Rodriguez E. Fernandez. Stability of C-peptide in blood specimens after delayed processing. <i>Biochim.Clin.</i> 37:S331, 2013.	Conference abstract
E. Graber, M. Regelman, E. Wallach, L. Waldman, M. Goldis, M. Klein, D. Chia, and R. Rapaport. C-peptide is detected in 40% of youth with long-	Conference abstract

Study	Reason for exclusion
standing type 1 diabetes: A pilot study. <i>Diabetes</i> 63:A320, 2014.	
M. Habu, R. Kuwabara, M. Okuno, J. Suzuki, T. Urakami, and S. Takahashi. Prevalences of antibodies to IA-2 and GAD at the time of diagnosis in children with type1 diabetes. <i>Pediatr Diabetes</i> 14:123, 2013.	Conference abstract
C. C. Johnson, K. A. Mclaughlin, D. Morgan, R. G. Feltbower, and M. R. Christie. Fine mapping of epitopes for antibodies to the juxtamembrane domain of IA-2 in type 1 diabetes. <i>Diabetes</i> 63:A430, 2014.	Conference abstract
C. B. Juhl, U. Bradley, J. J. Holst, R. D. Leslie, K. B. Yderstraede, and S. Hunter. Similar weight-adjusted insulin secretion and insulin sensitivity in short-duration late autoimmune diabetes of adulthood (LADA) and Type 2 diabetes: Action LADA 8. <i>Diabet Med</i> 31 (8):941-945, 2014.	N<50
ES Jung, Dong Kyun Han, Eun Mi Yang, Min Sun Kim, Dae Yeol Lee, and Chan Jong Kim. Thyroid autoimmunity in children and adolescents with newly diagnosed type 1 diabetes mellitus. <i>Ann.pediatr.endocrinol.metab.</i> 19 (2):76-79, 2014.	Wrong population: children
N Mohamed Kamal Alanani and AA Alsulaimani. Epidemiological pattern of newly diagnosed children with type 1 diabetes mellitus, Taif, Saudi Arabia. <i>ScientificWorldJournal</i> 2013:421569, 2013.	Already found this study in first set of reruns. Has been excluded from review as children population
S. Kanthimathi, S. Jahnvi, K. Balamurugan, H. Ranjani, J. Sonya, S. Goswami, S. Chowdhury, V. Mohan, and V. Radha. Glucokinase gene mutations (MODY 2) in Asian Indians. <i>Diabetes Technol.Ther.</i> 16 (3):180-185, 2014.	Wrong population: not diabetic
E. Kawasaki, T. Maruyama, A. Imagawa, T. Awata, H. Ikegami, Y. Uchigata, H. Osawa, Y. Kawabata, T. Kobayashi, A. Shimada, I. Shimizu, K. Takahashi, M. Nagata, H. Makino, and T. Hanafusa. Diagnostic criteria for acute-onset type 1 diabetes mellitus (2012): Report of the committee of Japan diabetes society on the research of fulminant and acute-onset type 1 diabetes mellitus. <i>J.diabetes investig.</i> 5 (1):115-118, 2014.	Wrong population: fulminant and acute T1D
E Kawasaki, Megumi Tanaka, Masaki Miwa, Norio Abiru, and Atsushi Kawakami. Novel enzyme-linked immunosorbent assay for bivalent ZnT8 autoantibodies. <i>Acta Diabetol</i> 51 (3):429-434, 2014.	Wrong population: all ages mixed
B. Khodaghalian, A. U. Nayak, G. I. Varughese, and P. Raffeeq. Association of anti-GAD antibodies at diagnosis with glycaemia at 6 months in children with type 1 diabetes. <i>Diabetes</i> 63:A627, 2014.	Conference abstract
I Kikkas, Roberto Mallone, Etienne Larger, Herve Volland, and Nathalie Morel. A Rapid Lateral Flow Immunoassay for the Detection of Tyrosine Phosphatase-Like Protein IA-2 Autoantibodies in Human Serum. <i>PLoS one</i> 9 (7):e103088, 2014.	Wrong sample size. N<50
YH Kong, Min Sun Kim, and Dae Yeol Lee. Comparison of the prevalence of islet autoantibodies according to age and disease duration in patients with type 1 diabetes mellitus. <i>Ann.pediatr.endocrinol.metab.</i> 18 (2):65-70, 2013.	Wrong sample size: adult subgroup is N<50; adult and young pple mixed subgroup isalso N<50
B Kyung Koo, Sehyun Chae, Kristine M. Kim, Min Jueng Kang, Eunhee G. Kim, Soo Heon Kwak, Hye Seung Jung, et al. Identification of novel autoantibodies in type 1 diabetic patients using a high-density protein microarray. <i>Diabetes</i> 63 (9):3022-3032, 2014.	Unable to obtain article
M. K. Koskinen, R. Hermann, J. Matomaki, J. Mykkanen, M. Vaha-Makila, T. Simell, S. Simell, M. Makinen, V. Simell, M. Saarinen, J. Ilonen, M. Knip, and O. Simell. Insulin resistance, beta cell function and the effect of non-HLA genetic variants in Finnish DIPP study children with HLA-conferred risk for type 1 diabetes. <i>Diabetologia</i> 56:S229, 2013.	Conference abstract
JE Lee, Ji Woo Lee, Tatsuyoshi Fujii, Noriyoshi Fujii, and Jong Weon Choi. The ratio of estimated average glucose to fasting plasma glucose level is superior to glycated albumin, hemoglobin A1c, fructosamine, and GA/A1c ratio for assessing beta-cell function in childhood diabetes. <i>Biomed Res Int</i> 2014:370790, 2014.	Wrong population: children and young people
J. Lempainen, A.-P. Laine, A. Hammals, R. Veijola, O. Simell, M. Knip, and J. Ilonen. PTPN2 rs45450798 polymorphism is associated with accelerated progression of beta cell autoimmunity to clinical type 1 diabetes. <i>Diabetologia</i> 56:S18, 2013.	Conference abstract
A. Lernmark. The environmental determinants of diabetes in the young (TEDDY) and prospects of prevention. <i>Pediatr Diabetes</i> 14:1-2, 2013.	Conference abstract
J. Lilleker, V. Biswas, and R. Mohanraj. Relevance of gad antibodies in adults with epilepsy: Experience in a tertiary clinic. <i>J.Neurol.Neurosurg.Psychiatry</i> 84 (11), 2013.	Conference abstract
J. Ludvigsson, D. Krisky, R. Casas, T. Battelino, L. Castano, J. Greening, O. Kordonouri, T. Otonkoski, P. Pozzilli, J. J. Robert, H. J. Veeze, and J. Palmer. GAD65 antigen therapy in recently diagnosed type 1 diabetes mellitus. <i>Diabetes Technol.Ther.</i> 15 (SUPPL.1):S92-S93, 2013.	Conference abstract
E. Maddaloni, N. Lessan, A. A. Tikriti, P. Pozzilli, and M. T. Barakat. Prevalence and features of adult-onset autoimmune diabetes in the United Arab Emirates (UAE). <i>Diabetes</i> 63:A399, 2014.	Conference abstract
S. Majidi, A. R. Fouts, T. Armstrong, R. M. Sippl, K. Colclough, Z. Wang, D. S. Batish, M. Jaremkos, S. Ellard, A. T. Hattersley, G. J. Klingensmith, and A. K.	Conference abstract

Study	Reason for exclusion
Steck. Hla typing and C-peptide measurement to target moty genetic testing in antibody-negative diabetes. <i>Diabetes</i> 63:A354, 2014.	
S Masala, Davide Cossu, Simona Piccinini, Novella Rapini, Arianna Massimi, Ottavia Porzio, Silvia Pietrosanti, Roberta Lidano, Maria Luisa Manca Bitti, and Leonardo Antonio Sechi. Recognition of zinc transporter 8 and MAP3865c homologous epitopes by new-onset type 1 diabetes children from continental Italy. <i>Acta Diabetol</i> 51 (4):577-585, 2014.	Wrong population: children and young people
R. Matter, A. Adly, M. M. Abd El Aziz, and D. Toima. Serum CXC chemokine ligand 10 (CXCL10) in type 1 diabetic children, adolescents, and subjects at high risk of type 1 diabetes. <i>Pediatr Diabetes</i> 14:44, 2013.	Conference abstract
A. Maurizi, R. Strollo, P. Pozzilli, and N. Napoli. Osteocalcin and residual beta-cell function in type 1 diabetes. <i>J.Bone Miner.Res.</i> 26, 2011.	Conference abstract
M L Max Andersen, Lotte B. Nielsen, Jannet Svensson, Sven Porksen, Philip Hougaard, Craig Beam, Carla Greenbaum, Dorothy Becker, Jacob S. Petersen, Lars Hansen, and Henrik B. Mortensen. Disease progression among 446 children with newly diagnosed type 1 diabetes located in Scandinavia, Europe, and North America during the last 27yr. <i>Pediatr Diabetes</i> 15 (5):345-354, 2014.	Wrong population: children and young people
A. Messaaoui, S. Tenoutasse, C. Melot, and H. Dorchy. Inverse relationship between increased glomerular filtration rate and C-peptide level at diagnosis of type 1 diabetes in children and adolescents. <i>Pediatr Diabetes</i> 14:21-22, 2013.	Conference abstract
D. Mul, T. C. Sas, J. J. Schermer-Rotte, and H. J. Veeze. Completeness of immunological testing at diagnosis of diabetes mellitus in the Paediatric Diabetes Registry in the Netherlands (PDR.NL). <i>Pediatr Diabetes</i> 14:123-124, 2013.	Conference abstract
K. Nugent, C. M. McDonnell, and N. P. Murphy. Autoantibodies in type 1 diabetes: Are we different? <i>Ir.J.Med.Sci.</i> 181:S105, 2012.	Conference abstract
R. A. Oram, T. J. McDonald, B. M. Shields, E. R. Pearson, and A. T. Hattersley. A large, population-based study demonstrates that most people with long duration Type 1 diabetes are insulin microsecretors and produce their own endogenous insulin. <i>Diabet Med</i> 31:10, 2014.	Conference abstract
C. J. Padoa, P. Rheeder, and N. J. Crowther. Phenotypic and genotypic characterisation of type 1 diabetes mellitus in black South African patients. <i>J.Endocrinol.Metab.Diabetes S.Afr.</i> 18 (1):37, 2013.	Conference abstract
M L Pedersen, Peter Bjerregaard, and Marit Eika Jorgensen. GAD65 antibodies among Greenland Inuit and its relation to glucose intolerance. <i>Acta Diabetol</i> 51 (4):641-646, 2014.	Wrong population: not generalizable / applicable to UK population
R. Piekarski, J. Tabarkiewicz, A. Bojarska-Junak, and L. Szweczyk. Dynamic changes of the TH17 cell population in children with new-onset type 1 diabetes. <i>Diabetes</i> 63:A625-A626, 2014.	Conference abstract
R. Piekarski, B. Wilczyn'ska, A. Bojarska-Junak, and J. Tabarkiewicz. Th17 cells in children with new onset type 1 diabetes-preliminary report. <i>Pediatr Diabetes</i> 14:123, 2013.	Conference abstract
W. E. Powell, C. N. Janicki, A. Howell, A. Bishop, C. M. Dayan, and F. S. Wong. Developing an assay to detect B-cell responses to autoantigens GAD and IA-2 in Type 1 diabetes. <i>Diabet Med</i> 31:47, 2014.	Conference abstract
F Prodam, Francesco Cadario, Simonetta Bellone, Letizia Trovato, Stefania Moia, Erica Pozzi, Silvia Savastio, and Gianni Bona. Obestatin levels are associated with C-peptide and antiinsulin antibodies at the onset, whereas unacylated and acylated ghrelin levels are not predictive of long-term metabolic control in children with type 1 diabetes. <i>J Clin Endocrinol Metab</i> 99 (4):E599-E607, 2014.	Unable to obtain article
M. J. Redondo, N. Bansal, L. M. Rodriguez, J. A. Kushner, C. S. Hampe, and A. Balasubramanyam. Dpd epitope-specific GAD65 autoantibody is associated with older age of onset and obesity in pediatric type 1 diabetes. <i>Diabetes</i> 63:A8, 2014.	Conference abstract
M. Rewers, K. Waugh, K. Barriga, J. Norris, and J. Snell-Bergeon. Lower physical activity in children with persistent islet autoantibodies than in matched controls. <i>Diabetologia</i> 56:S132-S133, 2013.	Conference abstract
V. Serban, F. Fiera, and B. Timar. Basal C-peptide behavior and its clinical significance in Romanian children with type 1 diabetes. <i>Pediatr Diabetes</i> 14:80, 2013.	Conference abstract
B. M. Shields, M. Hudson, M. Shepherd, R. Oram, T. J. McDonald, S. Ellard, E. R. Pearson, and A. T. Hattersley. Comparison of screening using clinical criteria and biomarkers to identify maturity-onset diabetes of the young (MODY) in a community based setting. <i>Diabet Med</i> 31:20, 2014.	Conference abstract
H. Siljander, A. Peet, V. Tillmann, T. Harkonen, O. Niemela, J. Ilonen, Herten L. Von, T. Haahtela, Mutius E. Von, and M. Knip. Relation between beta cell autoimmunity and levels of allergen-specific IgEs in young Finnish and Estonian children. <i>Diabetologia</i> 56:S18, 2013.	Conference abstract
H. Skarstrand, F. Vaziri-Sani, C. Andersson, H. Elding-Larsson, S. Ivarsson, and A. Lernmark. NPY minor autoantibodies in newly diagnosed type 1 diabetes patients. <i>Diabetologia</i> 56:S19, 2013.	Conference abstract
J. V. Stidsen, R. W. Thomsen, J. S. Nielsen, J. Rungby, S. P. Ulrichsen, K.	Conference abstract

Study	Reason for exclusion
Berensci, S. Friborg, I. Brandslund, A. A. Nielsen, J. S. Christiansen, H. Sorensen, A. A. Vaag, T. B. Olesen, M. H. Olsen, J. E. Henriksen, and H. Beck-Nielsen. Pathophysiological phenotypes of clinically diagnosed type 2 diabetes. <i>Diabetes</i> 63:A354-A355, 2014.	
M. S. Sunni, M. Farah, J. Smith, A. Dhunkal, M. D. Bellin, B. M. Nathan, P. A. Gottlieb, L. Yu, S. Babu, T. Armstrong, and A. Moran. HLA alleles and diabetes autoantibodies in a group of Somali children with type 1 diabetes in the Twin Cities, Minnesota: A pilot study. <i>Pediatr Diabetes</i> 14:129, 2013.	Conference abstract
J Takezawa, Kouichi Yamada, Akemi Morita, Naomi Aiba, and Shaw Watanabe. Preproghrelin gene polymorphisms in obese Japanese: Association with diabetes mellitus in men and with metabolic syndrome parameters in women. <i>Obes Res Clin Pract</i> 3 (4):179-191, 2009.	Wrong population: mixed diabetes subgroup
J. Urbanova, B. Rypackova, Z. Prochazkova, P. Kucera, M. Cerna, M. Anel, and P. Heneberg. Positivity for islet cell autoantibodies in patients with monogenic diabetes is associated with later diabetes onset and higher HbA1c level. <i>Diabet Med</i> 31 (4):466-471, 2014.	Wrong population: mixed ages, and N<50
I. Wallace, S. Chan, M. Naidu, B. Secret, G. Braatvedt, and M. Khanolkar. A 6 year retrospective observational study: Autoantibodies to glutamic acid decarboxylase (GAD) and insulinoma antigen 2 (IA-2) in patients newly diagnosed with adult diabetes presenting with diabetic ketoacidosis. <i>Diabet Med</i> 31:181, 2014.	Conference abstract
K Warncke, Miriam Krasmann, Ramona Puff, Desiree Dunstheimer, Anette Gabriele Ziegler, and Andreas Beyerlein. Does diabetes appear in distinct phenotypes in young people? Results of the diabetes mellitus incidence Cohort Registry (DiMelli). <i>PLoS one</i> 8 (9):e74339, 2013.	Already found article in first reruns. Was excluded from review as wrong population – mixed ages
R. A. Watkins, C. Evans-Molina, J. Terrell, K. Day, L. Guindon, R. G. Mirmira, J. S. Blum, and L. A. Di Meglio. Persistence of beta cell stress in the initial period following diagnosis of T1D in children. <i>Pediatr Diabetes</i> 14:68, 2013.	Conference abstract
K. Wilhelm, K. Tornow, V. Lampasona, U. Walschus, I. Rjasanowski, W. Kerner, and M. Schlosser. Prognostic and diagnostic relevance of ZnT8 antibodies in autoimmune diabetes. <i>Diabetologia</i> 56:S133, 2013.	Conference abstract
P. Xu, X. Qian, D. A. Schatz, D. Cuthbertson, and J. P. Krischer. Distribution of C-peptide and its determinants in North American children at risk for type 1 diabetes. <i>Diabetes care</i> 37 (7):1959-1965, 2014.	Wrong population: not diabetes, only those at risk for diabetes
AS. Yilmaz, Z. Aycan, S. Cetinkaya, V. N. Bas, A. Onder, H. N. Peltek Kendirci, and S. Ceylaner. Screening for mutations in children with a clinical diagnosis of maturity onset diabetes of youth (MODY). <i>Pediatr Diabetes</i> 14:132, 2013.	Conference abstract
S. Zago, M. Fabris, M. Liguori, M. Trevisan, M. Zanatta, A. Comici, G. Zanette, E. Tonutti, and F. Curcio. Improving the diagnostic approach to type I diabetes: The introduction of anti-zinc transporter protein autoantibodies (ZnT8A). <i>FASEB J.</i> 28 (1 SUPPL. 1), 2014.	Conference abstract
A. Zubkiewicz-Kucharska, A. Noczyn'ska, and L. Usnarska-Zubkiewicz. Prognostic significance of T lymphocytes in type 1 diabetes in children. <i>Pediatr Diabetes</i> 14:124, 2013.	Conference abstract
G. J. Tobon, A. Arango, V. Abad, J. Garcia, H. Cuervo, A. Velasquez, I. D. Angel, P. Vega, A. Abad, and J. M. Anaya. Clinical and immunological characteristics of type 1 diabetes mellitus in a northwestern Colombian population. <i>Diabetes Res.Clin.Pract.</i> 72 (2):170-175, 2006.	Mixed population: all ages with no adult or young people subgroup analysis
M. Koga, J. Murai, H. Saito, S. Kasayama, T. Kobayashi, A. Imagawa, and T. Hanafusa. Correlation of glycated albumin but not hemoglobin A1c with endogenous insulin secretion in fulminant type 1 diabetes mellitus. <i>J.Diabetes Invest.</i> 1 (6):279-282, 2010.	Mixed population: all ages with no adult or young people subgroup analysis. Also wrong type of diabetes: fulminant T1D
M. K. Tulloch-Reid, M. S. Boyne, M. F. Smikle, E. G. Choo-Kang, R. H. Parkes, R. A. Wright-Pascoe, E. N. Barton, R. J. Wilks, and D. E. Williams. Clinical and laboratory features of youth onset type 2 diabetes in Jamaica. <i>West Indian Med.J.</i> 59 (2):131-138, 2010.	Mixed population: all ages with no adult or young people subgroup analysis
A Sifarikas, R.J. Johnston, MK. Bulsara, P O'Leary, TW. Jones, and EA. Davis. Early loss of the glucagon response to hypoglycemia in adolescents with type 1 diabetes. <i>Diabetes Care</i> 35 (8):1757-1762, 2012.	Mixed population: all ages with no adult or young people subgroup analysis
C. Y. Pan, W. Y. So, B. A. K. Khalid, V. Mohan, A. C. Thai, P. Zimmet, C. S. Cockram, L. N. Jorgensen, J. P. Yeo, and ASDIAB Study Group. Metabolic, immunological and clinical characteristics in newly diagnosed Asian diabetes patients aged 12-40 years. <i>Diabet.Med.</i> 21 (9):1007-1013, 2004.	Mixed population: all ages with no adult or young people subgroup analysis
A. L. Todd, W. Y. Ng, K. F. Lui, and A. C. Thai. Low prevalence of autoimmune diabetes markers in a mixed ethnic population of Singaporean diabetics. <i>Intern.Med.J.</i> 34 (1-2):24-30, 2004.	Mixed population: all ages with no adult or young people subgroup analysis
M Rodacki, L Zajdenverg, RP Tortora, FA Reis, MS. Albernaz, MRB Goncalves, A Milech, and JEP de Oliveira. Characteristics of childhood and adult-onset type 1 diabetes in a multi-ethnic population. <i>Diabetes Res.Clin.Pract.</i> 69 (1):22-28, 2005.	Mixed population: all ages with no adult or young people subgroup analysis
A Szybowska and A Skorka. The risk factors of ketoacidosis in children with newly diagnosed type 1 diabetes mellitus. <i>Pediatr Diabetes</i> 12 (4 Pt 1):302-306, 2011.	Wrong population: children and young people
S. Hameed, S. Ellard, H. J. Woodhead, K. A. Neville, J. L. Walker, M. E. Craig,	Wrong population: children and young

Study	Reason for exclusion
T. Armstrong, L. Yu, G. S. Eisenbarth, A. T. Hattersley, and C. F. Verge. Persistently autoantibody negative (PAN) type 1 diabetes mellitus in children. <i>Pediatr Diabetes</i> 12 (3 PART 1):142-149, 2011.	people
RB. Lipton, ML. Drum, KK. Danielson, S Aw Greeley, GI. Bell, and WA. Hagopian. Onset features and subsequent clinical evolution of childhood diabetes over several years. <i>Pediatr Diabetes</i> 12 (4 Pt 1):326-334, 2011.	Wrong population: children and young people
Y Xin, M Yang, X Juan Chen, YJ Tong, and LH Zhang. Clinical features at the onset of childhood type 1 diabetes mellitus in Shenyang, China. <i>J.Paediatr.Child Health</i> 46 (4):171-175, 2010.	Wrong population: children and young people
HB. Mortensen, P Hougaard, P Swift, L Hansen, RW. Holl, H Hoey, H Bjoerndalen, C de Beaufort, F Chiarelli, T Danne, EJ. Schoenle, J Aman, and Hvidoere Study Group on Childhood Diabetes. New definition for the partial remission period in children and adolescents with type 1 diabetes. <i>Diabetes Care</i> 32 (8):1384-1390, 2009.	Wrong population: children and young people
T. Reinehr, E. Schober, S. Wiegand, A. Thon, R. Holl, and DPV-Wiss Study Group. Beta-cell autoantibodies in children with type 2 diabetes mellitus: subgroup or misclassification? <i>Arch.Dis.Child.</i> 91 (6):473-477, 2006.	Wrong population: children and young people
A. Amutha, M. Datta, R. Unnikrishnan, R. M. Anjana, and V. Mohan. Clinical profile and complications of childhood- and adolescent-onset type 2 diabetes seen at a diabetes center in south India. <i>Diabetes Technol Ther</i> 14 (6):497-504, 2012.	Wrong population: children and young people
LE. Levitt Katz, SN Magge, ML. Hernandez, KM. Murphy, HM. McKnight, and T Lipman. Glycemic control in youth with type 2 diabetes declines as early as two years after diagnosis. <i>J.Pediatr.</i> 158 (1):106-111, 2011.	Wrong population: children and young people
J Matsui, N Tamasawa, J Tanabe, N Kasai, H Murakami, K Matsuki, and T Suda. Clinical characteristics of Japanese youth-onset type 2 diabetes with ketonuria. <i>Diabetes Res.Clin.Pract.</i> 70 (3):235-238, 2005.	Wrong population: children and young people
C Brorsson, F Vaziri-Sani, R Bergholdt, S Eising, A Nilsson, J Svensson, A Lernmark, F Pociot, and Danish Study Group of Childhood Diabetes. Correlations between islet autoantibody specificity and the SLC30A8 genotype with HLA-DQB1 and metabolic control in new onset type 1 diabetes. <i>Autoimmunity</i> 44 (2):107-114, 2011.	Wrong population: children and young people
H Manan, Al M Angham, and A Sitebanat. Genetic and diabetic auto-antibody markers in Saudi children with type 1 diabetes. <i>Hum.Immunol.</i> 71 (12):1238-1242, 2010.	Wrong population: children and young people
A. M. N. E. Abd El Baky, S. M. Abd El Dayem, H. A. Atwa, and H. Rasmy. Assessment of interleukin 18 in children with type 1 diabetes and their relatives: Its relation to autoantibodies. <i>J.Med.Sci.(Pakistan)</i> 6 (4):603-608, 2006.	Wrong population: children and young people
M. S. Ronkainen, K. Savola, and M. Kniip. Antibodies to GAD65 epitopes at diagnosis and over the first 10 years of clinical type 1 diabetes mellitus. <i>Scand.J.Immunol.</i> 59 (3):334-340, 2004.	Wrong population: children and young people
C. Andersson, K. Larsson, F. Vaziri-Sani, K. Lynch, A. Carlsson, E. Cedervall, B. Jonsson, J. Neiderud, M. Mansson, A. Nilsson, A. Lernmark, H. Elding Larsson, and S. A. Ivarsson. The three ZNT8 autoantibody variants together improve the diagnostic sensitivity of childhood and adolescent type 1 diabetes. <i>Autoimmunity</i> 44 (5):394-405, 2011.	Wrong population: children and young people
B. M. Brooks-Worrell, C. J. Greenbaum, J. P. Palmer, and C. Pihoker. Autoimmunity to Islet Proteins in Children Diagnosed with New-Onset Diabetes. <i>J.Clin.Endocrinol.Metab.</i> 89 (5):2222-2227, 2004.	Wrong population: children and young people
G Karaguzel, S Simsek, O Deger, and A Okten. Screening of diabetes, thyroid, and celiac diseases-related autoantibodies in a sample of Turkish children with type 1 diabetes and their siblings. <i>Diabetes Res.Clin.Pract.</i> 80 (2):238-243, 2008.	Wrong population: children and young people
A. Kaas, C. Pflieger, A. V. Kharagitsingh, N. C. Schloot, L. Hansen, K. Buschard, B. P. C. Koeleman, B. O. Roep, H. B. Mortensen, B. Z. Alizadeh, and Hvidoere Study Group on Childhood Diabetes. Association between age, IL-10, IFNgamma, stimulated C-peptide and disease progression in children with newly diagnosed Type 1 diabetes. <i>Diabet.Med.</i> 29 (6):734-741, 2012.	Wrong population: children and young people
F. Lombardo, M. Valenzise, M. Wasniewska, M. F. Messina, C. Ruggeri, T. Arrigo, and F. De Luca. Two-year prospective evaluation of the factors affecting honeymoon frequency and duration in children with insulin dependent diabetes mellitus: the key-role of age at diagnosis. <i>Diabetes Nutr Metab</i> 15 (4):246-251, 2002.	Wrong population: children and young people
S. Salardi, S. Zucchini, A. Cicognani, E. Corbelli, R. Santoni, L. Ragni, D. Elleri, and E. Cacciari. The severity of clinical presentation of type 1 diabetes in children does not significantly influence the pattern of residual beta-cell function and long-term metabolic control. <i>Pediatr Diabetes</i> 4 (1):4-9, 2003.	Wrong population: children and young people
LE. Levitt Katz, A. F. J, J. Ganesh, M. Abraham, K. Murphy, and T. H. Lipman. Fasting c-peptide and insulin-like growth factor-binding protein-1 levels help to distinguish childhood type 1 and type 2 diabetes at diagnosis. <i>Pediatr Diabetes</i> 8 (2):53-59, 2007.	Wrong population: children and young people
Fu Sung Lo, Min Hai Yang, Luan Yin Chang, Yung Chun Ou, and Yang Hau Van. Clinical features of type 1 diabetic children at initial diagnosis. <i>Acta Paediatr.Taiwan.</i> 45 (4):218-223, 2004.	Wrong population: children and young people

Study	Reason for exclusion
J. Ludvigsson, A. Carlsson, G. Forsander, S. Ivarsson, I. Kockum, A. Lernmark, B. Lindblad, C. Marcus, and U. Samuelsson. C-peptide in the classification of diabetes in children and adolescents. <i>Pediatr Diabetes</i> 13 (1):45-50, 2012.	Wrong population: children and young people
A Kaas, MLM Andersen, S Fredheim, P Hougaard, K Buschard, JS Petersen, C de Beaufort, KJ. Robertson, L Hansen, HB. Mortensen, LB. Nielsen, and Hvidoere Study Group on Childhood Diabetes. Proinsulin, GLP-1, and glucagon are associated with partial remission in children and adolescents with newly diagnosed type 1 diabetes. <i>Pediatr Diabetes</i> 13 (1):51-58, 2012.	Wrong population: children and young people
A. Zmyslowska, W. Mlynarski, A. Szadkowska, and J. Bodalski. Prediction of the clinical remission using the C-peptide level in type 1 diabetes in children. <i>Endokrynol.Diabetol.Choroby Przemiany Materii Wieku Rozwojowego</i> 13 (2):71-74, 2007.	Wrong population: children and young people
HB. Mortensen, PGF. Swift, RW. Holl, P. Hougaard, L Hansen, H Bjoerndalen, CE. de Beaufort, M Knip, and Hvidoere Study Group on Childhood Diabetes. Multinational study in children and adolescents with newly diagnosed type 1 diabetes: association of age, ketoacidosis, HLA status, and autoantibodies on residual beta-cell function and glycemic control 12 months after diagnosis. <i>Pediatr Diabetes</i> 11 (4):218-226, 2010.	Wrong population: children and young people
C Pflieger, HB. Mortensen, L Hansen, C Herder, BO. Roep, H Hoey, HJ Aanstoot, M Kocova, NC. Schloot, and Hvidore Study Group on Childhood Diabetes. Association of IL-1ra and adiponectin with C-peptide and remission in patients with type 1 diabetes. <i>Diabetes</i> 57 (4):929-937, 2008.	Wrong population: children and young people
K. C. Copeland, P. Zeitler, M. Geffner, C. Guandalini, J. Higgins, K. Hirst, F. R. Kaufman, B. Linder, S. Marcovina, P. McGuigan, L. Pyle, W. Tamborlane, and S. Willi. Characteristics of adolescents and youth with recent-onset type 2 diabetes: The TODAY cohort at baseline. <i>J.Clin.Endocrinol.Metab.</i> 96 (1):159-167, 2011.	Wrong population: children and young people
G.J. Klingensmith, L Pyle, S Arslanian, KC. Copeland, L Cuttler, F Kaufman, L Laffel, S Marcovina, SE. Tollefsen, RS. Weinstock, B Linder, and TODAY Study Group. The presence of GAD and IA-2 antibodies in youth with a type 2 diabetes phenotype: results from the TODAY study. <i>Diabetes Care</i> 33 (9):1970-1975, 2010.	Wrong population: children and young people
H Holmberg, O Vaarala, V Sadauskaite-Kuehne, J Ilonen, Z Padaiga, and J Ludvigsson. Higher prevalence of autoantibodies to insulin and GAD65 in Swedish compared to Lithuanian children with type 1 diabetes. <i>Diabetes Res.Clin.Pract.</i> 72 (3):308-314, 2006.	Wrong population: children and young people
M. Rodacki, L. Zajdenverg, M. S. Albemaz, M. R. Bencke-Goncalves, A. Milech, and J. E. P. Oliveira. Relationship between the prevalence of anti-glutamic acid decarboxylase autoantibodies and duration of type 1 diabetes mellitus in Brazilian patients. <i>Braz.J.Med.Biol.Res.</i> 37 (11):1645-1650, 2004.	Wrong sample size: adults and young people N<50
E. Astorri, C. Guglielmi, M. Bombardieri, C. Alessandri, R. Buzzetti, D. Maggi, G. Valesini, C. Pitzalis, and P. Pozzilli. Circulating Reg1alpha proteins and autoantibodies to Reg1alpha proteins as biomarkers of beta-cell regeneration and damage in type 1 diabetes. <i>Horm.Metab.Res.</i> 42 (13):955-960, 2010.	Wrong sample size: adults and young people N<50
C Zheng, Z Zhou, L Yang, J Lin, G Huang, X Li, W Zhou, X Wang, and Z Liu. Fulminant type 1 diabetes mellitus exhibits distinct clinical and autoimmunity features from classical type 1 diabetes mellitus in Chinese. <i>Diabetes.Metab.Res.Rev.</i> 27 (1):70-78, 2011.	Wrong sample size: adults and young people N<50
T Mimura, H Funatsu, Y Uchigata, S Kitano, E Shimizu, S Amano, S Yamagami, H Noma, M Araie, and S Hori. Glutamic acid decarboxylase autoantibody prevalence and association with HLA genotype in patients with younger-onset type 1 diabetes and proliferative diabetic retinopathy. <i>Ophthalmology</i> 112 (11):1904-1909, 2005.	Wrong sample size: adults and young people N<50
AG. Unnikrishnan, V Kumaravel, V Nair, A Rao, RV. Jayakumar, H Kumar, and CB. Sanjeevi. TSH receptor antibodies in subjects with type 1 diabetes mellitus. <i>Ann.N.Y.Acad.Sci.</i> 1079:220-225, 2006.	Wrong sample size: adults and young people N<50
L Yang, Z Guang Zhou, G Huang, L Li Ouyang, X Li, and X Yan. Six-year follow-up of pancreatic beta cell function in adults with latent autoimmune diabetes. <i>World J Gastroenterol</i> 11 (19):2900-2905, 2005.	Wrong sample size: adults N<50
T. Tankova, L. Dakovska, G. Kirilov, and D. Koev. Intravenous glucose tolerance test and anti-GAD65 antibodies in the diagnosis of the type of diabetes mellitus. <i>Pract.Diabetes Int.</i> 20 (1):13-17, 2003.	Wrong sample size: adults N<50
Z. Milicevic, J. Knezevic, A. Sabioncello, G. Roglic, and B. Rocic. Beta-cell secretory function and CD25 + lymphocyte subsets in the early stage of type 1 diabetes mellitus. <i>Exp.Clin.Endocrinol.Diabetes</i> 112 (4):181-186, 2004.	Wrong sample size: adults N<50
NG 2002 W. Y. Ng, K. F. Lui, J. S. Cheah, and A. C. Thai. IgG1 subclass dominates autoimmune response to tyrosine phosphatase-like molecule IA-2 in Chinese type 1 diabetes patients. <i>Horm.Metab.Res.</i> 34 (10):596-600, 2002.	Wrong sample size: adults N<50
JM Gomez, R Vila, P Catalina, J Soler, L Badimon, and M Sahun. The markers of inflammation and endothelial dysfunction in correlation with glycated haemoglobin are present in type 2 diabetes mellitus patients but not in their relatives. <i>Glycoconj.J.</i> 25 (6):573-579, 2008.	Wrong sample size: adults N<50
C.-Y. Huang and S.-M. Lai. Low prevalence of latent autoimmune diabetes in	Wrong sample size: adults N<50

Study	Reason for exclusion
adult type 2 diabetic patients with age of onset at 30-39 years in Taiwan. J.Intern.Med.Taiwan 15 (1):12-18, 2004.	
M. Kurowska, J. S. Tarach, J. Malicka, H. Jankowska, and A. Dabrowska. Islet GAD autoantibodies in patients with newly diagnosed type 2 diabetes. Ann.Univ.Mariae Curie-Sklodowska Sect.DDD Pharm. 23 (3):101-106, 2010.	Wrong sample size: adults N<50
K. Agarwal, D. E. Jones, A. K. Daly, O. F. James, B. Vaidya, S. Pearce, and M. F. Bassendine. CTLA-4 gene polymorphism confers susceptibility to primary biliary cirrhosis. J Hepatol 32 (4):538-541, 2000.	Wrong population: adults only
Ch Amrouche, H. Jamoussi Kamoun, N. Trabelsi, and S. Blouza Chabchoub. Latent autoimmune diabetes in Tunisian adults (LADA): identification of autoimmune markers. Tunis Med 86 (4):316-318, 2008.	Wrong population: adults only
M. K. Andersen, M. Sterner, T. Forsen, A. Karajamaki, O. Rolandsson, C. Forsblom, P.-H. Groop, K. Lahti, P. M. Nilsson, L. Groop, and T. Tuomi. Type 2 diabetes susceptibility gene variants predispose to adult-onset autoimmune diabetes. Diabetologia 57 (9):1859-1868, 2014.	Wrong population: adults only
Ender Arikan, Tefvik Sabuncu, Esref M. Ozer, and Husrev Hatemi. The clinical characteristics of latent autoimmune diabetes in adults and its relation with chronic complications in metabolically poor controlled Turkish patients with Type 2 diabetes mellitus. J.Diabetes Complications 19 (5):254-258, 2005.	Wrong population: adults only
D Arslan, Alparslan Merdin, Deniz Tural, Mustafa Temizel, Olgun Akin, Seyda Gunduz, Ali Murat Tatli, Fatma Avci, and Mukremin Uysal. The effect of autoimmunity on the development time of microvascular complications in patients with type 1 diabetes mellitus. Med Sci Monit 20:1176-1179, 2014.	Wrong population: adults only
A. Barker, A. Lauria, N. Schloot, N. Hosszufalusi, J. Ludvigsson, C. Mathieu, D. Mauricio, M. Nordwall, B. Van Der Schueren, T. Mandrup-Poulsen, W. A. Scherbaum, I. Weets, F. K. Gorus, N. Wareham, R. D. Leslie, and P. Pozzilli. Age-dependent decline of beta-cell function in type 1 diabetes after diagnosis: a multi-centre longitudinal study. Diabetes Obesity and Metabolism 16 (3):262-267, 2014.	Wrong population: adults only
DS. H. Bell and Fernando Ovalle. The role of C-peptide levels in screening for latent autoimmune diabetes in adults. Am.J.Ther. 11 (4):308-311, 2004.	Wrong population: adults only
J. Bodalska-Lipinska, A. Szadkowska, and L. Markuszewski. Principles of diagnosis of latent autoimmune diabetes in adults (LADA). Diabetol.Dosw.Klin. 6 (2):69-74, 2006.	Wrong population: adults only
G. F. Bottazzo, E. Bosi, C. A. Cull, E. Bonifacio, M. Locatelli, P. Zimmet, I. R. Mackay, and R. R. Holman. IA-2 antibody prevalence and risk assessment of early insulin requirement in subjects presenting with type 2 diabetes (UKPDS 71). Diabetologia 48 (4):703-708, 2005.	Wrong population: adults only
H. A. J. Castleden, B. Shields, P. J. Bingley, A. J. K. Williams, M. Sampson, M. Walker, J. M. Gibson, M. I. McCarthy, G. A. Hitman, J. C. Levy, A. T. Hattersley, B. Vaidya, and E. R. Pearson. GAD antibodies in probands and their relatives in a cohort clinically selected for Type 2 diabetes. Diabet.Med. 23 (8):834-838, 2006.	Wrong population: adults only
M. Cerna, P. Novota, K. Kolostova, P. Cejkova, E. Zdarsky, D. Novakova, P. Kucera, J. Novak, and M. Andel. HLA in Czech adult patients with autoimmune diabetes mellitus: comparison with Czech children with type 1 diabetes and patients with type 2 diabetes. Eur.J.Immunogenet. 30 (6):401-407, 2003.	Wrong population: adults only
M. N. Chowta, P. M. Adhikari, N. K. Chowta, A. K. Shenoy, and S. D'Souza. Serum C peptide level and renal function in diabetes mellitus. Indian J.Nephrol. 20 (1):25-28, 2010.	Wrong population: adults only
H. Davies, S. Brophy, A. Fielding, P. Bingley, M. Chandler, I. Hilldrup, C. Brooks, and R. Williams. Latent autoimmune diabetes in adults (LADA) in South Wales: incidence and characterization. Diabet.Med. 25 (11):1354-1357, 2008.	Wrong population: adults only
T. M. E. Davis, Z. Mehta, I. R. Mackay, C. A. Cull, D. G. Bruce, S. Fida, M. J. Rowley, and R. R. Holman. Autoantibodies to the islet cell antigen SOX-13 are associated with duration but not type of diabetes. Diabet.Med. 20 (3):198-204, 2003.	Wrong population: adults only
M. Desai, C. A. Cull, V. A. Horton, M. R. Christie, E. Bonifacio, V. Lampasona, P. J. Bingley, J. C. Levy, I. R. Mackay, P. Zimmet, R. R. Holman, and A. Clark. GAD autoantibodies and epitope reactivities persist after diagnosis in latent autoimmune diabetes in adults but do not predict disease progression: UKPDS 77. Diabetologia 50 (10):2052-2060, 2007.	Wrong population: adults only
K Hamaguchi, Akinori Kimura, Yoichiro Kusuda, Tsutomu Yamashita, Michio Yasunami, Megumi Takahasi, Nobuyuki Abe, and Hironobu Yoshimatsu. Clinical and genetic characteristics of GAD-antibody positive patients initially diagnosed as having type 2 diabetes. Diabetes Res.Clin.Pract. 66 (2):163-171, 2004.	Wrong population: adults only
C S. Hampe, Murray E. Maitland, Lisa K. Gilliam, Thanh H. T. Phan, Ian R. Sweet, Jared R. Radtke, Vasile Bota, Bruce R. Ransom, and Irl B. Hirsch. High titers of autoantibodies to glutamate decarboxylase in type 1 diabetes patients: epitope analysis and inhibition of enzyme activity. Endocr Pract 19 (4):663-668, 2013.	Wrong population: adults only
Ml. Hawa, Hubert Kolb, Nanette Schloot, Huriya Beyan, Stavroula A. Paschou,	Wrong population: adults only

Study	Reason for exclusion
Raffaella Buzzetti, Didac Mauricio, Alberto de Leiva, Knud Yderstraede, Henning Beck-Neilsen, Jaakko Tuomilehto, Cinzia Sarti, Charles Thivolet, David Hadden, Steven Hunter, Guntram Schernthaner, Werner A. Scherbaum, Rhys Williams, Sinead Brophy, Paolo Pozzilli, Richard David Leslie, and Action LADA consortium. Adult-onset autoimmune diabetes in Europe is prevalent with a broad clinical phenotype: Action LADA 7. <i>Diabetes Care</i> 36 (4):908-913, 2013.	
M. Hillman, C. Torn, M. Landin-Olsson, and DISS study group. The glutamic acid decarboxylase 65 immunoglobulin G subclass profile differs between adult-onset type 1 diabetes and latent autoimmune diabetes in adults (LADA) up to 3 years after clinical onset. <i>Clin.Exp.Immunol.</i> 157 (2):255-260, 2009.	Wrong population: adults only
S. V. Hope, A. G. Jones, E. Goodchild, M. Shepherd, R. E. J. Besser, B. Shields, T. McDonald, B. A. Knight, and A. Hattersley. Urinary C-peptide creatinine ratio detects absolute insulin deficiency in Type 2 diabetes. <i>Diabet.Med.</i> 30 (11):1342-1348, 2013.	Wrong population: adults only
N Hosszofalusi, Agnes Vatay, Katalin Rajczy, Zoltan Prohaszka, Eva Pozsonyi, Laura Horvath, Andrea Grosz, Laszlo Gero, Laszlo Madacsy, Laszlo Romics, Istvan Karadi, George Fust, and Pal Panczel. Similar genetic features and different islet cell autoantibody pattern of latent autoimmune diabetes in adults (LADA) compared with adult-onset type 1 diabetes with rapid progression. <i>Diabetes Care</i> 26 (2):452-457, 2003.	Wrong population: adults only
G Huang, Yufei Xiang, Lingling Pan, Xia Li, Shuoming Luo, and Zhiguang Zhou. Zinc transporter 8 autoantibody (ZnT8A) could help differentiate latent autoimmune diabetes in adults (LADA) from phenotypic type 2 diabetes mellitus. <i>Diabetes.Metab.Res.Rev.</i> 29 (5):363-368, 2013.	Wrong population: adults only
Y Hwangbo, Jin Taek Kim, Eun Ky Kim, Ah Reum Khang, Tae Jung Oh, Hak Chul Jang, Kyong Soo Park, Seong Yeon Kim, Hong Kyu Lee, and Young Min Cho. Prevalence and clinical characteristics of recently diagnosed type 2 diabetes patients with positive anti-glutamic Acid decarboxylase antibody. <i>Diabetes & Metabolism</i> 36 (2):136-143, 2012.	Wrong population: adults only
C. S. Kim, M. K. Song, J. S. Park, M. H. Cho, H. J. Kim, J. S. Nam, E. S. Kang, C. W. Ahn, B. S. Cha, E. G. Lee, S. K. Lim, K. R. Kim, H. C. Lee, and K. B. Huh. The clinical and immunogenetic characteristics of adult-onset type 1 diabetes mellitus in Korea. <i>Acta Diabetol.</i> 44 (2):45-54, 2007.	Wrong population: adults only
S. A. Lee, W. J. Lee, E. H. Kim, J. H. Yu, C. H. Jung, E. H. Koh, M. S. Kim, J. Y. Park, and K. U. Lee. Progression to insulin deficiency in Korean patients with Type 2 diabetes mellitus positive for anti-GAD antibody. <i>Diabet.Med.</i> 28 (3):319-324, 2011.	Wrong population: adults only
E Lindholm, Bengt Hallengren, and Carl David Agardh. Gender differences in GAD antibody-positive diabetes mellitus in relation to age at onset, C-peptide and other endocrine autoimmune diseases. <i>Diabetes.Metab.Res.Rev.</i> 20 (2):158-164, 2004.	Wrong population: adults only
YP. Mahadeb, Damien Gruson, Martin Buyschaert, and Michel P. Hermans. What are the characteristics of phenotypic type 2 diabetic patients with low-titer GAD65 antibodies? <i>Acta Diabetol.</i> 51 (1):103-111, 2014.	Wrong population: adults only
M. Maioli, G. M. Pes, G. Delitala, L. Puddu, A. Falorni, F. Tolu, R. Lampis, V. Orru, G. Secchi, A. M. Cicalo, R. Floris, G. F. Madau, R. M. Pilosu, M. Whalen, and F. Cucca. Number of autoantibodies and HLA genotype, more than high titers of glutamic acid decarboxylase autoantibodies, predict insulin dependence in latent autoimmune diabetes of adults. <i>EUR.J.ENDOCRINOL.</i> 163 (4):541-549, 2010.	Wrong population: adults only
J de Faria Maraschin, Leticia Scherz Weinert, Nadia Murussi, Vanessa Witter, Ticiane da Costa Rodrigues, Egna Regina Rossato, and Sandra Pinho Silveiro. Influence of age at diagnosis and duration of diabetes on the positivity of glutamic acid decarboxylase antibody in South-Brazilian type 1 diabetes mellitus. <i>Ann.Clin.Biochem.</i> 50 (Pt 3):262-266, 2013.	Wrong population: adults only
T. J. McDonald, K. Colclough, R. Brown, B. Shields, M. Shepherd, P. Bingley, A. Williams, A. T. Hattersley, and Sian Ellard. Islet autoantibodies can discriminate maturity-onset diabetes of the young (MODY) from Type 1 diabetes. <i>Diabet.Med.</i> 28 (9):1028-1033, 2011.	Wrong population: adults only
L. Monge, G. Bruno, S. Pinach, G. Grassi, G. Maghzenzani, F. Dani, and G. Pagano. A clinically orientated approach increases the efficiency of screening for latent autoimmune diabetes in adults (LADA) in a large clinic-based cohort of patients with diabetes onset over 50 years. <i>Diabet.Med.</i> 21 (5):456-459, 2004.	Wrong population: adults only
S Murao, Shiori Kondo, Jun Ohashi, Yasuhisa Fujii, Ikki Shimizu, Masao Fujiyama, Keizo Ohno, Yasuharu Takada, Kazuaki Nakai, Yukio Yamane, Haruhiko Osawa, and Hideichi Makino. Anti-thyroid peroxidase antibody, IA-2 antibody, and fasting C-peptide levels predict beta cell failure in patients with latent autoimmune diabetes in adults (LADA)--a 5-year follow-up of the Ehime study. <i>Diabetes Res.Clin.Pract.</i> 80 (1):114-121, 2008.	Wrong population: adults only
A Paschke, Agata Grzelka, Agnieszka Zawada, and Dorota Zozulinska-Ziolkiewicz. Clinical characteristics and autoantibody pattern in newly diagnosed adult-onset autoimmune diabetes. <i>Pol.Arch.Med.Wewn.</i> 123 (7-8):401-408, 2013.	Wrong population: adults only

Study	Reason for exclusion
MA. Radtke, Kristian Midthjell, Tom I. L. Nilsen, and Valdemar Grill. Heterogeneity of patients with latent autoimmune diabetes in adults: linkage to autoimmunity is apparent only in those with perceived need for insulin treatment: results from the Nord-Trøndelag Health (HUNT) study. <i>Diabetes Care</i> 32 (2):245-250, 2009.	Wrong population: adults only
A Rogowicz-Frontczak, Dorota Zozulińska-Ziolkiewicz, Monika Litwinowicz, Paweł Niedzwiecki, Krystyna Wyka, and Bogna Wierusz-Wysocka. Are zinc transporter type 8 antibodies a marker of autoimmune thyroiditis in non-obese adults with new-onset diabetes? <i>EUR.J.ENDOCRINOL.</i> 170 (4):651-658, 2014.	Wrong population: adults only
Mi Oh Roh, Chan Hee Jung, Bo Yeon Kim, Ji Oh Mok, and Chul Hee Kim. The prevalence and characteristics of latent autoimmune diabetes in adults (LADA) and its relation with chronic complications in a clinical department of a university hospital in Korea. <i>Acta Diabetol.</i> 50 (2):129-134, 2013.	Wrong population: adults only
K. Shishikura, K. Tanimoto, S. Sakai, Y. Tanimoto, J. Terasaki, and T. Hanafusa. Association between skeletal muscle mass and insulin secretion in patients with type 2 diabetes mellitus. <i>Endocr.J.</i> 61 (3):281-287, 2014.	Wrong population: adults only
E. P. Sorgjerd, F. Skorpen, K. Kvaloy, K. Midthjell, and V. Grill. Time dynamics of autoantibodies are coupled to phenotypes and add to the heterogeneity of autoimmune diabetes in adults: the HUNT study, Norway. <i>Diabetologia</i> 55 (5):1310-1318, 2012.	Wrong population: adults only
A. Szybowska, A. Ramotowska, K. Dzygalo, and D. Golicki. Beneficial effect of real-time continuous glucose monitoring system on glycemic control in type 1 diabetic patients: systematic review and meta-analysis of randomized trials. <i>EUR.J.ENDOCRINOL.</i> 166:567-574, 2012.	Wrong population: adults only
G Thanabalasingham, Aparna Pal, Mary P. Selwood, Christina Dudley, Karen Fisher, Polly J. Bingley, Sian Ellard, Andrew J. Farmer, Mark I. McCarthy, and Katharine R. Owen. Systematic assessment of etiology in adults with a clinical diagnosis of young-onset type 2 diabetes is a successful strategy for identifying maturity-onset diabetes of the young. <i>Diabetes Care</i> 35 (6):1206-1212, 2012.	Wrong population: adults only
A Trabucchi, Natalia I. Faccinetti, Luciano L. Guerra, Felix M. Puchulu, Gustavo D. Frechtel, Edgardo Poskus, and Silvina N. Valdez. Detection and characterization of ZnT8 autoantibodies could help to screen latent autoimmune diabetes in adult-onset patients with type 2 phenotype. <i>Autoimmunity</i> 45 (2):137-142, 2012.	Wrong population: adults only
F Vaziri-Sani, Shilpa Oak, Jared Radtke, Ke Lernmark, Kristian Lynch, Carl D. Agardh, Corrado M. Cilio, Asa L. Lethagen, Eva Ortvist, Mona Landin-Olsson, Carina Torn, and Christiane S. Hampe. ZnT8 autoantibody titers in type 1 diabetes patients decline rapidly after clinical onset. <i>Autoimmunity</i> 43 (8):598-606, 2010.	Wrong population: adults only
I. Vermeulen, I. Weets, M. Asanghanwa, J. Ruige, Gaal L. Van, C. Mathieu, B. Keymeulen, V. Lampasona, J. M. Wenzlau, J. C. Hutton, D. G. Pipeleers, and F. K. Gorus. Contribution of antibodies against IA-2beta and zinc transporter 8 to classification of diabetes diagnosed under 40 years of age. <i>Diabetes Care</i> 34 (8):1760-1765, 2011.	Wrong population: adults only
A. Vlad, V. Serban, Alexandra Sima, R. Timar, and Mihaela Rosu. The value of basal C peptide and its relationship with pancreatic autoantibodies in young adults with type 2 diabetes mellitus. <i>Rom.J.Intern.Med.</i> 42 (2):333-341, 2004.	Wrong population: adults only
H. Wilmot-Roussel, D. J. Levy, C. Carette, S. Caillat-Zucman, C. Boitard, J. Timsit, and D. Dubois-Laforgue. Factors associated with the presence of glutamic acid decarboxylase and islet antigen-2 autoantibodies in patients with long-standing type 1 diabetes. <i>Diabetes & Metabolism</i> 39 (3):244-249, 2013.	Wrong population: adults only
L. Yang, Z. G. Zhou, S. Z. Tan, G. Huang, P. Jin, X. Yan, X. Li, H. Peng, and W. Hagopian. Carboxypeptidase-H autoantibodies differentiate a more latent subset of autoimmune diabetes from phenotypic type 2 diabetes among Chinese adults. <i>Ann.N.Y.Acad.Sci.</i> 1150:263-266, 2008.	Wrong population: adults only
S Zampetti, Marco Capizzi, Marialuisa Spoletini, Giuseppe Campagna, Gaetano Leto, Laura Cipolloni, Claudio Tiberti, Emanuele Bosi, Alberto Falorni, Raffaella Buzzetti, and NIRAD Study Group. GADA titer-related risk for organ-specific autoimmunity in LADA subjects subdivided according to gender (NIRAD study 6). <i>J.Clin.Endocrinol.Metab.</i> 97 (10):3759-3765, 2012.	Wrong population: adults only
S Zhang, Qi Sun, Kai Feng, Yong Fu, Ou Wang, Fan Ping, and Yuxiu Li. Clinical, biochemical, and immunological characteristics of newly diagnosed nonobese diabetic patients aged 18-45 years in China. <i>J.Diabetes Complications</i> 26 (1):40-43, 2012.	Wrong population: adults only

H.2 Type 1 diabetes – education

Review question

What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

Study	Reason for exclusion
Ambrosino,J.M., Fennie,K., Whittemore,R., Jaser,S., Dowd,M.F., Grey,M., Short-term effects of coping skills training in school-age children with type 1 diabetes, <i>Pediatric Diabetes</i> , 9, 74-82, 2008	PICO not met: intervention not considered to be a form of structured education
Anderson,B.J., Wolf,F.M., Burkhart,M.T., Cornell,R.G., Bacon,G.E, Effects of peer-group intervention on metabolic control of adolescents with IDDM. Randomized outpatient study, <i>Diabetes Care</i> , 12, 179-183, 1989	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (did not consider a structured form of education)
Armour,T.A., Norris,S.L., Jack,L.,Jr., Zhang,X., Fisher,L., The effectiveness of family interventions in people with diabetes mellitus: a systematic review. [47 refs], <i>Diabetic Medicine</i> , 22, 1295-1305, 2005	Systematic review: individual randomised controlled trials have been considered for inclusion
Barnes,L.P., The illiterate client: strategies in patient teaching, <i>MCN: The American Journal of Maternal Child Nursing</i> , 17, 127-127, 1992	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not an RCT)
Bin-Abbas,B., Jabbari,M., Al-Fares,A., El-Dali,A., Al-Orifi,F., Effect of mobile phone short text messages on glycaemic control in children with type 1 diabetes, <i>Journal of Telemedicine and Telecare</i> , 20, 153-156, 2014	The study was not randomised, and included only 1 group using the intervention
Bloomfield,S., Calder,J.E., Chisholm,V., Kelnar,C.J., Steel,J.M., Farquhar,J.W., Elton,R., A project in diabetes education for children, <i>Diabetic Medicine</i> , 7, 137-142, 1990	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (study population unclear)
Brown,S.J., Lieberman,D.A., Germeny,B.A., Fan,Y.C., Wilson,D.M., Pasta,D.J., Educational video game for juvenile diabetes: results of a controlled trial, <i>Medical Informatics</i> , 22, 77-89, 1997	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (did not consider a structured form of education)
Chaney,D., Coates,V., Shevlin,M., Carson,D., McDougall,A., Long,A., Bunting,B., Evaluation of the Carbohydrate, Insulin Collaborative Education (CHOICE) programme for young people with Type 1 diabetes, <i>Diabetic Medicine</i> , 28, 25-, 2011	Conference abstract
Chaney,David, Coates,Vivien, Shevlin,Mark, Running a complex educational intervention for adolescents with type 1 diabetes -- lessons learnt, <i>Journal of Diabetes Nursing</i> , 14, 370-, 2010	Discussion of issues from a randomised controlled trial
Christie,D., Strange,V., Allen,E., Oliver,S., Wong,I.C., Smith,F., Cairns,J., Thompson,R., Hindmarsh,P., O'Neill,S., Bull,C., Viner,R., Elbourne,D., Maximising engagement, motivation and long term change in a Structured Intensive Education Programme in Diabetes for children, young people and their families: Child and Adolescent Structured Competencies Approach to Diabetes Education (CASCADE), <i>BMC Pediatrics</i> , 9, 57-, 2009	Protocol for a randomised controlled study (CASCADE)
Couch,R., Jetha,M., Dryden,D.M., Hooten,N., Liang,Y., Durec,T., Sumamo,E., Spooner,C., Milne,A., O'Gorman,K., Klassen,T.P., Diabetes education for children with type 1 diabetes mellitus and their families. [122 refs], <i>Evidence Report/Technology Assessment</i> , 1-144, 2008	Systematic review: individual randomised controlled trials have been considered for inclusion
DeShazo,J., Harris,L., Pratt,W., Effective intervention or child's play? A review of video games for diabetes education, <i>Diabetes Technology and Therapeutics</i> , 12, 815-822, 2010	Systematic review: individual randomised controlled trials have been considered for inclusion
Diabetes Education Program in Bulgaria (DEPB) Project Group., Diabetes education program in Bulgaria, <i>Patient Education and Counseling</i> , 43, 111-114, 2001	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (no separate paediatric data reported)
Elamin,A., Eltayeb,B., Hasan,M., Hofvander,Y., Tuvemo,T., Effect of dietary education on metabolic control in children and adolescents with Type I diabetes mellitus, <i>Diabetes, Nutrition and Metabolism - Clinical and Experimental</i> , 6, 223-229, 1993	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (length of follow-up too short)
Ellis,D.A., Yopp,J., Templin,T., Naar-King,S., Frey,M.A., Cunningham,P.B., Idalski,A., Niec,L.N., Family mediators and moderators of treatment outcomes among youths with poorly controlled type 1 diabetes: results from a randomized controlled trial, <i>Journal of Pediatric Psychology</i> , 32, 194-205, 2007	Did not consider a structured form of education
Gage,H., Hampson,S., Skinner,T.C., Hart,J., Storey,L., Foxcroft,D., Kimber,A., Craddock,S., McEvilly,E.A., Educational and psychosocial programmes for adolescents with diabetes: approaches, outcomes and cost-effectiveness. [122 refs], <i>Patient Education and Counseling</i> ,	Systematic review: individual randomised controlled trials have been considered for inclusion

Diagnosis and management of type 1 diabetes in children and young people
Excluded studies

Study	Reason for exclusion
53, 333-346, 2004	
Grey,M., Jaser,S.S., Whittemore,R., Jeon,S., Lindemann,E., Coping skills training for parents of children with type 1 diabetes: 12-month outcomes, <i>Nursing Research</i> , 60, 173-181, 2011	Conference abstract
Grey,M., Whittemore,R., Jaser,S., Ambrosino,J., Lindemann,E., Liberti,L., Northrup,V., Dziura,J., Effects of coping skills training in school-age children with type 1 diabetes, <i>Research in Nursing and Health</i> , 32, 405-418, 2009	PICO not met: intervention not considered to be a form of structured education
Grey,M., Whittemore,R., Jeon,S., Jaser,S., Murphy,K., Faulkner,M., Delamater,A., Internet programs for youth with type 1 diabetes (T1D) improve outcomes, <i>Diabetes</i> , 61, A90-, 2012	PICO not met: intervention not considered to be a form of structured education
Hackett,A.F., Court,S., Mathews,J.N., McCowen,C., Do education groups help diabetics and their parents?, <i>Archives of Disease in ChildhoodArch.Dis.Child.</i> , 64, 997-1003, 1989	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (study design unclear; not clearly an RCT)
Hampson,S.E., Skinner,T.C., Hart,J., Storey,L., Gage,H., Foxcroft,D., Kimber,A., Shaw,K., Walker,J., Effects of educational and psychosocial interventions for adolescents with diabetes mellitus: a systematic review (Structured abstract), <i>Health Technology Assessment Database</i> , -, 2013	Abstract for a systematic review published in 2001
Hampson,S.E., Skinner,T.C., Hart,J., Storey,L., Gage,H., Foxcroft,D., Kimber,A., Craddock,S., McEvilly,E.A., Behavioral interventions for adolescents with type 1 diabetes: how effective are they?. [68 refs], <i>Diabetes Care</i> , 23, 1416-1422, 2000	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (individual RCTs are included in the guideline review)
Hampson,S.E., Skinner,T.C., Hart,J., Storey,L., Gage,H., Foxcroft,D., Kimber,A., Shaw,K., Walker,J., Effects of educational and psychosocial interventions for adolescents with diabetes mellitus: a systematic review. [148 refs], <i>Health Technology Assessment (Winchester, England)</i> , 5, 1-79, 2001	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (individual RCTs are included in the guideline review)
Hanberger,L., Ludvigsson,J., Nordfeldt,S., Use of a web 2.0 portal to improve education and communication in young patients with families: randomized controlled trial, <i>Journal of medical Internet research</i> , 15, e175-, 2013	Web 2.0 portal was not a 'structured' education programme (there was no structured curriculum); the use of the portal was designed to be self-initiated by participants and their parents whenever needed, although there was access to communication with healthcare professionals
Hill-Briggs,F., Gemmell,L., Problem solving in diabetes self-management and control: A systematic review of the literature, <i>Diabetes Educator</i> , 33, 1032-1050, 2007	Systematic review: individual randomised controlled trials have been considered for inclusion
Hoff,A.L., Mullins,L.L., Gillaspay,S.R., Page,M.C., Van,PeltJ, Chaney,J.M., An intervention to decrease uncertainty and distress among parents of children newly diagnosed with diabetes: A pilot study, <i>Families, Systems and Health</i> , 23, 329-342, 2005	PICO not met: population was specifically the parents of children with diabetes
Holmes,C.S., Chen,R., Mackey,E., Grey,M., Streisand,R., Randomized clinical trial of clinic-integrated, low-intensity treatment to prevent deterioration of disease care in adolescents with type 1 diabetes, <i>Diabetes Care</i> , 37, 1535-1543, 2014	Wrong intervention (behavioural intervention)
Hood,K.K., Rohan,J.M., Peterson,C.M., Drotar,D., Interventions with adherence-promoting components in pediatric type 1 diabetes: meta-analysis of their impact on glycaemic control, <i>Diabetes Care</i> , 33, 1658-1664, 2010	Systematic review: individual randomised controlled trials have been considered for inclusion
Howells,L., Wilson,A.C., Skinner,T.C., Newton,R., Morris,A.D., Greene,S.A., A randomized control trial of the effect of negotiated telephone support on glycaemic control in young people with Type 1 diabetes, <i>Diabetic Medicine</i> , 19, 643-648, 2002	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (did not consider a structured form of education)
Husted,G.R., Thorsteinsson,B., Esbensen,B.A., Hommel,E., Zoffmann,V., Improving glycaemic control and life skills in adolescents with type 1 diabetes: a randomised, controlled intervention study using the Guided Self-Determination-Young method in triads of adolescents, parents and health care providers integrated into routine paediatric outpatient clinics, <i>BMC Pediatrics</i> , 11, 55-, 2011	PICO not met: intervention not considered to be a form of structured education
Izquierdo,R., Morin,P.C., Bratt,K., Moreau,Z., Meyer,S., Ploutz-Snyder,R., Wade,M., Weinstock,R.S., School-centered telemedicine for children with type 1 diabetes mellitus, <i>Journal of Pediatrics</i> , 155, 374-379, 2009	PICO not met: intervention intended for improvement in education for school staff
Jonsson,L., Hallstrom,I., Lundqvist,A., A multi-disciplinary education process related to the discharging of children from hospital when the child has been diagnosed with type 1 diabetes--a qualitative study, <i>BMC Pediatrics</i> , 10, 36-, 2010	Not a randomised controlled trial

Study	Reason for exclusion
Laffel,L.M.B., Vangsnest,L., Connell,A., Goebel-Fabbri,A., Butler,D., Anderson,B.J., Impact of ambulatory, family-focused teamwork intervention on glycemic control in youth with type 1 diabetes, <i>Journal of Pediatrics</i> , 142, 409-416, 2003	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (intervention not considered to be a form of structured education)
Mannucci,E., Pala,L., Rotella,C.M., Long-term interactive group education for type 1 diabetic patients, <i>Acta Diabetologica</i> , 42, 1-6, 2005	Not a randomised controlled trial
Massouh,S.R., Steele,T.M., Alseth,E.R., Diekmann,J.M., The effect of social learning intervention on metabolic control of insulin-dependent diabetes mellitus in adolescents, <i>Diabetes Educator</i> , 15, 518-521, 1989	Included in 2004 guideline review - did not meet inclusion criteria for 2015 update review (closer to a behavioural intervention than a structured education programme)
McBroom,L.A., Enriquez,M., Review of family-centered interventions to enhance the health outcomes of children with type 1 diabetes. [36 refs], <i>Diabetes Educator</i> , 35, 428-438, 2009	Systematic review: individual randomised controlled trials have been considered for inclusion
McNabb,W.L., Quinn,M.T., Murphy,D.M., Thorp,F.K., Cook,S., Increasing children's responsibility for diabetes self-care: the In Control study, <i>Diabetes Educator</i> , 20, 121-124, 1994	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (follow-up period insufficient)
Mcperson,A.C., Price,K., Does an interactive website provide additional support to young people participating in an educational intervention for type 1 diabetes?, <i>Pediatric Diabetes</i> , 13, 139-, 2012	Conference abstract
Moattari,Marzieh, Hashemi,Maryam, Dabbaghmanesh,Mohammad, The impact of electronic education on metabolic control indicators in patients with diabetes who need insulin: a randomised clinical control trial, <i>Journal of Clinical Nursing</i> , 22, 32-38, 2013	PICO not met: adult participants only
Muller,Nicolle, Kloos,Christof, Samann,Alexander, Wolf,Gunter, Muller,Ulrich Alfons, Evaluation of a treatment and teaching refresher programme for the optimization of intensified insulin therapy in type 1 diabetes, <i>Patient Education and Counseling</i> , 93, 108-113, 2013	Participants aged between 16 and 70 years
Mulvaney,S.A., Rothman,R.L., Osborn,C.Y., Lybarger,C., Dietrich,M.S., Wallston,K.A., Self-management problem solving for adolescents with type 1 diabetes: intervention processes associated with an Internet program, <i>Patient Education and Counseling</i> , 85, 140-142, 2011	Outcomes not compared between the comparative groups
Mulvaney,S.A., Rothman,R.L., Wallston,K.A., Lybarger,C., Dietrich,M.S., An internet-based program to improve self-management in adolescents with type 1 diabetes, <i>Diabetes Care</i> , 33, 602-604, 2010	PICO not met: intervention not considered to be a form of structured education
Murphy,H.R., Rayman,G., Skinner,T.C., Psycho-educational interventions for children and young people with Type 1 diabetes. [52 refs], <i>Diabetic Medicine</i> , 23, 935-943, 2006	Systematic review: individual randomised controlled trials have been considered for inclusion
Nansel,T.R., Iannotti,R.J., Simons-Morton,B.G., Cox,C., Plotnick,L.P., Clark,L.M., Zeitzoff,L., Diabetes personal trainer outcomes: short-term and 1-year outcomes of a diabetes personal trainer intervention among youth with type 1 diabetes, <i>Diabetes Care</i> , 30, 2471-2477, 2007	PICO not met: intervention not considered to be a form of structured education
Nansel,T.R., Iannotti,R.J., Simons-Morton,B.G., Plotnick,L.P., Clark,L.M., Zeitzoff,L., Long-term maintenance of treatment outcomes: diabetes personal trainer intervention for youth with type 1 diabetes, <i>Diabetes Care</i> , 32, 807-809, 2009	A follow-up study of a randomised controlled trial
Nicholas,D.B., Fellner,K.D., Frank,M., Small,M., Hetherington,R., Slater,R., Daneman,D., Evaluation of an online education and support intervention for adolescents with diabetes, <i>Social Work in Health Care</i> , 51, 815-827, 2012	Process evaluation
Nordfeldt,S., Johansson,C., Carlsson,E., Hammersjo,J.A., Persistent effects of a pedagogical device targeted at prevention of severe hypoglycaemia: a randomized, controlled study, <i>Acta Paediatrica</i> , 94, 1395-1401, 2005	A follow-up study of a randomised controlled trial
Nordfeldt,S., Johansson,C., Carlsson,E., Hammersjo,J.A., Prevention of severe hypoglycaemia in type I diabetes: a randomised controlled population study, <i>Archives of Disease in Childhood</i> , 88, 240-245, 2003	Included in 2004 guideline review - does not meet criteria for 2015 update review (not a structured education programme)
Olmsted,M.P., Daneman,D., Rydall,A.C., Lawson,M.L., Rodin,G., The effects of psychoeducation on disturbed eating attitudes and behavior in young women with type 1 diabetes mellitus, <i>International Journal of Eating Disorders</i> , 32, 230-239, 2002	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population limited to young women with eating disturbance)
Pichert,J.W., Smeltzer,C., Snyder,G.M., Gregory,R.P.,	Included in 2004 guideline review - does not meet inclusion

Study	Reason for exclusion
Smeltzer,R., Kinzer,C.K., Traditional vs anchored instruction for diabetes-related nutritional knowledge, skills, and behavior, <i>Diabetes Educator</i> , 20, 45-48, 1994	criteria for 2015 review (no outcomes of interest reported)
Pichert,J.W., Snyder,G.M., Kinzer,C.K., Boswell,E.J., Problem solving anchored instruction about sick days for adolescents with diabetes, <i>Patient Education and Counseling</i> , 23, 115-124, 1994	Included in 2004 guideline review - does not meet inclusion criteria for 2015 review (no outcomes of interest reported)
Price,K.J., Wales,J., Eiser,C., Knowles,J., Heller,S., Freeman,J., Brennan,A., McPherson,A., Wellington,J., Does an intensive self-management structured education course improve outcomes for children and young people with type 1 diabetes? The Kids In Control OF Food (KICK-OFF) cluster-randomised controlled trial protocol, <i>BMJ Open</i> , 3, -, 2013	A protocol for a randomised controlled trial (KICK-OFF)
Sansom-Daly,U.M., Peate,M., Wakefield,C.E., Bryant,R.A., Cohn,R.J., A systematic review of psychological interventions for adolescents and young adults living with chronic illness, <i>Health Psychology</i> , 31, 380-393, 2012	Systematic review: individual randomised controlled trials have been considered for inclusion
Satin,W., La Greca,A.M., Zigo,M.A., Skyler,J.S., Diabetes in adolescence: effects of multifamily group intervention and parent simulation of diabetes, <i>Journal of Pediatric Psychology</i> J.Pediatr.Psychol., 14, 259-275, 1989	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not considered to be a structured education programme)
Savage,E., Farrell,D., McManus,V., Grey,M., The science of intervention development for type 1 diabetes in childhood: systematic review, <i>Journal of Advanced Nursing</i> , 66, 2604-2619, 2010	Systematic review: individual randomised controlled trials have been considered for inclusion
Sherifali,D., A case manager plus psychoeducation reduced adverse outcomes in youth with type 1 diabetes, <i>Evidence Based Nursing</i> , 7, 42-42, 2004	Abstract
Spiegel,G., Bortsov,A., Bishop,F.K., Owen,D., Klingensmith,G.J., Mayer-Davis,E.J., Maahs,D.M., Randomized Nutrition Education Intervention to Improve Carbohydrate Counting in Adolescents with Type 1 Diabetes Study: Is More Intensive Education Needed?, <i>Journal of the Academy of Nutrition and Dietetics</i> , , 1736-1746, 2012	PICO not met: outcomes of interest not reported
Srinivasan,B., Davies,M., Lawrence,I., Diabetes: glycaemic control in type 1, <i>Clinical Evidence</i> , 2008, 2008., -, 2008	Systematic review: individual randomised controlled trials have been considered for inclusion
Suh,S., Jean,C., Koo,M., Lee,S.Y., Cho,M.J., Sim,K.H., Jin,S.M., Bae,J.C., Kim,J.H., A randomized controlled trial of an internet-based mentoring program for type 1 diabetes patients with inadequate glycermic control, <i>Diabetes and Metabolism Journal</i> , 38, 134-142, 2014	Adult population
Sullivan-Bolyai,Susan, Bova,Carol, Leung,Katherine, Trudeau,Allison, Lee,Mary, Gruppuso,Philip, Social Support to Empower Parents (STEP): An intervention for parents of young children newly diagnosed with type 1 diabetes, <i>The Diabetes Educator</i> , 36, 88-97, 2010	Population was mothers of children with type 1 diabetes
Sundelin,J., Forsander,G., Mattsson,S.E, Family-oriented support at the onset of diabetes mellitus: a comparison of two group conditions during 2 years following diagnosis, <i>Acta Paediatrica</i> Acta Paediatr., 85, 49-55, 1996	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not a form of structured education)
Urban,A.D., Berry,D., Grey,M., Optimizing outcomes in adolescents with type 1 diabetes and their families, <i>Journal of Clinical Outcomes Management</i> , 11, 299-306, 2004	Systematic review: individual randomised controlled trials have been considered for inclusion
Viklund,G., Ortqvist,E., Wikblad,K., Assessment of an empowerment education programme. A randomized study in teenagers with diabetes, <i>Diabetic medicine : a journal of the British Diabetic Association</i> , 24, 550-556, 2007	PICO not met: intervention not considered to be a form of structured education
Wang,Y.C., Stewart,S.M., Mackenzie,M., Nakonezny,P.A., Edwards,D., White,P.C., A randomized controlled trial comparing motivational interviewing in education to structured diabetes education in teens with type 1 diabetes, <i>Diabetes Care</i> , 33, 1741-1743, 2010	This is a process evaluation study, not a clinical trial
Whittemore,R., Jaser,S.S., Jeon,S., Liberti,L., Delamater,A., Murphy,K., Faulkner,M.S., Grey,M., An internet coping skills training program for youth with type 1 diabetes: six-month outcomes, <i>Nursing Research</i> , 61, 395-404, 2012	PICO not met: intervention not considered to be a form of structured education
Wysocki,T., Harris,M.A, Greco,P., Harvey,L.M., McDonnell,K, Elder Danda,C.L, Bubb,J, White,N.H., Social validity of support group and behavior therapy interventions for families of adolescents with insulin-dependent diabetes mellitus, <i>Journal of Pediatric Psychology</i> J.Pediatr.Psychol., 22, 635-649, 1997	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (no outcomes of interest reported and the original study was also excluded)
Wysocki,T., Harris,M.A., Buckloh,L.M., Mertlich,D., Lochrie,A.S., Taylor,A., Sadler,M., White,N.H., Randomized, controlled trial of Behavioral Family Systems Therapy for	Maintenance study for a randomised controlled trial

Study	Reason for exclusion
Diabetes: maintenance and generalization of effects on parent-adolescent communication, Behavior Therapy, 39, 33-46, 2008	
Wysocki,T., Harris,M.A., Greco,P., Bubb,J., Danda,C.E., Harvey,L.M., McDonnell,K., Taylor,A., White,N.H., Randomized, controlled trial of behavior therapy for families of adolescents with insulin-dependent diabetes mellitus, Journal of Pediatric Psychology, 25, 23-33, 2000	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (the original study Wysocki 1997 was excluded; this article has also been excluded as only results from the 3-month follow-up are reported)

H.3 Type 1 diabetes – behavioural interventions

Review question

What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 1 diabetes?

Study	Reason for exclusion
Ambrosino,J.M., Fennie,K., Whittemore,R., Jaser,S., Dowd,M.F., Grey,M., Short-term effects of coping skills training in school-age children with type 1 diabetes, Pediatric Diabetes, 9, 74-82, 2008	PICO not met - follow-up length insufficient
Anderson,B.J., Wolf,F.M., Burkhart,M.T., Cornell,R.G., Bacon,G.E, Effects of peer-group intervention on metabolic control of adolescents with IDDM. Randomized outpatient study, Diabetes Care, 12, 179-183, 1989	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not an intervention specified in the review protocol)
Berger,G., Muehlechner,M., Brunmayr,F., Waldhoer,T., Wondratsch,C., Lonsky,J., Koenig,M., Horak,E., Wagner,G., Hoertenhuber,T., Fritsch,M., Schober,E., Rami-Merhar,B., Motivational interviewing to improve metabolic control in adolescents with type 1 diabetes: It's worth talking to boys?, Pediatric Diabetes, 13, 27-, 2012	Conference abstract
Boardway,R.H., Delamater,A.M., Tomakowsky,J., Gutai,J.P., Stress management training for adolescents with diabetes, Journal of Pediatric Psychology, 18, 29-45, 1993	Included in 2004 guideline review “ does not meet inclusion criteria for 2015 update review (follow-up does not meet required duration)
Cakan,N., Ellis,D.A., Templin,T., Frey,M., Naar-King,S., The effects of weight status on treatment outcomes in a randomized clinical trial of multisystemic therapy for adolescents with type 1 diabetes and chronically poor metabolic control, Pediatric Diabetes, 8, 206-213, 2007	Secondary publication
Channon,S., Smith,V.J., Gregory,J.W., A pilot study of motivational interviewing in adolescents with diabetes, Archives of Disease in Childhood, 88, 680-683, 2003	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not an RCT)
Chernoff,R.G., Ireys,H.T., DeVet,K.A., Kim,Y.J., A randomized, controlled trial of a community-based support program for families of children with chronic illness: pediatric outcomes, Archives of Pediatrics and Adolescent Medicine, 156, 533-539, 2002	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population does not match the inclusion criteria of the 2015 update review)
Chisholm,V., Gonzalez,A., Atkinson,L., Interpersonal engagement mediates the relation between maternal affect and externalising behaviour in young children with type 1 diabetes, PLoS ONE [Electronic Resource], 9, e97672-, 2014	Interventions are not of interest
Cho,E., Shin,S.H., Eun,S.H., Kim,J.Y., Nam,H.K., Lee,K.H., Rhie,Y.J., Psychological characteristics of Korean children and adolescents with type 1 diabetes mellitus, Annals of Pediatric Endocrinology and Metabolism, 18, 122-127, 2013	Wrong study design (case-control, not RCT)
Christie,D., Thompson,R., Sawtell,M., Allen,E., Cairns,J., Smith,F., Jamieson,E., Hargreaves,K., Ingold,A., Brooks,L., Wiggins,M., Oliver,S., Jones,R., Elbourne,D., Santos,A., Wong,I.C., O'Neill,S., Strange,V., Hindmarsh,P., Annan,F., Viner,R., Structured, intensive education maximising engagement, motivation and long-term change for children and young people with diabetes: a cluster randomised controlled trial with integral process and economic evaluation - the CASCADE study, Health Technology Assessment (Winchester, England), 18, 1-202, 2014	Wrong intervention (education)
Daley,B.J., Sponsorship for adolescents with diabetes, Health and Social Work, 17, 173-182, 1992	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population unclear, stated as teenagers with diabetes)
Delamater,A.M., Bubb,J., Davis,S.G., Smith,J.A., Schmidt,L., White,N.H., Santiago,J.V., Randomized prospective study of self-management training with newly diagnosed diabetic children. [erratum appears in Diabetes Care 1990 Jul;13(7):819], Diabetes Care, 13, 492-498, 1990	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (intervention is an education programme rather than a behavioural intervention)
Ellis,D., Naar-King,S., Templin,T., Frey,M., Cunningham,P., Sheidow,A., Cakan,N., Idalski,A., Multisystemic therapy for adolescents with poorly controlled type 1 diabetes: reduced diabetic ketoacidosis admissions and related costs over	Secondary publication

Study	Reason for exclusion
24 months, <i>Diabetes Care</i> , 31, 1746-1747, 2008	
Ellis,D.A., Frey,M.A., Naar-King,S., Templin,T., Cunningham,P.B., Cakan,N., The effects of multisystemic therapy on diabetes stress among adolescents with chronically poorly controlled type 1 diabetes: findings from a randomized, controlled trial, <i>Pediatrics</i> , 116, e826-e832, 2005	Secondary publication
Ellis,D.A., Naar-King,S., Chen,X., Moltz,K., Cunningham,P.B., Idalski-Carcone,A., Multisystemic therapy compared to telephone support for youth with poorly controlled diabetes: findings from a randomized controlled trial, <i>Annals of Behavioral Medicine</i> , 44, 207-215, 2012	Secondary publication
Ellis,D.A., Naar-King,S., Frey,M., Templin,T., Rowland,M., Cakan,N., Multisystemic treatment of poorly controlled type 1 diabetes: effects on medical resource utilization, <i>Journal of Pediatric Psychology</i> , 30, 656-666, 2005	Secondary publication
Ellis,D.A., Naar-King,S., Templin,T., Frey,M.A., Cunningham,P.B., Improving health outcomes among youth with poorly controlled type I diabetes: the role of treatment fidelity in a randomized clinical trial of multisystemic therapy, <i>Journal of Family Psychology</i> , 21, 363-371, 2007	Secondary publication
Ellis,D.A., Templin,T., Naar-King,S., Frey,M.A., Cunningham,P.B., Podolski,C.L., Cakan,N., Multisystemic therapy for adolescents with poorly controlled type I diabetes: Stability of treatment effects in a randomized controlled trial, <i>Journal of Consulting and Clinical Psychology</i> , 75, 168-174, 2007	Secondary publication
Ellis,D.A., Yopp,J., Templin,T., Naar-King,S., Frey,M.A., Cunningham,P.B., Idalski,A., Niec,L.N., Family mediators and moderators of treatment outcomes among youths with poorly controlled type 1 diabetes: results from a randomized controlled trial, <i>Journal of Pediatric Psychology</i> , 32, 194-205, 2007	Secondary publication
Franklin,V.L., Waller,A., Pagliari,C., Greene,S.A., A randomized controlled trial of Sweet Talk, a text-messaging system to support young people with diabetes, <i>Diabetic Medicine</i> , 23, 1332-1338, 2006	PICO not met - support delivered by clinical staff not peers
Freeman,K.A., Duke,D.C., Harris,M.A., Behavioral health care for adolescents with poorly controlled diabetes via Skype: does working alliance remain intact?, <i>Journal of Diabetes Science and Technology</i> , 7, 727-735, 2013	Outcomes examined (working alliance inventory (WAI) subscale scores and the association between them and HbA1c) not of interest
Garcia-Perez,L., Perestelo-Perez,L., Serrano-Aguilar,P., Del,Mar Trujillo-Martin, Effectiveness of a psychoeducative intervention in a summer camp for children with type 1 diabetes mellitus, <i>Diabetes Educator</i> , 36, 310-317, 2010	PICO not met - intervention not relevant to this question
Gayes,L.A., Steele,R.G., A meta-analysis of motivational interviewing interventions for pediatric health behavior change, <i>Journal of Consulting and Clinical Psychology</i> , 82, 521-535, 2014	Meta-analysis - individual studies considered for guideline review
Greco,P., Pendley,J.S., McDonell,K., Reeves,G., A peer group intervention for adolescents with type 1 diabetes and their best friends, <i>Journal of Pediatric Psychology</i> , 26, 485-490, 2001	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not a comparative study and therefore does not meet the study design inclusion criteria)
Gregory,J., Robling,M., Bennert,K., Channon,S., Cohen,D., Crowne,E., Hambly,H., Hawthorne,K., Hood,K., Longo,M., Lowes,L., McNamara,R., Pickles,T., Playle,R., Rollnick,S., Thomas-Jones,E., Development and evaluation by a cluster randomised trial of a psychosocial intervention in children and teenagers experiencing diabetes: the DEPICTED study, <i>Health Technology Assessment (Winchester, England)</i> , 15, 1-202, 2011	Secondary publication
Gregory,J.W., Channon,S., Motivational interviewing to improve blood-glucose control in childhood diabetes, <i>Paediatrics and Child Health</i> , 19, 331-334, 2009	Commentary
Grey,M., Jaser,S.S., Whittemore,R., Jeon,S., Lindemann,E., Coping skills training for parents of children with type 1 diabetes: 12-month outcomes, <i>Nursing Research</i> , 60, 173-181, 2011	Pooled analysis of two separate randomised controlled trials
Grey,M., Whittemore,R., Jaser,S., Ambrosino,J., Lindemann,E., Liberti,L., Northrup,V., Dziura,J., Effects of coping skills training in school-age children with type 1 diabetes, <i>Research in Nursing and Health</i> , 32, 405-418, 2009	PICO not met - outcome results not presented in a usable manner
Grey,M., Whittemore,R., Jeon,S., Murphy,K., Faulkner,M.S., Delamater,A., TeenCope Study Group., Internet psycho-education programs improve outcomes in youth with type 1 diabetes, <i>Diabetes Care</i> , 36, 2475-2482, 2013	Education rather than behavioural intervention programme
Grey,M., Whittemore,R., Liberti,L., Delamater,A., Murphy,K., Faulkner,M.S., A comparison of two internet programs for adolescents with type 1 diabetes: design and methods, <i>Contemporary Clinical Trials</i> , 33, 769-776, 2012	Protocol for a randomised controlled trial
Grey,M., Boland,E.A., Davidson,M., Li,J., Tamborlane,W.V., Coping skills training for youth with diabetes mellitus has long-lasting effects on metabolic control and quality of life, <i>Journal of Pediatrics</i> , 137, 107-113, 2000	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population included participants up to the age of 20 years with no subgroups of younger participants reported)
Grey,M., Boland,E.A., Davidson,M., Yu,C., Sullivan-Bolyai,S., Tamborlane,W.V., Short-term effects of coping skills training as adjunct to intensive therapy in adolescents, <i>Diabetes Care</i> , 21, 902-908, 1998	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population includes participants up to the age of 20 years but does not report subgroups for younger participants, and length of

Study	Reason for exclusion
	follow-up does not meet the inclusion criteria)
Grey,M., Boland,E.A., Davidson,M., Yu,C., Tamborlane,W.V., Coping skills training for youths with diabetes on intensive therapy, <i>Applied Nursing Research</i> , 12, 3-12, 1999	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (participants aged < 20 years and no subgroup analysis for ages relevant to guideline)
Gross,A.M., Heimann,L., Shapiro,R., Schulz,R.M., Children with diabetes. Social skills training and hemoglobin A1c levels, <i>Behavior ModificationBehav.Modif.</i> , 7, 151-164, 1983	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (data are not extractable and therefore the study is excluded from the 2015 update)
Gross,AM, Magalnick,LJ, Richardson,P, Self management training with families of insulin dependent diabetic children: a controlled long term investigation, <i>Child and Family Behavior Therapy</i> , 7, 35-50, 1985	Included in 2004 guideline review –“ does not meet inclusion criteria for 2015 update review (follow-up is not required duration)
Hampson,S.E., Skinner,T.C., Hart,J., Storey,L., Gage,H., Foxcroft,D., Kimber,A., Cradock,S., McEvelly,E.A., Behavioral interventions for adolescents with type 1 diabetes: how effective are they?. [68 refs], <i>Diabetes Care</i> , 23, 1416-1422, 2000	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (includes participants aged up to 21 years and does not report any subgroup analyses for younger participants)
Hampson,S.E., Skinner,T.C., Hart,J., Storey,L., Gage,H., Foxcroft,D., Kimber,A., Shaw,K., Walker,J., Effects of educational and psychosocial interventions for adolescents with diabetes mellitus: a systematic review. [148 refs], <i>Health Technology Assessment (Winchester, England)</i> , 5, 1-79, 2001	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (the broad inclusion criteria for this health technology assessment (HTA) report did not match the 2015 review update criteria, but the report was checked for relevance of individual studies)
Harris,MA, Greco,P, Wysocki,T, White,NH, Family therapy with adolescents with diabetes: a litmus test for clinically meaningful change, <i>Families, Systems and Health</i> , 24, 441-446, 2001	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (no outcomes of interest)
Harris,MA, Mertlich,D, Piloting home-based behavioral family systems therapy for adolescents with poorly controlled diabetes, <i>Children's Health Care</i> , 32, 65-79, 2003	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not an RCT)
Hernandez,C.A., Family focused teamwork prevented deterioration in diabetes control in children and adolescents, <i>Evidence Based Nursing</i> , 7, 10-10, 2004	Commentary
Hoff,A.L., Mullins,L.L., Gillaspay,S.R., Page,M.C., Van,PeltJ, Chaney,J.M., An intervention to decrease uncertainty and distress among parents of children newly diagnosed with diabetes: A pilot study, <i>Families, Systems and Health</i> , 23, 329-342, 2005	PICO not met - intervention not relevant to this question
Holmes,C.S., Chen,R., Mackey,E., Grey,M., Streisand,R., Randomized clinical trial of clinic-integrated, low-intensity treatment to prevent deterioration of disease care in adolescents with type 1 diabetes, <i>Diabetes Care</i> , 37, 1535-1543, 2014	Data in study cannot be extracted
Hood,K.K., Nansel,T.R., Commonalities in effective behavioral interventions for children and adolescents with type 1 diabetes: A review of reviews, <i>Diabetes Spectrum</i> , 20, 251-253, 2007	Review of reviews
Howe,C.J., Jawad,A.F., Tuttle,A.K., Moser,J.T., Preis,C., Buzby,M., Murphy,K.M., Education and telephone case management for children with type 1 diabetes: A randomized controlled trial, <i>Journal of Pediatric Nursing</i> , 20, 83-95, 2005	PICO not met - intervention not relevant to this question
Husted,G.R., Thorsteinsson,B., Esbensen,B.A., Hommel,E., Zoffmann,V., Improving glycaemic control and life skills in adolescents with type 1 diabetes: a randomised, controlled intervention study using the Guided Self-Determination-Young method in triads of adolescents, parents and health care providers integrated into routine paediatric outpatient clinics, <i>BMC Pediatrics</i> , 11, 55-, 2011	Protocol for a randomised controlled trial
Insabella,G., Grey,M., Knafel,G., Tamborlane,W., The transition to young adulthood in youth with type 1 diabetes on intensive treatment, <i>Pediatric Diabetes</i> , 8, 228-234, 2007	PICO not met - age range of participants in original study was 12 to 20 years
Ireys,H.T., Chernoff,R., DeVet,K.A., Kim,Y., Maternal outcomes of a randomized controlled trial of a community-based support program for families of children with chronic illnesses, <i>Archives of Pediatrics and Adolescent Medicine</i> , 155, 771-777, 2001	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population not exclusively type 1 diabetes)
Jaser,S.S., Whittemore,R., Ambrosino,J.M., Lindemann,E., Grey,M., Mediators of depressive symptoms in children with type 1 diabetes and their mothers, <i>Journal of Pediatric Psychology</i> , 33, 509-519, 2008	Secondary publication
Kaplan,R.M., Chadwick,M.W., Schimmel,L.E., Social learning intervention to promote metabolic control in type 1 diabetes mellitus: pilot experiment results, <i>Diabetes Care</i> , 8, 152-155, 1985	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (length of follow-up did not meet the inclusion criteria)
Kawamura,T., Kawamura,K., Hirose,M., Hashimoto,T., Higashide,T., Kashihara,Y., Aono,S., Okajima,M., Oguru,M., Harai,H., Training of motivational interviewing to parents improved the glycemic control of the childhood and	Conference abstract

Diagnosis and management of type 1 diabetes in children and young people
Excluded studies

Study	Reason for exclusion
adolescent type 1 diabetes: A prospective randomized control trial, <i>Pediatric Diabetes</i> , 13, 26-, 2012	
Kharrazi,H., Improving healthy behaviors in type 1 diabetic patients by interactive frameworks, AMIA ..., Annual Symposium Proceedings/AMIA Symposium. 2009, 322-326, 2009	PICO not met - no clinical outcomes reported
Kumar,V.S., Wentzell,K.J., Mikkelsen,T., Pentland,A., Laffel,L.M., The DAILY (Daily Automated Intensive Log for Youth) trial: a wireless, portable system to improve adherence and glycemic control in youth with diabetes, <i>Diabetes Technology and Therapeutics</i> , 6, 445-453, 2004	PICO not met - study included children and young people with either type 1 diabetes or type 2 diabetes
LÅ,ding,R.N., Wold,J.E., Skavhaug,A., Graue,M., Evaluation of peer-group support and problem-solving training in the treatment of adolescents with type 1 diabetes, <i>European Diabetes Nursing</i> , 4, 28-33, 2007	Study is non-randomised
Lapp,J., White,N.H., Social networking and peer support (SNAPS) in adolescents with type 1 diabetes mellitus (T1D): A pilot study, <i>Diabetes</i> , 61, A195-, 2012	Conference abstract
Lehmkuhl,H.D., Storch,E.A., Cammarata,C., Meyer,K., Rahman,O., Silverstein,J., Malasanos,T., Geffken,G., Telehealth behavior therapy for the management of type 1 diabetes in adolescents, <i>Journal of Diabetes Science and Technology</i> , 4, 199-208, 2010	PICO not met: follow-up length insufficient
Marrero,DG, Myers,G, Golden,MP, West,D, Adjustment to misfortune: the use of a social support group for adolescent diabetes, <i>Pediatric and Adolescent Endocrinology</i> , 10, 213-218, 1982	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (length of follow-up did not meet the inclusion criteria for the 2015 update review)
Matam,P., Kumaraiah,V., Munichoodappa,C., Kumar,K.M., Aravind,S., Behavioural intervention in the management of compliance in young type-I diabetics, <i>Journal of the Association of Physicians of India</i> , 48, 967-971, 2000	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (participants aged < 22 years with no subgroup analysis for ages relevant to the guideline)
McNamara,R., Robling,M., Hood,K., Bennert,K., Channon,S., Cohen,D., Crowne,E., Hambly,H., Hawthorne,K., Longo,M., Lowes,L., Playle,R., Rollnick,S., Gregory,J.W., Development and Evaluation of a Psychosocial Intervention for Children and Teenagers Experiencing Diabetes (DEPICTED): a protocol for a cluster randomised controlled trial of the effectiveness of a communication skills training programme for healthcare professionals working with young people with type 1 diabetes, <i>BMC Health Services Research</i> , 10, 36-, 2010	Secondary publication
Mendez,F.J., Belendez,M., Effects of a behavioral intervention on treatment adherence and stress management in adolescents with IDDM, <i>Diabetes Care</i> , 20, 1370-1375, 1997	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not a comparative study)
Mulvaney,S.A., Rothman,R.L., Osborn,C.Y., Lybarger,C., Dietrich,M.S., Wallston,K.A., Self-management problem solving for adolescents with type 1 diabetes: intervention processes associated with an Internet program, <i>Patient Education and Counseling</i> , 85, 140-142, 2011	Secondary publication
Mulvaney,S.A., Rothman,R.L., Wallston,K.A., Lybarger,C., Dietrich,M.S., An internet-based program to improve self-management in adolescents with type 1 diabetes, <i>Diabetes Care</i> , 33, 602-604, 2010	PICO not met: insufficient follow-up period (12 weeks)
Murphy,H.R., Wadham,C., Hassler-Hurst,J., Rayman,G., Skinner,T.C., Families and Adolescents Communication and Teamwork Study (FACTS) Group., Randomized trial of a diabetes self-management education and family teamwork intervention in adolescents with Type 1 diabetes, <i>Diabetic Medicine</i> , 29, e249-e254, 2012	PICO not met - intervention not relevant to this question
Murphy,H.R., Wadham,C., Rayman,G., Skinner,T.C., Approaches to integrating paediatric diabetes care and structured education: experiences from the Families, Adolescents, and Children's Teamwork Study (FACTS), <i>Diabetic Medicine</i> , 24, 1261-1268, 2007	PICO not met - intervention not relevant to this question
Naar-King,S., Ellis,D.A., Idalski,A., Frey,M.A., Cunningham,P., Multisystemic therapy decreases parental overestimation of adolescent responsibility for Type 1 diabetes management in urban youth, <i>Families, Systems and Health</i> , 25, 178-189, 2007	Secondary publication
Nansel,T.R., Iannotti,R.J., Liu,A., Clinic-integrated behavioral intervention for families of youth with type 1 diabetes: randomized clinical trial, <i>Pediatrics</i> , 129, e866-e873, 2012	PICO not met - outcomes not reported in sufficient detail
Nansel,T.R., Iannotti,R.J., Simons-Morton,B.G., Plotnick,L.P., Clark,L.M., Zeitoff,L., Long-term maintenance of treatment outcomes: diabetes personal trainer intervention for youth with type 1 diabetes, <i>Diabetes Care</i> , 32, 807-809, 2009	Secondary publication
Nardi,L., Zucchini,S., Petracci,E., Cavrini,G., Maltoni,G., Scipione,M., D'Alberon,F., A randomized controlled study on the effect of a group therapy for parents of youths with type 1 diabetes on quality of life, <i>Pediatric Diabetes</i> , 13, 156-, 2012	Conference abstract
Newton,K.T., Ashley,A., Pilot study of a web-based intervention for adolescents with type 1 diabetes, <i>Journal of Telemedicine and Telecare</i> , 19, 443-449, 2013	7-week intervention outcomes were assessed through an exit survey
Nunn,E., King,B., Smart,C., Anderson,D., A randomized controlled trial of telephone calls to young patients with poorly controlled type 1 diabetes, <i>Pediatric</i>	PICO not met - intervention was support from a healthcare professional

Diagnosis and management of type 1 diabetes in children and young people
Excluded studies

Study	Reason for exclusion
Diabetes, 7, 254-279, 2006	not peer support
Patel,A, Maissi,E., Chang,H.C., Rodrigues,I., Smith,M., Thomas,S., Chalder,T., Schmidt,U., Treasure,J., Ismail,K., Motivational enhancement therapy with and without cognitive behaviour therapy for Type 1 diabetes: economic evaluation from a randomized controlled trial, Diabetic medicine : a journal of the British Diabetic Association, 28, 470-479, 2011	PICO not met - study included adults
Paterson,B.L., Multisystemic therapy improved adherence to blood glucose testing in adolescents with type 1 diabetes, Evidence Based Nursing, 9, 14-14, 2006	Commentary
Pendley,J.S., Kasmien,L.J., Miller,D.L., Donze,J., Swenson,C., Reeves,G., Peer and family support in children and adolescents with type 1 diabetes, Journal of Pediatric Psychology, 27, 429-438, 2002	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (non-comparative study and therefore does not meet the study design inclusion criteria)
Powell,P.W., Hilliard,M.E., Anderson,B.J., Motivational interviewing to promote adherence behaviors in pediatric type 1 diabetes, Current Diabetes Reports, 14, 531-, 2014	This is a literature review
Ridge,K., Bartlett,J., Cheah,Y., Thomas,S., Lawrence-Smith,G., Winkley,K., Ismail,K., Do the effects of psychological treatments on improving glycaemic control in type 1 diabetes persist over time? A long-term follow-up of a randomized controlled trial, Psychosomatic Medicine, 74, 319-323, 2012	Secondary publication
Ryden,O., Nevander,L., Johnsson,P., Hansson,K., Kronvall,P., Sjoblad,S., Westbom,L., Family therapy in poorly controlled juvenile IDDM: Effects on diabetic control, self-evaluation and behavioural symptoms, Acta Paediatrica, International Journal of Paediatrics, 83, 285-291, 1994	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (follow-up period not sufficient)
Sassmann,H., de,Hair M., Danne,T., Lange,K., Reducing stress and supporting positive relations in families of young children with type 1 diabetes: a randomized controlled study for evaluating the effects of the DELFIN parenting program, BMC Pediatrics, 12, 152-, 2012	Although families with children aged 2 to 10 years were selected for the study, the main target population of the intervention was parents; for outcomes related to children, only mean Hb1Ac at 3-month follow-up was reported
Satin,W., La Greca,A.M, Zigo,M.A, Skyler,J.S, Diabetes in adolescence: effects of multifamily group intervention and parent simulation of diabetes, Journal of Pediatric Psychology, 14, 259-275, 1989	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (follow-up does not meet required length)
Scaramuzza,A., Castellani,G., Lorini,R., Insulin abuse in an adolescent with insulin-dependent diabetes mellitus, European Journal of Pediatrics, 155, 526-, 1996	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (this is a letter)
Schachinger,H., Hegar,K., Hermannus,N., Straumann,M., Keller,U., Fehm-Wolfsdorf,G., Berger,W., Cox,D., Randomized controlled clinical trial of Blood Glucose Awareness Training (BGAT III) in Switzerland and Germany, Journal of Behavioral Medicine, 28, 587-594, 2005	Study involving adults
Schafer,L.C., Glasgow,R.E., McCaul,K.D., Increasing the adherence of diabetic adolescents, Journal of Behavioral Medicine, 5, 353-362, 1982	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (case series, not an RCT)
Serlachius,A., Frydenberg,E., Northam,E., Cameron,F., A randomised trial of a psychosocial program to improve glycaemic control and psychosocial wellbeing in adolescents with type 1 diabetes, Pediatric Diabetes, 12, 20-, 2011	Conference abstract
Skocic,Milena, Rudan,Vlasta, Brajkovic,Lovorka, Marcinko,Darko, Relationship among psychopathological dimensions, coping mechanisms, and glycaemic control in a Croatian sample of adolescents with diabetes mellitus type 1, European Child & Adolescent Psychiatry, 19, 525-533, 2010	Wrong study design (cohort study not an RCT)
Suh,S., Jean,C., Koo,M., Lee,S.Y., Cho,M.J., Sim,K.H., Jin,S.M., Bae,J.C., Kim,J.H., A randomized controlled trial of an internet-based mentoring program for type 1 diabetes patients with inadequate glycaemic control, Diabetes and Metabolism Journal, 38, 134-142, 2014	Adult population
Sullivan-Bolyai,S., Bova,C., Lee,M., Johnson,K., Development and pilot testing of a parent education intervention for type 1 diabetes: parent education through simulation-diabetes, Diabetes Educator, 38, 50-57, 2012	PICO not met - outcomes of interest not reported
Sullivan-Bolyai,S., Bova,C., Leung,K., Trudeau,A., Lee,M., Gruppuso,P., Social Support to Empower Parents (STEP): an intervention for parents of young children newly diagnosed with type 1 diabetes, Diabetes Educator, 36, 88-97, 2010	PICO not met - outcomes of interest not reported
Sullivan-Bolyai,S., Grey,M., Deatrick,J., Gruppuso,P., Giraitis,P., Tamborlane,W., Helping other mothers effectively work at raising young children with type 1 diabetes, Diabetes Educator, 30, 476-484, 2004	PICO not met - outcomes of interest not reported
Sullivan-Bolyai,Susan, Bova,Carol, Leung,Katherine, Trudeau,Allison, Lee,Mary, Gruppuso,Philip, Social Support to Empower Parents (STEP): An intervention for parents of young children newly diagnosed with type 1 diabetes, The Diabetes Educator, 36, 88-97, 2010	Intervention not of interest
Sundelin,J., Forsander,G., Mattsson,S.E, Family-oriented support at the onset of diabetes mellitus: a comparison of two group conditions during 2 years following diagnosis, Acta PaediatricaActa Paediatr., 85, 49-55, 1996	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not intervention of

Study	Reason for exclusion
	interest)
Svoren,B.M., Butler,D., Levine,B.S., Anderson,B.J., Laffel,L.M., Reducing acute adverse outcomes in youths with type 1 diabetes: a randomized, controlled trial, Pediatrics, 112, 914-922, 2003	PICO not met - support given by a healthcare professional, not peers
Urban,A.D., Berry,D., Grey,M., Optimizing outcomes in adolescents with type 1 diabetes and their families, Journal of Clinical Outcomes Management, 11, 299-306, 2004	Clinical review, background reading
Viklund,G., Ortqvist,E., Wikblad,K., Assessment of an empowerment education programme. A randomized study in teenagers with diabetes, Diabetic medicine : a journal of the British Diabetic Association, 24, 550-556, 2007	PICO not met - intervention not of interest for this review
Weinger,K., Beverly,E.A., Lee,Y., Sitnikov,L., Ganda,O.P., Caballero,A.E., The effect of a structured behavioral intervention on poorly controlled diabetes: a randomized controlled trial, Archives of Internal Medicine, 171, 1990-1999, 2011	PICO not met - study included adults
Whittemore,R., Grey,M., Lindemann,E., Ambrosino,J., Jaser,S., Development of an Internet coping skills training program for teenagers with type 1 diabetes, CIN: Computers, Informatics, Nursing, 28, 103-111, 2010	Process evaluation
Whittemore,R., Jaser,S.S., Jeon,S., Liberti,L., Delamater,A., Murphy,K., Faulkner.M.S., Grey,M., An internet coping skills training program for youth with type 1 diabetes: six-month outcomes, Nursing Research, 61, 395-404, 2012	PICO not met - outcome results not presented in a usable manner
Wolanski,R., Sigman,T., Polychronakos,C., Assessment of blood glucose self-monitoring skills in a camp for diabetic children: the effects of individualized feedback counselling, Patient Education and CounselingPatient Educ.Couns., 29, 5-11, 1996	Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (follow-up period insufficient)
Wysocki,T., Iannotti,R., Weissberg-Benchell,J., Laffel,L., Hood,K., Anderson,B., Chen,R., Family Management of Childhood Diabetes Steering Committee., Diabetes problem solving by youths with type 1 diabetes and their caregivers: measurement, validation, and longitudinal associations with glycemic control, Journal of Pediatric Psychology, 33, 875-884, 2008	PICO not met: outcome data not reported in sufficient detail
Wysocki,T., Harris,M.A., Buckloh,L.M., Mertlich,D., Lochrie,A.S., Taylor,A., Sadler,M., White,N.H. Randomized, controlled trial of Behavioral Family Systems Therapy for Diabetes: maintenance and generalization of effects on parent-adolescent communication , Behavior Therapy, Vol. 39, Issue 1, 33-46, 2008	Does not report outcomes of interest
Yopp,Justin M., - The impact of family functioning on treatment adherence and metabolic control for adolescents with poorly controlled type 1 diabetes, - Dissertation Abstracts International: Section B: The Sciences and Engineering, 66, 1744-, -32676	Dissertation abstract
Zoffmann,V., Lauritzen,T., Guided self-determination improves life skills with type 1 diabetes and A1C in randomized controlled trial, Patient Education and Counseling, 64, 78-86, 2006	PICO not met - study included adults

H.4 Type 1 diabetes – multiple daily injections

Review question

What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

Study	Reason for exclusion
Influence of intensive diabetes treatment on quality-of-life outcomes in the diabetes control and complications trial, Diabetes Care, 19, 195-203, 1996	PICO criteria not met - comparison is between 3 or more injections per day and 1-2 injections per day
Effect of intensive diabetes treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus: Diabetes Control and Complications Trial. Diabetes Control and Complications Trial Research Group, Journal of Pediatrics, 125, 177-188, 1994	PICO criteria not met - comparison is between 3 or more injections per day and 1-2 injections per day
Weight gain associated with intensive therapy in the diabetes control and complications trial. The DCCT Research Group, Diabetes Care, 11, 567-573, 1988	PICO criteria not met - comparison is between 3 or more injections per day and 1-2 injections per day
Effects of intensive diabetes therapy on neuropsychological function in adults in the Diabetes Control and Complications Trial, Annals of Internal Medicine, 124, 379-388, 1996	PICO criteria not met - comparison is between 3 or more injections per day and 1-2 injections per day
Acharya,S.H., Philip,S., Viswanath,A.K., Boroujerdi,M., Waugh,N.R., Pearson,D.W.M., Glycaemic control and body mass index in late-adolescents and young adults with Type 1 diabetes mellitus: A population-based study, Diabetic	PICO (Patient Intervention Comparator Outcome) criteria not met - age range is 15-25 years, data for insulin regimen comparisons not reported separately for guideline age range

Study	Reason for exclusion
Medicine, 25, 360-364, 2008	
Al-Khawari,M., Al-Ruwayeh,A., Al-Doub,K., Allgrove,J., Adolescents on basal-bolus insulin can fast during Ramadan, <i>Pediatric Diabetes</i> , 11, 96-100, 2010	PICO criteria not met - participants are fasting during Ramadan with follow-up < 4 months
Allen,C., LeCaire,T., Palta,M., Daniels,K., Meredith,M., D'Alessio,D.J., Wisconsin Diabetes Registry Project, Risk factors for frequent and severe hypoglycemia in type 1 diabetes, <i>Diabetes Care</i> , 24, 1878-1881, 2001	PICO criteria not met - comparison is between 3 or more injections per day or continuous subcutaneous insulin infusion (CSII) and less than 3 injections per day
Anderson,D.G., Multiple daily injections in young patients using the ezy-BICC bolus insulin calculation card, compared to mixed insulin and CSII, <i>Pediatric Diabetes</i> , 10, 304-309, 2009	PICO criteria not met - age range is 1-20 years and data for relevant comparisons not reported separately for guideline age range
Azar,S.T., Birbari,A., Nocturnal blood pressure elevation in patients with type 1 diabetes receiving intensive insulin therapy compared with that in patients receiving conventional insulin therapy, <i>Journal of Clinical Endocrinology and Metabolism</i> , 83, 3190-3193, 1998	PICO criteria not met - comparison is between 2 and 3 or more injections per day
Azar,S.T., Zalloua,P.A., Zantout,M.S., Shahine,C.H., Salti,I., Leptin levels in patients with type 1 diabetes receiving intensive insulin therapy compared with those in patients receiving conventional insulin therapy, <i>Journal of Endocrinological Investigation</i> , 25, 724-726, 2002	PICO criteria not met - age range includes 18 years, guideline age range not reported separately
Bangstad,H.J., Danne,T., Deeb,L., Jarosz-Chobot,P., Urakami,T., Hanas,R., Insulin treatment in children and adolescents with diabetes, <i>Pediatric Diabetes</i> , 10, 82-99, 2009	Study criteria not met - consensus guideline
Baroni,M., Vialettes,B., Pozzilli,P., The glucose evaluation trial for remission (GETREM): A european effort to evaluate insulin-dependent diabetes mellitus in the first year after diagnosis, <i>Diabetes and Metabolism</i> , 23, 264-265, 1997	Study criteria not met - description of trial protocol only
Bayrakdar,A., Noureddine,S., Farhood,L., Nasrallah,M.P., Comparison of quality of life in a group of Lebanese type 1 diabetics on insulin pump and those on multiple daily injections, <i>Journal Medical Libanais - Lebanese Medical Journal</i> , 62, 22-26, 2014	The study does not show how many injections were given in the MDI group, wrong study design (cross-sectional study)
Beck,J.K., Lewis,T.V., Logan,K.J., Harrison,D.L., Gardner,A.W., Copeland,K.C., Intensive vs. conventional insulin management initiated at diagnosis in children with diabetes: should payer source influence the choice of therapy?, <i>Pediatric Diabetes</i> , 10, 368-373, 2009	PICO criteria not met - cannot separate CSII and multiple daily injection results
Blair,J.C., Peak,M., Gregory,J.W., What is the best way to deliver subcutaneous insulin to infants, children, and young people with type 1 diabetes mellitus?, <i>BMJ (Online)</i> , 343, -, 2011	PICO criteria not met - continuous subcutaneous insulin infusion versus multiple daily injections
Blasetti,A., Di,Giulio C., Tocco,A.M., Verrotti,A., Tumini,S., Chiarelli,F., Altobelli,E., Variables associated with severe hypoglycemia in children and adolescents with type 1 diabetes: a population-based study, <i>Pediatric Diabetes</i> , 12, 4-10, 2011	PICO criteria not met - all participants were using multiple daily injections
Bloomgarden,Z.T., Diabetes issues in women and children, <i>Diabetes Care</i> , 26, 2457-2463, 2003	Study criteria not met - narrative review
Bolli,G.B., Rationale for using combinations of short-acting insulin analogue and NPH insulin at mealtime in the treatment of type 1 diabetes mellitus. [18 refs], <i>Journal of Pediatric Endocrinology</i> , 12 Suppl 3, 737-744, 1999	Study criteria not met - narrative review
Bougneres,P.F., Landais,P., Mairesse,A.M., Jais,J.P., Jos,J., Peyraud,J., Wieliczko,M.C., Chavoix,P., Garandeau,P., Asensi,D., Improvement of diabetic control and acceptability of a three-injection insulin regimen in diabetic adolescents. A multicenter controlled study, <i>Diabetes Care</i> , 16, 94-102, 1993	PICO criteria not met - comparison is between 2 and 3 injections per day
Brinchmann-Hansen,O., Dahl-Jorgensen,K., Hanssen,K.F., Sandvik,L., Effects of intensified insulin treatment on various lesions of diabetic retinopathy, <i>American Journal of Ophthalmology</i> , , 644-653, 1985	PICO criteria not met - age range 18-45 years
Bulsara,M.K., Holman,C.D., Davis,E.A., Jones,T.W., The impact of a decade of changing treatment on rates of severe hypoglycemia in a population-based cohort of children with type 1 diabetes, <i>Diabetes Care</i> , 27, 2293-2298, 2004	PICO criteria not met - comparison is between 2 and 3 injections per day

Study	Reason for exclusion
Callaghan,Brian C., Little,Ann A., Feldman,Eva L., Hughes,AC Richard, Enhanced glucose control for preventing and treating diabetic neuropathy, Cochrane Database of Systematic Reviews, -, 2012	PICO criteria not met - interventions are a mixture of advice, insulin, and pancreas transplant; data for young people included but not reported separately; references checked
Cemeroglu,A.P., Kleis,L., Wood,A., Parkes,C., Wood,M.A., Davis,A.T., Comparison of the effect of insulin glulisine to insulin aspart on breakfast postprandial blood glucose levels in children with type 1 diabetes mellitus on multiple daily injections, Endocrine Practice, 19, 614-619, 2013	Case study, cross-over, not clear about frequency of MDI
Cengiz,E., Swan,K.L., Tamborlane,W.V., Sherr,J.L., Martin,M., Weinzimer,S.A., The alteration of aspart insulin pharmacodynamics when mixed with detemir insulin, Diabetes Care, 35, 690-692, 2012	PICO criteria not met - follow-up < 4 months
Cengiz,E., Tamborlane,W.V., Martin-Fredericksen,M., Dziura,J., Weinzimer,S.A., Early pharmacokinetic and pharmacodynamic effects of mixing lispro with glargine insulin: results of glucose clamp studies in youth with type 1 diabetes, Diabetes Care, 33, 1009-1012, 2010	PICO criteria not met - follow-up < 4 months
Centre for Reviews and Dissemination., Effect of intensive therapy on early macrovascular disease in young individuals with type 1 diabetes: a systematic review and meta-analysis (Structured abstract), Database of Abstracts of Reviews of Effects, -, 2012	PICO criteria not met - age range is 18-50 years
Chapman,T.M., Noble,S., Goa,K.L., Insulin aspart: a review of its use in the management of type 1 and 2 diabetes mellitus. [100 refs][Erratum appears in Drugs. 2003;63(5):512.], Drugs, 62, 1945-1981, 2002	PICO criteria not met - comparison is between two multiple daily injection regimens
Chapman,T.M., Perry,C.M., Spotlight on insulin detemir in type 1 and 2 diabetes mellitus, Biodrugs, 19, 67-69, 2005	Study criteria not met - summary article; references checked
Chase,H.P., Rose,B., Hoops,S., Archer,P.G., Cribari,J.M., Techniques for improving glucose control in type I diabetes, Pediatrician, 12, 229-235, 1983	PICO criteria not met - number of injections per day not reported for all participants
Chase,H.P., Dixon,B., Pearson,J., Fiallo-Scharer,R., Walravens,P., Klingensmith,G., Rewers,M., Garg,S.K., Reduced hypoglycemic episodes and improved glycemic control in children with type 1 diabetes using insulin glargine and neutral protamine Hagedorn insulin, Journal of Pediatrics, 143, 737-740, 2003	PICO criteria not met - participants had a mixture of treatments before switching to basal-bolus regimen but these were not reported separately
Chase,H.P., Garg,S.K., Hoops,S.L., Harris,S., Wilcox,W., Use of the pen delivery system for intensive insulin therapy in college-age students with type I diabetes, Journal of Adolescent Health, 12, 373-376, 1991	PICO criteria not met - age range includes 18 years, but data for guideline age range not reported separately
Clarke,W.L., The Diabetes Control and Complications Trial: new challenges for the primary physician, Virginia Medical Quarterly, 121, 185-188, 1994	PICO criteria not met - multiple daily injections defined as 3 injections per day
Craig,M.E., Jones,T.W., Silink,M., Ping,Y.J., Diabetes care, glycemic control, and complications in children with type 1 diabetes from Asia and the Western Pacific Region, Journal of Diabetes and its Complications, 21, 280-287, 2007	Incomplete data for comparisons of interest
Craig,M.E., Handelsman,P., Donaghue,K.C., Chan,A., Blades,B., Laina,R., Bradford,D., Middlehurst,A., Ambler,G., Verge,C.F., Crock,P., Moore,P., Silink,M., ACT,HbA, Predictors of glycaemic control and hypoglycaemia in children and adolescents with type 1 diabetes from NSW and the ACT, Medical Journal of Australia, 177, 235-238, 2002	Incomplete data for comparisons of interest
Da,SilvaJoseL, Cardoso-Demartini,A.D.A., Liberatore,JuniorR, Paulino,M.F.V.M., De,Lemos MariniS, Guerra-Junior,G., Rodrigues,A.G., Clinical and laboratory profile of pediatric and adolescent patients with type 1 diabetes, Jornal de Pediatria, 85, 490-494, 2009	PICO criteria not met - participants received 1, 2 or 3 injections per day; age range is 3-26 years
DAFNE Study Group, Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: dose adjustment for normal eating (DAFNE) randomised controlled trial, BMJ, 746-748, 2002	PICO criteria not met - age range is 18 years or older
Dahl-Jorgensen,K., Near-normoglycemia and late diabetic complications. The Oslo Study, Acta Endocrinologica, , 1-38, 1987	PICO criteria not met - age range 18-45 years

Study	Reason for exclusion
Dahl-Jorgensen,K., Bjoro,T., Kierulf,P., Sandvik,L., Bangstad,H.J., Hanssen,K.F., Long-term glyceemic control and kidney function in insulin-dependent diabetes mellitus, <i>Kidney International</i> , , 920-923, 1992	PICO criteria not met - age range 18-45 years
Dahl-Jorgensen,K., Brinchmann-Hansen,O., Hanssen,K.F., Sandvik,L., Aagenaes,O., Rapid tightening of blood glucose control leads to transient deterioration of retinopathy in insulin dependent diabetes mellitus: the Oslo study, <i>British Medical Journal Clinical Research Ed.</i> , , 811-815, 1985	PICO criteria not met - age range 18-45 years
Dahl-Jorgensen,K., Hanssen,K.F., Kierulf,P., Bjoro,T., Sandvik,L., Aagenaes,O., Reduction of urinary albumin excretion after 4 years of continuous subcutaneous excretion after 4 years of continuous subcutaneous infusion in insulin-dependent diabetes mellitus. The Oslo Study, <i>Acta Endocrinologica</i> , , 19-25, 1988	PICO criteria not met - age range 18-45 years
Dahl-Jorgensen,K., Torjesen,P., Hanssen,K.F., Sandvik,L., Aagenaes,O., Increase in insulin antibodies during continuous subcutaneous insulin infusion and multiple-injection therapy in contrast to conventional treatment, <i>Diabetes</i> , , 1-5, 1987	PICO criteria not met - age range 18-42 years
Daneman,D., Wolfson,D.H., Becker,D.J., Drash,A.L., Factors affecting glycosylated hemoglobin values in children with insulin-dependent diabetes, <i>Journal of Pediatrics</i> , 99, 847-853, 1981	PICO criteria not met - comparison is between 1 and 2 injections per day
Danne,T., Mortensen,H.B., Hougaard,P., Lynggaard,H., Aanstoot,H.J., Chiarelli,F., Daneman,D., Dorchy,H., Garandeau,P., Greene,S.A., Hoey,H., Holl,R.W., Kaprio,E.A., Kocova,M., Martul,P., Matsuura,N., Robertson,K.J., Schoenle,E.J., Sovik,O., Swift,P.G., Tsou,R.M., Vanelli,M., Aman,J., Hvidore Study Group on Childhood Diabetes., Persistent differences among centers over 3 years in glyceemic control and hypoglycemia in a study of 3,805 children and adolescents with type 1 diabetes from the Hvidore Study Group, <i>Diabetes Care</i> , 24, 1342-1347, 2001	PICO criteria not met - no data reported on absolute number of injections (change in number only)
de,BeaufortC, Hypoglycemia during intensified insulin therapy of young children, <i>Journal of Pediatric Endocrinology and Metabolism</i> , 11, 153-158, 1998	PICO criteria not met - comparison is between 1-2 and 3 or more injections per day
Deiss,D., Kordonouri,O., Hartmann,R., Hopfenmuller,W., Lupke,K., Danne,T., Treatment with insulin glargine reduces asymptomatic hypoglycemia detected by continuous subcutaneous glucose monitoring in children and adolescents with type 1 diabetes, <i>Pediatric Diabetes</i> , 8, 157-162, 2007	PICO criteria not met - follow up < 4 months
Deja,G., Jarosz-Chobot,P., Polanska,J., The rate of improvement in metabolic control in children with diabetes mellitus type 1 on insulin glargine depends on age, <i>Experimental and Clinical Endocrinology and Diabetes</i> , 115, 662-668, 2007	PICO criteria not met - comparison is between two versions of a multiple daily injection regimen
Distiller,L.A., Robertson,L.I., Moore,R., Bonnici,F., A bolus/basal multiple injection regimen in type I diabetes. A multicentre trial using a new 'fountain-pen' device for short-acting human insulin as well as long-acting human insulin, <i>South African Medical Journal, Suid-Afrikaanse Tydskrif Vir Geneeskunde</i> . 71, 749-752, 1987	PICO criteria not met - follow up < 4 months
Downie,E., Craig,M.E., Hing,S., Cusumano,J., Chan,A.K., Donaghue,K.C., Continued reduction in the prevalence of retinopathy in adolescents with type 1 diabetes: role of insulin therapy and glyceemic control, <i>Diabetes Care</i> , 34, 2368-2373, 2011	PICO criteria not met - multiple daily injections defined as 3 injections per day and results combined with those for CSII
Dunn,C.J., Plosker,G.L., Keating,G.M., McKeage,K., Scott,L.J., Insulin glargine: an updated review of its use in the management of diabetes mellitus. [111 refs], <i>Drugs</i> , 63, 1743-1778, 2003	PICO criteria not met - comparison is between two multiple daily injection regimens
Ebeling,P., Jansson,P.A., Smith,U., Lalli,C., Bolli,G.B., Koivisto,V.A., Strategies toward improved control during insulin lispro therapy in IDDM. Importance of basal insulin, <i>Diabetes Care</i> , 20, 1287-1289, 1997	PICO criteria not met - age range 18-60 years
Egger,M, Smith,GD, Stettler,C, Diem,P, Risk of adverse effects of intensified treatment in insulin-dependent diabetes mellitus: a meta-analysis, <i>Diabetic Medicine</i> , , 919-928, 1997	PICO criteria not met - all included trials are in adults (outside guideline age range)

Study	Reason for exclusion
Fairchild,J.M., Ambler,G.R., Genoud-Lawton,C.H., Westman,E.A., Chan,A., Howard,N.J., Crock,P.A., Nunn,E.A., Silink,M., Insulin lispro versus regular insulin in children with type 1 diabetes on twice daily insulin, <i>Pediatric Diabetes</i> , 1, 135-141, 2000	PICO criteria not met - both treatment arms received 2 injections per day of mixed insulins
Fasching,P., Derfler,K., Maca,T., Kurzemann,S., Howorka,K., Schneider,B., Zirm,M., Waldhausl,W., Feasibility and efficacy of intensive insulin therapy in type 1 diabetes mellitus in primary care, <i>Diabetic Medicine</i> , 11, 836-842, 1994	PICO criteria not met - age range is 8-57 years
Fiallo-Scharer,R., Horner,B., McFann,K., Walravens,P., Chase,H.P., Mixing rapid-acting insulin analogues with insulin glargine in children with type 1 diabetes mellitus, <i>Journal of Pediatrics</i> , 148, 481-484, 2006	PICO criteria not met - comparison is between two versions of a multiple daily injection regimen
Franklin,V.L., Khan,F., Kennedy,G., Belch,J.J., Greene,S.A., Intensive insulin therapy improves endothelial function and microvascular reactivity in young people with type 1 diabetes, <i>Diabetologia</i> , 51, 353-360, 2008	PICO criteria not met - cannot separate CSII and multiple daily injection results
Franklin,V.L., Waller,A., Pagliari,C., Greene,S.A., A randomized controlled trial of Sweet Talk, a text-messaging system to support young people with diabetes, <i>Diabetic Medicine</i> , 23, 1332-1338, 2006	PICO criteria not met - cannot separate CSII and multiple daily injection results
Garg,S.K., Carmain,J.A., Braddy,K.C., Anderson,J.H., Vignati,L., Jennings,M.K., Chase,H.P., Pre-meal insulin analogue insulin lispro vs Humulin R insulin treatment in young subjects with type 1 diabetes, <i>Diabetic Medicine</i> , 13, 47-52, 1996	PICO criteria not met - age range includes 18 years, with the guideline age range not reported separately
Garnock-Jones,K.P., Plosker,G.L., Insulin glulisine: A review of its use in the management of diabetes mellitus, <i>Drugs</i> , 69, 1035-1057, 2009	PICO criteria not met - comparison is between two multiple daily injection regimens
Gerstl,E.M., Rabl,W., Rosenbauer,J., Grobe,H., Hofer,S.E., Krause,U., Holl,R.W., Metabolic control as reflected by HbA1c in children, adolescents and young adults with type-1 diabetes mellitus: Combined longitudinal analysis including 27,035 patients from 207 centers in Germany and Austria during the last decade, <i>European Journal of Pediatrics</i> , 167, 447-453, 2008	PICO criteria not met - no data reported on insulin regimens
Gibb,D.M., Foot,A.B., May,B., Parish,H., Strang,S., Grant,D.B., Dunger,D.B., Human isophane or lente insulin? A double blind crossover trial in insulin dependent diabetes mellitus, <i>Archives of Disease in Childhood</i> , 65, 1334-1337, 1990	PICO criteria not met - both treatment arms received < 4 injections per day
Golden,M.P., Russell,B.P., Ingersoll,G.M., Gray,D.L., Hummer,K.M., Management of diabetes mellitus in children younger than 5 years of age, <i>American Journal of Diseases of Children</i> , 139, 448-452, 1985	PICO criteria not met - all participants on two injections per day
Golenko,A., Noczynska,A., An evaluation of physical development and metabolic control in children with type 1 diabetes mellitus receiving treatment with various insulin regimens. Part 1, <i>Diabetologia Doswiadczalna i Kliniczna</i> , 8, 115-123, 2008	PICO criteria not met - number of injections not reported
Gomes,M.B., Negrato,C.A., Cobas,R., Tannus,L.R.M., Goncalves,P.R., Da,SilvaP, Carneiro,J.R.I., Matheus,A.S.M., Dib,S.A., Azevedo,M.J., Nery,M., Rodacki,M., Zajdenverg,L., Montenegro,JuniorR, Sepulveda,J., Calliari,L.E., Jezini,D., Braga,N., Luescher,J.L., Berardo,R.S., rruda-Marques,M.C., Noronha,R.M., Manna,T.D., Salvodelli,R., Penha,F.G., Foss,M.C., Foss-Freitas,M.C., Pires,A.C., Robles,F.C., Guedes,M.D.F.S., Dualib,P., Silva,S.C., Sampaio,E., Rea,R., Faria,A.C.R., Tschiedel,B., Lavigne,S., Canani,L.H., Zucatti,A.T., Coral,M.H.C., Pereira,D.A., Araujo,L.A., Tolentino,M., Pedrosa,H.C., Prado,F.A., Rassi,N., Araujo,L.B., Fonseca,R.M.C., Guedes,A.D., Matos,O.S., Palma,C.C., Azulay,R., Forti,A.C., Facanha,C., Montenegro,A.P., Melo,N.H., Rezende,K.F., Ramos,A., Felicio,J.S., Santos,F.M., Determinants of intensive insulin therapeutic regimens in patients with type 1 diabetes: Data from a nationwide multicenter survey in Brazil, <i>Diabetology and Metabolic Syndrome</i> , 6, -, 2014	Interventions were 1-2 mixed vs monotherapy
Granado,F., Olmedilla,B., Botella,F., Simal,A., Blanco,I.,	PICO criteria not met - age range is 14-35 years

Study	Reason for exclusion
Retinol and alpha-tocopherol in serum of type 1 diabetic patients with intensive insulin therapy: a long term follow-up study, <i>Nutrition</i> , 19, 128-132, 2003	
Greene,S.A., Robertson,L., Royle,P., Robertson,A., Waugh,N., Rae,P., Patterson,C., A longitudinal observational study of insulin therapy and glycaemic control in Scottish children with Type 1 diabetes: DIABAUD 3, <i>Diabetic Medicine</i> , 23, 1216-1221, 2006	PICO criteria not met - data reported for 2 and 3 injections per day only
Grey,M., Boland,E.A., Tamborlane,W.V., Use of lispro insulin and quality of life in adolescents on intensive therapy, <i>Diabetes Educator</i> , 25, 934-941, 1999	PICO criteria not met - comparison is between two versions of a multiple daily injection regimen
Hanberger,L., Ludvigsson,J., Nordfeldt,S., Health-related quality of life in intensively treated young patients with type 1 diabetes, <i>Pediatric Diabetes</i> , 10, 374-381, 2009	Incomplete data for comparisons of interest
Hanssen,K.F., Dahl-Jorgensen,K., Brinchmann-Hansen,O., The influence of strict control on diabetic complications, <i>Acta Endocrinologica</i> , , 57-60, 1985	PICO criteria not met - age range is 18-42 years
Haugstvedt,A., Wentzel-Larsen,T., Rokne,B., Graue,M., Psychosocial family factors and glycemic control among children aged 1-15 years with type 1 diabetes: A population-based survey, <i>BMC Pediatrics</i> , 11 , 2011. Article Number, -, 2011	PICO criteria not met - all participants received multiple daily injections or CSII
Hayes,R.L., Garnett,S.P., Clarke,S.L., Harkin,N.M., Chan,A.K., Ambler,G.R., A flexible diet using an insulin to carbohydrate ratio for adolescents with type 1 diabetes - a pilot study, <i>Clinical Nutrition</i> , 31, 705-709, 2012	PICO criteria not met - all participants were using multiple daily injections
Heath,V., Diabetes: Basal insulin glargine decreases adolescent glycemic variability, <i>Nature Reviews Endocrinology</i> , 5, 183-, 2009	Summary of trial reported elsewhere (White et al 2009, weeded out)
Hecker,W., Grabert,M., Holl,R.W., Quality of paediatric IDDM care in germany: A multicentre analysis, <i>Journal of Pediatric Endocrinology and Metabolism</i> , 12, 31-38, 1999	PICO criteria not met - no comparative data reported
Hershey,T, Bhargava,N, Sadler,M, White,NH, Craft,S, Conventional versus intensive diabetes therapy in children with type 1 diabetes: effects on memory and motor speed, <i>Diabetes Care</i> , 1318-1324, 1999	PICO criteria not met - comparison is between 3 or more injections per day and 1-2 injections per day
Holl,R.W., Swift,P.G., Mortensen,H.B., Lynggaard,H., Hougaard,P., Aanstoot,H.J., Chiarelli,F., Daneman,D., Danne,T., Dorchy,H., Garandeanu,P., Greene,S., Hoey,H.M., Kaprio,E.A., Kocova,M., Martul,P., Matsuura,N., Robertson,K.J., Schoenle,E.J., Sovik,O., Tsou,R.M., Vanelli,M., Aman,J., Insulin injection regimens and metabolic control in an international survey of adolescents with type 1 diabetes over 3 years: results from the Hvidore study group, <i>European Journal of Pediatrics</i> , 162, 22-29, 2003	PICO criteria not met - cannot separate CSII and multiple daily injection results
Holman,RR, Mayon-White,V, Orde-Peckar,C, Steemson,J, Smith,B, McPerson,K, Prevention of deterioration of renal and sensory-nerve function by more intensive management of insulin-dependent diabetic patients. A two-year randomised prospective study, <i>Lancet</i> , 204-208, 1983	PICO criteria not met - age range is 21-60 years
HOSTOMSKA,L., KOPECKY,A., Insulin mixtures in the treatment of diabetes in children, <i>Review of Czechoslovak Medicine</i> , 2, 261-264, 1956	PICO criteria not met - no comparisons of interest reported
Houtzaggers,C.M., van,der,V, Multiple daily insulin injections: a multicentre study on acceptability and efficacy, <i>Netherlands Journal of Medicine</i> , 33, 16-25, 1988	PICO criteria not met - age range is 14-70 years, and follow-up < 4 months
Houtzaggers,CM, Berntzen,PA, van der Stap,H, van Maarschalkerweerd,WW, Lanting,P, Boen-Tan,I, Efficacy and acceptance of two intensified conventional insulin therapy regimens: a long-term cross-over comparison, <i>Diabetic Medicine</i> , 416-421, 1989	PICO criteria not met - age range is 18-63 years
Houtzaggers,CM, Visser,SP, Berntzen,PA, van der Stap,H, van Maarschalkerweerd,WW, Heine,RJ, Multiple daily insulin injections improve self-confidence, <i>Diabetic Medicine</i> , 512-519, 1989	PICO criteria not met - age range is 18-65 years
Institut fuer Qualitaet und Wirtschaftlichkeit im,Gesundheitswesen., Rapid-acting insulin analogues in the treatment of diabetes mellitus type 1 (Structured abstract), <i>Health Technology Assessment Database</i> , -, 2012	Non-English language

Study	Reason for exclusion
Jabbari,M., Bin-Abbas,B., Al-Fares,A., Basal-bolus insulin regimen using insulin detemir in type 1 diabetic Saudi children, <i>Current Pediatric Research</i> , 14, 108-110, 2010	PICO criteria not met - follow-up < 4 months, < 10 participants
Jackson,A., Ternand,C., Brunzell,C., Kleinschmidt,T., Dew,D., Milla,C., Moran,A., Insulin glargine improves hemoglobin A1c in children and adolescents with poorly controlled type 1 diabetes, <i>Pediatric Diabetes</i> , 4, 64-69, 2003	PICO criteria not met - comparison is between two versions of a multiple daily injection regimen
Jarosz-Chobot,P., Guthrie,D.W., Otto-Buczowska,E., Koehler,B., Self-care of young diabetics in practice, <i>Medical Science Monitor</i> , 6, 129-132, 2000	PICO criteria not met - details of insulin regimens not reported
Kaplan,W., Rodriguez,L.M., Smith,O.E., Haymond,M.W., Heptulla,R.A., Effects of mixing glargine and short-acting insulin analogs on glucose control, <i>Diabetes Care</i> , 27, 2739-2740, 2004	PICO criteria not met - follow-up < 4 months
Karaguzel,G., Satilmis,A., Akcurin,S., Bircan,I., Comparison of breakfast and bedtime administration of insulin glargine in children and adolescents with Type 1 diabetes, <i>Diabetes Research and Clinical Practice</i> , 74, 15-20, 2006	PICO criteria not met - comparison is between two versions of a multiple daily injection regimen
Katz,M.L., Volkening,L.K., Anderson,B.J., Laffel,L.M., Contemporary rates of severe hypoglycaemia in youth with Type 1 diabetes: variability by insulin regimen, <i>Diabetic Medicine</i> , 29, 926-932, 2012	PICO criteria not met - number of injections not stated and regimens unclear
Khadilkar,V.V., Khadilkar,A.V., Concomitant use of insulin glargine and NPH in type I diabetes, <i>Indian Pediatrics</i> , 42, 796-800, 2005	PICO criteria not met - comparison is between two regimens of 2 injections per day
Kimura,S., Nose,O., Tajiri,H., Miki,K., Yabuuchi,H., Shichiri,M., Harada,T., Efficacy of a multiple insulin injection regimen in teenagers with insulin-dependent diabetes. Carbohydrate and lipid oxidation measured by continuous indirect calorimetry, <i>Diabetes Research and Clinical Practice</i> , 4, 77-79, 1987	Study criteria not met - < 10 participants
Knerr,I., Hofer,S.E., Holterhus,P.M., Nake,A., Rosenbauer,J., Weitzel,D., Wolf,J., Holl,R.W., Prevailing therapeutic regimes and predictive factors for prandial insulin substitution in 26 687 children and adolescents with Type 1 diabetes in Germany and Austria, <i>Diabetic Medicine</i> , 24, 1478-1481, 2007	PICO criteria not met - age range includes > 18 years, guideline age range not reported separately
Laron,Z., Childhood diabetes towards the 21st century, <i>Journal of Pediatric Endocrinology and Metabolism</i> , 11, 387-402, 1998	Study criteria not met - narrative review
Lawson,M.L., Gerstein,H.C., Tsui,E., Zinman,B., Effect of intensive therapy on early macrovascular disease in young individuals with type 1 diabetes. A systematic review and meta-analysis, <i>Diabetes Care</i> , 22 Suppl 2, B35-B39, 1999	PICO criteria not met - all included trials were in adults
Leelarathna,L., Guzder,R., Muralidhara,K., Evans,M.L., Diabetes: glycaemic control in type 1, <i>Clinical Evidence</i> , 2011, 2011., -, 2011	PICO criteria not met - multiple daily injections versus CSII
Limbert,C., Schwingshandl,J., Haas,J., Roth,R., Borkenstein,M., Severe hypoglycemia in children and adolescents with IDDM: frequency and associated factors, <i>Journal of Diabetes and its Complications</i> , 7, 216-220, 1993	PICO criteria not met - age range is 4-25 years
Linn,T., Ortac,K., Laube,H., Federlin,K., Intensive therapy in adult insulin-dependent diabetes mellitus is associated with improved insulin sensitivity and reserve: a randomized, controlled, prospective study over 5 years in newly diagnosed patients, <i>Metabolism: Clinical and Experimental</i> , 45, 1508-1513, 1996	PICO criteria not met - comparison is between 3 or more injections per day and 1-2 injections per day
Maiorino,M.I., Bellastella,G., Petrizzo,M., Improta,M.R., Brancario,C., Castaldo,F., Olita,L., Giugliano,D., Treatment satisfaction and glycemic control in young Type 1 diabetic patients in transition from pediatric health care: CSII versus MDI, <i>Endocrine</i> , 46, 256-262, 2014	Age group 18-25 years
Martin,D., Licha-Muntz,G., Grasset,E., Greneche,M.O., Nouet,D., Francois,L., Legrand,C., Polak,M., ugendre-Ferrante,B., Tubiana-Rufi,N., Robert,J.J., Efficacy of Humalog injections before an afternoon meal and their acceptance by children and adolescents with type 1 diabetes, <i>Diabetic Medicine</i> , 19, 1026-1031, 2002	PICO criteria not met - boths arms had fewer than 4 injections per day

Study	Reason for exclusion
McCaughey, E.S., Betts, P.R., Rowe, D.J., Improved diabetic control in adolescents using the Penject syringe for multiple insulin injections, <i>Diabetic Medicine</i> , 3, 234-236, 1986	PICO criteria not met - length of follow-up < 4 months
McKeage, K., Goa, K.L., Insulin glargine: a review of its therapeutic use as a long-acting agent for the management of type 1 and 2 diabetes mellitus. [70 refs], <i>Drugs</i> , 61, 1599-1624, 2001	PICO criteria not met - comparison is between two multiple daily injection regimens
Menon, P.S.N., Virmani, A., Rationale of insulin therapy in insulin-dependent diabetes mellitus in children, <i>Indian Pediatrics</i> , 27, 1201-1208, 1990	Study criteria not met - narrative review
Microalbuminuria Collaborative Study Group, Intensive therapy and progression to clinical albuminuria in patients with insulin-dependent diabetes mellitus and microalbuminuria, <i>BMJ</i> , 973-977, 1995	PICO criteria not met - age range 17-59 years
Mohn, A., Strang, S., Wernicke-Panten, K., Lang, A.M., Edge, J.A., Dunger, D.B., Nocturnal glucose control and free insulin levels in children with type 1 diabetes by use of the long-acting insulin HOE 901 as part of a three-injection regimen, <i>Diabetes Care</i> , 23, 557-559, 2000	PICO criteria not met - both treatment arms include fewer than 4 injections per day
Mortensen, H.B., Outcome of quality management in pediatric diabetes care, <i>Hormone Research</i> , 50, 57-61, 1998	Incomplete data for comparisons of interest
Mortensen, H.B., Hougaard, P., Comparison of metabolic control in a cross-sectional study of 2,873 children and adolescents with IDDM from 18 countries. The Hvidovre Study Group on Childhood Diabetes. [Erratum appears in <i>Diabetes Care</i> 1997 Jul;20(7):1216], <i>Diabetes Care</i> , 20, 714-720, 1997	Incomplete data for comparisons of interest
Mortensen, H.B., Robertson, K.J., Aanstoot, H.J., Danne, T., Holl, R.W., Hougaard, P., Atchison, J.A., Chiarelli, F., Daneman, D., Dinesen, B., Dorchy, H., Garandeau, P., Greene, S., Hoey, H., Kaprio, E.A., Kocova, M., Martul, P., Matsuura, N., Schoenle, E.J., Sovik, O., Swift, P.G., Tsou, R.M., Vanelli, M., Aman, J., Insulin management and metabolic control of type 1 diabetes mellitus in childhood and adolescence in 18 countries. Hvidovre Study Group on Childhood Diabetes, <i>Diabetic Medicine</i> , 15, 752-759, 1998	PICO criteria not met - no relevant comparisons reported
Mortensen, H.B., Villumsen, J., Volund, A., Petersen, K.E., Nerup, J., Relationship between insulin injection regimen and metabolic control in young Danish type 1 diabetic patients. The Danish Study Group of Diabetes in Childhood, <i>Diabetic Medicine</i> , 9, 834-839, 1992	PICO criteria not met - multiple daily injections defined as 3 injections per day
Muhlhauser, I., Bruckner, I., Berger, M., Cheta, D., Jorgens, V., Ionescu-Tirgoviste, C., Scholz, V., Mincu, I., Evaluation of an intensified insulin treatment and teaching programme as routine management of type 1 (insulin-dependent) diabetes. The Bucharest-Dusseldorf Study, <i>Diabetologia</i> , 30, 681-690, 1987	PICO criteria not met - comparison is between 2 and > 2 injections per day
Nathan, D.M., McKittrick, C., Larkin, M., Schaffran, R., Singer, D.E., Glycemic control in diabetes mellitus: Have changes in therapy made a difference?, <i>American Journal of Medicine</i> , 100, 157-163, 1996	PICO criteria not met - age range includes over 18 years, data for relevant comparisons not reported separately for guideline age range
Neu, A., Beyer, P., Burger-Busing, J., Danne, T., Etspuler, J., Heidtmann, B., Holl, R.W., Karges, B., Kiess, W., Knerr, I., Kordonouri, O., Lange, K., Lepler, R., Marg, W., Nake, A., Petersen, M., Podeswik, A., Stachow, R., Von, Sengbusch, S., Wagner, V., Ziegler, R., Holterhus, P.M., Diagnosis, therapy and control of diabetes mellitus in children and adolescents, <i>Experimental and Clinical Endocrinology and Diabetes</i> , 122, 425-434, 2014	This is a review
Nguyen, T.M., Renukuntla, V.S., Heptulla, R.A., Mixing insulin aspart with detemir does not affect glucose excursion in children with type 1 diabetes, <i>Diabetes Care</i> , 33, 1750-1752, 2010	PICO criteria not met - follow-up < 4 months
Nordfeldt, S., Ludvigsson, J., Severe hypoglycemia in children with IDDM. A prospective population study, 1992-1994, <i>Diabetes Care</i> , 20, 497-503, 1997	PICO criteria not met - no comparison of insulin regimens
Ollenschlager, G., Hummerich, W., Steffen, M., Reincke, M., Allolio, B., Winelmann, W., Management and efficacy of intensified insulin therapy - starting in outpatients, <i>Klinische</i>	PICO criteria not met - mean age of participants outside guideline age range

Study	Reason for exclusion
Wochenschrift, 60-65, 1989	
Olsen,B.S., Johannesen,J., Sjolie,A.K., Borch-Johnsen,K., Hougaard,P., Thorsteinsson,B., Pramming,S., Marinelli,K., Mortensen,H.B., Metabolic control and prevalence of microvascular complications in young Danish patients with Type 1 diabetes mellitus, <i>Diabetic Medicine</i> , 16, 79-85, 1999	Incomplete data for comparisons of interest
Olsen,B.S., Sjolie,A.K., Hougaard,P., Johannesen,J., Borch-Johnsen,K., Marinelli,K., Thorsteinsson,B., Pramming,S., Mortensen,H.B., A 6-year nationwide cohort study of glycaemic control in young people with Type 1 diabetes: Risk markers for the development of retinopathy, nephropathy and neuropathy, <i>Journal of Diabetes and its Complications</i> , 14, 295-300, 2000	PICO criteria not met - no information on insulin regimens reported
Pais,V., Burkot,I., Buccino,J., Daneman,D., Is there a relationship between type of insulin regimen and dietary intake in adolescents with type 1 diabetes?, <i>Canadian Journal of Diabetes</i> , 34, 334-339, 2010	PICO criteria not met - no relevant outcomes reported
Palta,M., Shen,G., Allen,C., Klein,R., D'Alessio,D., Longitudinal patterns of glycemic control and diabetes care from diagnosis in a population-based cohort with type 1 diabetes, <i>American Journal of Epidemiology</i> , 144, 954-961, 1996	PICO criteria not met - no relevant comparisons reported
Paus,P.N., Jervell,J., Berg,T.J., Frosta,T., Larsen,S., [NovoPen. An aid in multi-injection insulin therapy], <i>Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke</i> , 106, 1943-1946, 1986	Non-English language
Pieber,T.R., Treichel,H.C., Hompesch,B., Philotheou,A., Mordhorst,L., Gall,M.A., Robertson,L.L., Comparison of insulin detemir and insulin glargine in subjects with Type 1 diabetes using intensive insulin therapy, <i>Diabetic Medicine</i> , 24, 635-642, 2007	PICO criteria not met - age range is 18 years and older
Rabbone,I., Scaramuzza,A.E., Ignaccolo,M.G., Tinti,D., Sicignano,S., Redaelli,F., De,Angelis L., Bosetti,A., Zuccotti,G.V., Cerutti,F., Carbohydrate counting with an automated bolus calculator helps to improve glycaemic control in children with type 1 diabetes using multiple daily injection therapy: an 18-month observational study, <i>Diabetes Research and Clinical Practice</i> , 103, 388-394, 2014	This study is an observational study
Reichard,P, Berglund,A, Britz,A, Levander,S, Rosenqvist,U, Hypoglycaemic episodes during intensified insulin treatment: increased frequency but no effect on cognitive function, <i>Journal of Internal Medicine</i> , 9-16, 1991	PICO criteria not met - mean age of participants is outside guideline age range
Reichard,P, Berglund,B, Britz,A, Cars,I, Nilsson,BY, Rosenqvist,U, Intensified conventional insulin treatment retards the microvascular complications of insulin-dependent diabetes mellitus (IDDM): the Stockholm Diabetes Intervention Study (SDIS) after 5 years, <i>Journal of Internal Medicine</i> , 101-108, 1991	PICO criteria not met - mean age of participants is outside guideline age range
Rewers,M., Pihoker,C., Donaghue,K., Hanas,R., Swift,P., Klingensmith,G.J., Assessment and monitoring of glycemic control in children and adolescents with diabetes, <i>Pediatric Diabetes</i> , 10, 71-81, 2009	Study criteria not met - consensus guideline
Reynolds,N.A., Wagstaff,A.J., Insulin aspart: a review of its use in the management of type 1 or 2 diabetes mellitus. [63 refs], <i>Drugs</i> , 64, 1957-1974, 2004	PICO criteria not met - comparison is between two multiple daily injection regimens
Rogers,D.G., The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus, <i>Clinical Pediatrics</i> , 33, 378-, 1994	Study criteria not met - commentary article
Rosenbauer,J., Dost,A., Karges,B., Hungele,A., Stahl,A., Bachle,C., Gerstl,E.M., Kastendieck,C., Hofer,S.E., Holl,R.W., DPV Initiative and the German BMBF Competence Network Diabetes Mellitus., Improved metabolic control in children and adolescents with type 1 diabetes: a trend analysis using prospective multicenter data from Germany and Austria, <i>Diabetes Care</i> , 35, 80-86, 2012	PICO criteria not met - age of participants is <20 years, data for comparisons of interest not reported separately for guideline age range
Rosengren,A., Adlerberth,A., Bresater,L.E., Ehnberg,S., Welin,L., Multiple insulin injection therapy using an insulin pen - who benefits? A clinical 3-year follow-up study of 100 type 1 and 51 type 2 diabetic patients, <i>Diabetes Research</i>	PICO criteria not met - age range is 17-72 years

Study	Reason for exclusion
and Clinical Practice, 20, 69-74, 1993	
Rosilio,M., Cotton,J.B., Wieliczko,M.C., Gendrault,B., Carel,J.C., Couvaras,O., Ser,N., Gillet,P., Soskin,S., Garandeau,P., Stuckens,C., Luyer,B.L.E., Jos,J., Bony-Trifunovic,H., Bertrand,A.M., Letlrq,F., Lafuma,A., Bougneres,P.F., Factors associated with glycemic control: A cross-sectional nationwide study in 2,579 french children with type 1 diabetes, Diabetes Care, , 1146-1153, 1998	PICO criteria not met - comparison is between 1-2 and > 3 injections per day
Rosilio,M., Cotton,J.B., Wieliczko,M.C., Gendrault,B., Carel,J.C., Couvaras,O., Ser,N., Gillet,P., Soskin,S., Garandeau,P., Stuckens,C., Le,Luyer B., Jos,J., Bony-Trifunovic,H., Bertrand,A.M., Leturcq,F., Lafuma,A., French Pediatric Diabetes Group, Bougneres,P.F., Factors associated with glycemic control. A cross-sectional nationwide study in 2,579 French children with type 1 diabetes. The French Pediatric Diabetes Group, Diabetes Care, 21, 1146-1153, 1998	PICO criteria not met - data reported for 2 versus 3 injections per day only
Rudolf,M.C., Sherwin,R.S., Markowitz,R., Bates,S.E., Genel,M., Hochstadt,J., Tamborlane,W.V., Effect of intensive insulin treatment on linear growth in the young diabetic patient, Journal of Pediatrics, 101, 333-339, 1982	Study criteria not met - < 10 participants
Salardi,S., Cacciari,E., Zucchini,S., Donati,S., Steri,L., Gualandi,S., Mazzanti,L., Calliva,R., Modifications of metabolic control in type 1 diabetic children and adolescents: experience over the last 20 years, Journal of Pediatric Endocrinology, 10, 569-578, 1997	PICO criteria not met - comparison is between 3 and fewer than 3 injections per day
Schiffrin,A., Treatment of insulin-dependent diabetes with multiple subcutaneous insulin injections. [64 refs], Medical Clinics of North America, 66, 1251-1267, 1982	Study criteria not met - narrative review
Schiffrin,A.D., Desrosiers,M., Aleyassine,H., Belmonte,M.M., Intensified insulin therapy in the type I diabetic adolescent: a controlled trial, Diabetes Care, 7, 107-113, 1984	PICO criteria not met - multiple daily injections versus CSII
Schober,E., Schoenle,E., Van,Dyk J., Wernicke-Panten,K., Pediatric Study Group of Insulin Glargine, Comparative trial between insulin glargine and NPH insulin in children and adolescents with type 1 diabetes, Diabetes Care, 24, 2005-2006, 2001	PICO criteria not met - comparison is between two multiple daily injection regimens
Schober,E., Schoenle,E., Van,Dyk J., Wernicke-Panten,K., Pediatric Study Group of Insulin Glargine., Comparative trial between insulin glargine and NPH insulin in children and adolescents with type 1 diabetes mellitus, Journal of Pediatric Endocrinology, 15, 369-376, 2002	PICO criteria not met - comparison is between two multiple daily injection regimens
Service,F.J., Daube,J.R., O'Brien,P.C., Zimmerman,B.R., Swanson,C.J., Brennan,M.D., Dyck,P.J., Effect of blood glucose control on peripheral nerve function in diabetic patients, Mayo Clinic Proceedings, 58, 283-289, 1983	PICO criteria not met - median age is 31 years
Shah,S.C., Malone,J.I., Simpson,N.E., A randomized trial of intensive insulin therapy in newly diagnosed insulin-dependent diabetes mellitus, New England Journal of Medicine, 320, 550-554, 1989	PICO criteria not met - comparison is between 2 injections per day and continuous subcutaneous insulin infusion
Shalitin,S., Phillip,M., Which factors predict glycemic control in children diagnosed with type 1 diabetes before 6.5 years of age?, Acta Diabetologica, 49, 355-362, 2012	PICO criteria not met - comparison is between multiple daily injections and CSII
Shamoon,H., Duffly,H., Fleischer,N., Engel,S., Saenger,P., Strelzyn,M., Litwak,M., Wylie-Rosett,J., Farkash,A., Geiger,D., Engel,H., Fleischman,J., Pompei,D., Ginsberg,N., Glover,M., Brisman,M., Walker,E., Thomashunis,A., Gonzalez,J., The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus, New England Journal of Medicine, 329, 977-986, 1993	PICO criteria not met - comparison is between 3 or more injections per day and 1-2 injections per day
Shukla,V.K., Otten,N., Insulin lispro: a critical evaluation (Structured abstract), Health Technology Assessment Database, -, 2012	Study criteria not met - abstract only
Simpson,D., McCormack,P.L., Keating,G.M., Lyseng-Williamson,K.A., Insulin lispro: A review of its use in the management of diabetes mellitus, Drugs, 67, 407-434, 2007	PICO criteria not met - comparison is between two multiple daily injection regimens
Siu,A., Poon,C.Y., Pharmacologic management in pediatric type 1 diabetes mellitus, U.S, 33, -, 2008	Study criteria not met - narrative review

Study	Reason for exclusion
Small,M, MacRury,S, Boal,A, Paterson,KR, MacCuish,AC, Comparison of conventional twice daily subcutaneous insulin administration and a multiple injection regimen (using the NovoPen) in insulin-dependent diabetes mellitus, <i>Diabetes Research</i> , 85-89, 1988	PICO criteria not met - mean age of participants outside guideline age range
Smith,C.P., Dunger,D.B., Mitten,S., Hewitt,J., Spowart,K., Grant,D.B., Savage,M.O., A comparison of morning and bed-time ultralente administration when using multiple injections in adolescence, <i>Diabetic Medicine</i> , 5, 352-355, 1988	PICO criteria not met - follow-up < 4 months
Soliman,A.T., Omar,M., Rizk,M.M., El,Awwa A., AlGhobashy,F.M., Glycaemic control with modified intensive insulin injections (MI) using insulin pens and premixed insulin in children with type-1 diabetes: a randomized controlled trial, <i>Journal of Tropical Pediatrics</i> , 52, 276-281, 2006	PICO criteria not met - both treatment arms received fewer than 4 injections per day
Srinivasan,B., Davies,M., Lawrence,I., Diabetes: glycaemic control in type 1, <i>Clinical Evidence</i> , 2008, 2008., -, 2008	PICO criteria not met - multiple daily injections versus CSII
Sundelin,J., Forsander,G., Mattson,S.E., Family-oriented support at the onset of diabetes mellitus: a comparison of two group conditions during 2 years following diagnosis, <i>Acta Paediatrica</i> , 85, 49-55, 1996	PICO criteria not met - educational intervention
Svensson,J., Johannesen,J., Mortensen,H.B., Nordly,S., Improved metabolic outcome in a Danish diabetic paediatric population aged 0-18 yr: Results from a nationwide continuous Registration, <i>Pediatric Diabetes</i> , 10, 461-467, 2009	PICO criteria not met - no direct comparisons of interventions of interest
Svoren,B.M., Volkening,L.K., Butler,D.A., Moreland,E.C., Anderson,B.J., Laffel,L.M., Temporal trends in the treatment of pediatric type 1 diabetes and impact on acute outcomes, <i>Journal of Pediatrics</i> , 150, 279-285, 2007	PICO criteria not met - multiple daily injections defined as 3 or more injections per day
Swift,P.G., Diabetes in the young: from Leicester to Siena (via Oslo, Bethesda and Hvidore), <i>Acta Bio-Medica de l Ateneo Parmense</i> , 76 Suppl 3, 7-13, 2005	Study criteria not met - narrative review
Swift,P.G., Kennedy,J.D., Gerlis,L.S., Change to U-100 insulin does not appear to affect insulin absorption, <i>British Medical Journal Clinical Research Ed.</i> , 286, 1015-, 1983	PICO criteria not met - follow-up < 4 months
Tan,S.H., Lee,B.W., The use of twice-daily insulin regimes in insulin-dependent diabetic children, <i>Journal of the Singapore Paediatric Society</i> , 25, 70-74, 1983	PICO criteria not met - comparison is between 1 and 2 injections per day
The Writing Team for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group, Effect of intensive therapy on the microvascular complications of type 1 diabetes mellitus, <i>JAMA</i> , 2563-2569, 2002	PICO criteria not met - comparison is between 3 or more injections per day and 1-2 injections per day
Thompson,R.J., Agostini,K., Potts,L., Luscombe,J., Christie,D., Viner,R., White,B., Hindmarsh,P.C., Deprivation and ethnicity impact on diabetes control and use of treatment regimen, <i>Diabetic Medicine</i> , 30, 491-494, 2013	The study only reported that the highest HbA1c was the highest in the twice-daily group and the lowest in the insulin therapy group in text; no comparison between MDI and mixed insulin injection was made.
Thomsett,M., Shield,G., Batch,J., Cotterill,A., How well are we doing? Metabolic control in patients with diabetes, <i>Journal of Paediatrics and Child Health</i> , 35, 479-482, 1999	PICO criteria not met - comparison is between 1-2 and > 2 injections per day
Tonella,P., Fluck,C.E., Mullis,P.E., Metabolic control of type 1 diabetic patients followed at the University Children's Hospital in Berne: have we reached the goal?, <i>Swiss Medical Weekly</i> , 140, w13057-, 2010	Incomplete data for comparisons of interest
Tubiana-Rufi,N., Levy-Marchal,C., Mugnier,E., Czernichow,P., Long term feasibility of multiple daily injections with insulin pens in children and adolescents with diabetes, <i>European Journal of Pediatrics</i> , 149, 80-83, 1989	PICO criteria not met - age range is 5-19.5 years, guideline age range not reported separately
Tupola,S., Rajantie,J., Maenpaa,J., Severe hypoglycaemia in children and adolescents during multiple-dose insulin therapy, <i>Diabetic Medicine</i> , 15, 695-699, 1998	PICO criteria not met - age range is 2-21 years, guideline age range not reported separately
Urakami,T., Kuwabara,R., Habu,M., Okuno,M., Suzuki,J., Takahashi,S., Basal insulin requirement of youth with type 1 diabetes differs according to age, <i>Journal of Diabetes Investigation</i> , 5, 442-444, 2014	No information on outcomes of interest
Urakami,T., Suzuki,J., Yoshida,A., Saito,H., Ishige,M.,	PICO criteria not met - insulin regimen data not reported

Study	Reason for exclusion
Takahashi,S., Mugishima,H., Association between sex, age, insulin regimens and glycemic control in children and adolescents with type 1 diabetes, <i>Clinical Pediatric Endocrinology</i> , 19, 1-6, 2010	separately for guideline age range
Viberti,G.C., Intensive therapy and progression to clinical albuminuria in patients with insulin dependent diabetes mellitus and microalbuminuria, <i>British Medical Journal</i> , 311, 973-977, 1995	PICO criteria not met - age range 17-59 years
Vicens-Calvet,E., Gussinye,M., Albisu,M.A., Potau,N., Ibanez,L., Insulin treatment in adolescence, <i>Journal of Endocrinological Investigation</i> , 12, 109-112, 1989	Study criteria not met - < 10 participants in multiple daily injections arm
Wagner,V.M., Muller-Godeffroy,E., von,Sengbusch S., Hager,S., Thyen,U., Age, metabolic control and type of insulin regime influences health-related quality of life in children and adolescents with type 1 diabetes mellitus, <i>European Journal of Pediatrics</i> , 164, 491-496, 2005	PICO criteria not met - multiple daily injections defined as > 3 injections per day
Wagner,V.M., Grabert,M., Holl,R.W., Severe hypoglycaemia, metabolic control and diabetes management in children with type 1 diabetes in the decade after the Diabetes Control and Complications Trial -- a large-scale multicentre study, <i>European Journal of Pediatrics</i> , 164, 73-79, 2005	PICO criteria not met - cannot separate CSII data from multiple daily injections
Wang,PH, Lau,J, Chalmers,TC, Meta-analysis of effects of intensive blood-glucose control on late complications of type 1 diabetes, <i>Lancet</i> , 1306-1309, 1993	Study criteria not met - brief report of systematic review. References checked.
Wheeler,K.A., Ahmed,M.L., Edge,J.A., Dunger,D.B., Comparison of cartridge insulin Penmix 50:50/Isophane with soluble/Isophane in type I diabetic adolescents using a multiple injection regimen, <i>Diabetes Research</i> , 22, 59-65, 1993	PICO criteria not met - comparison is between two multiple daily injection regimens
White,N.H., Intensive diabetes therapy is effective in children, <i>American Family Physician</i> , 50, 407-, 1994	PICO criteria not met - comparison is between 1-2 and 2-4 injections per day
White,N.H., Waltman,S.R., Krupin,T., Santiago,J.V., Reversal of neuropathic and gastrointestinal complications related to diabetes mellitus in adolescents with improved metabolic control, <i>Journal of Pediatrics</i> , 99, 41-45, 1981	Study criteria not met - < 10 participants
Wierusz-Wysocka,B., Wysocki,H., Byks,H., Zozulinska,D., Wykretowicz,A., Kazmierczak,M., Metabolic control quality and free radical activity in diabetic patients, <i>Diabetes Research and Clinical Practice</i> , 27, 193-197, 1995	PICO criteria not met - age range 17-51 years and follow-up < 4 months
Williams,R.M., Dunger,D.B., Insulin treatment in children and adolescents. [50 refs], <i>Acta Paediatrica</i> , 93, 440-446, 2004	Study criteria not met - narrative review
Wilson,D.P., Fesmire,J.D., Endres,R.K., Blackett,P.R., Increased levels of HDL-cholesterol and apolipoprotein A-I after intensified insulin therapy for diabetes, <i>Southern Medical Journal</i> , 78, 636-638, 1985	PICO criteria not met - age range is 9-21 years, guideline age range not reported separately
Wintergerst,K.A., Hinkle,K.M., Barnes,C.N., Omoruyi,A.O., Foster,M.B., The impact of health insurance coverage on pediatric diabetes management, <i>Diabetes Research and Clinical Practice</i> , 90, 40-44, 2010	PICO criteria not met - age range includes 18 years, guideline age range not reported separately
Wolfsdorf,J.I., How effective is biphasic insulin aspart in the treatment of adolescents with type 1 diabetes?, <i>Nature Clinical Practice Endocrinology and Metabolism</i> , 2, 486-487, 2006	Summary of trial reported elsewhere (Mortensen et al 2006, weeded out)
Wysocki,T., Diabetes self-management profile for flexible insulin regimens: Cross-sectional and longitudinal analysis of psychometric properties in a pediatric sample, <i>Diabetes Care</i> , 28, 2034-2035, 2005	PICO criteria not met - comparison is continuous glucose monitoring versus usual monitoring
Wysocki,T., Harris,M.A., Buckloh,L.M., Wilkinson,K., Sadler,M., Mauras,N., White,N.H., Self-care autonomy and outcomes of intensive therapy or usual care in youth with type 1 diabetes, <i>Journal of Pediatric Psychology</i> , 31, 1036-1045, 2006	PICO criteria not met - cannot separate CSII and multiple daily injection results
Ying,A.K., Lairson,D.R., Giardino,A.P., Bondy,M.L., Zaheer,I., Haymond,M.W., Heptulla,R.A., Predictors of direct costs of diabetes care in pediatric patients with type 1 diabetes, <i>Pediatric Diabetes</i> , 12, 177-182, 2011	PICO criteria not met - multiple daily injections defined as 3 or more injections per day

H.5 Type 1 diabetes – HbA1c targets

Review question

What is the optimal haemoglobin A1c (HbA1c) target for children and young people with type 1 diabetes?

Study	Reason for exclusion
Jarosz-Chobot,P., Polanska,J., Mysliwiec,M., Szadkowska,A., Fendler,W., Kaminska,H., Chumiecki,M., Mianowska,B., Techmanska,I., Sztangierska,B., Mlynarski,W., PolPeDiab study group., Multicenter cross-sectional analysis of values of glycosylated haemoglobin (HbA1c) in Polish children and adolescents with long-term type 1 diabetes in Poland: PolPeDiab study group, <i>Pediatric endocrinology, diabetes, and metabolism</i> , 18, 125-129, 2012	No targets specified. No threshold for HbA1c in analysis. No relevant outcomes reported. Study assesses whether children and young people with different HbA1c values have stable HbA1c levels.
Swift,P.G., Skinner,T.C., de Beaufort,C.E., Cameron,F.J., Aman,J., Aanstoot,H.J., Castano,L., Chiarelli,F., Daneman,D., Danne,T., Dorchy,H., Hoey,H., Kaprio,E.A., Kaufman,F., Kocova,M., Mortensen,H.B., Njolstad,P.R., Phillip,M., Robertson,K.J., Schoenle,E.J., Urakami,T., Vanelli,M., Ackermann,R.W., Skovlund,S.E., Hvidoere Study Group on Childhood Diabetes., Target setting in intensive insulin management is associated with metabolic control: the Hvidoere childhood diabetes study group centre differences study 2005, <i>Pediatric Diabetes</i> , 11, 271-278, 2010	No relevant outcomes were reported. Study addresses whether specifying tighter targets means a lower HbA1c is achieved, rather than the effect of a tighter HbA1c target on adverse outcomes.

H.6 Type 1 diabetes – blood glucose targets

Review question

What are the optimal blood glucose targets for children and young people with type 1 diabetes?

Study	Reason for exclusion
Ashwell,S.G., Gebbie,J., Home,P.D., Optimal timing of injection of once-daily insulin glargine in people with Type 1 diabetes using insulin lispro at meal-times, <i>Diabetic Medicine</i> , 23, 46-52, 2006	PICO not met: adult participants only
Boot,M., Volkening,L.K., Butler,D.A., Laffel,L.M., The impact of blood glucose and HbA(1c) goals on glycaemic control in children and adolescents with Type 1 diabetes, <i>Diabetic Medicine</i> , 30, 333-337, 2013	PICO not met: outcomes of interest not given
Fullerton,B., Jeitler,K., Seitz,M., Horvath,K., Berghold,A., Siebenhofer,A., Intensive glucose control versus conventional glucose control for type 1 diabetes mellitus, <i>Cochrane Database of Systematic Reviews</i> , 2, CD009122-, 2014	The review was about both children and adults. The study on children (Wysocki et al. 2003) does not meet the protocol in terms of intervention (that is, the comparison groups (intensive and usual care)not only differed in terms of Hb1Ac targets during treatment, but also other interventions such as education and behavioural interventions).
Fullerton,Birgit, Berghold,Andrea, Jeitler,Klaus, Siebenhofer,Andrea, Intensive glucose control versus conventional glucose control for type 1 diabetes mellitus, <i>Cochrane Database of Systematic Reviews</i> , -, 2011	Protocol for a systematic review
Imran,S.A., Rabasa-Lhoret,R., Ross,S., Targets for Glycemic Control, <i>Canadian Journal of Diabetes</i> , 37, S31-S34, 2013	Clinical practice management guideline
Marcason,W., Is There a Recommended Target Range for Blood Glucose for the Type 1 Diabetic Endurance Athlete?, <i>Journal of the Academy of Nutrition and Dietetics</i> , 112, 2092-, 2012	Neither a study nor a systematic review
Nguyen,T.M., Mason,K.J., Sanders,C.G., Yazdani,P., Heptulla,R.A., Targeting blood glucose management in school improves glycemic control in children with poorly controlled type 1 diabetes mellitus, <i>Journal of Pediatrics</i> , 153, 575-578, 2008	PICO not met - interventions used did not include blood glucose targets
Rankin,D., Cooke,D.D., Heller,S., Elliott,J., Amiel,S., Lawton,J., UK National Institute for Health Research (NIHR)	PICO not met: adult participants only

Study	Reason for exclusion
Dose Adjustment for Normal Eating (DAFNE) Study Group., Experiences of using blood glucose targets when following an intensive insulin regimen: a qualitative longitudinal investigation involving patients with Type 1 diabetes, <i>Diabetic Medicine</i> , 29, 1079-1084, 2012	
Scaramuzza,A.E., Iafusco,D., Santoro,L., Bosetti,A., De,Palma A., Spiri,D., Mameli,C., Zuccotti,G.V., Timing of bolus in children with type 1 diabetes using continuous subcutaneous insulin infusion (TiBoDi Study), <i>Diabetes Technology and Therapeutics</i> , 12, 149-152, 2010	PICO not met: no long-term outcomes assessed
Svoren,B.M., Volkening,L.K., Butler,D.A., Moreland,E.C., Anderson,B.J., Laffel,L.M., Temporal trends in the treatment of pediatric type 1 diabetes and impact on acute outcomes, <i>Journal of Pediatrics</i> , 150, 279-285, 2007	PICO not met - intervention examined did not include blood glucose targets
Swift,P.G., Skinner,T.C., de Beaufort,C.E., Cameron,F.J., Aman,J., Aanstoot,H.J., Castano,L., Chiarelli,F., Daneman,D., Danne,T., Dorchy,H., Hoey,H., Kaprio,E.A., Kaufman,F., Kocova,M., Mortensen,H.B., Njolstad,P.R., Phillip,M., Robertson,K.J., Schoenle,E.J., Urakami,T., Vanelli,M., Ackermann,R.W., Skovlund,S.E., Hvidoere Study Group on Childhood Diabetes., Target setting in intensive insulin management is associated with metabolic control: the Hvidoere childhood diabetes study group centre differences study 2005, <i>Pediatric Diabetes</i> , 11, 271-278, 2010	PICO not met - study does not report relationship between blood glucose levels and HbA1c

H.7 Type 1 diabetes – blood glucose monitoring

Review questions

How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?

Study	Reason for exclusion
Allen,C., LeCaire,T., Palta,M., Daniels,K., Meredith,M., D'Alessio,D.J., Wisconsin Diabetes,Registry Project, Risk factors for frequent and severe hypoglycemia in type 1 diabetes, <i>Diabetes Care</i> , 24, 1878-1881, 2001	PICO not met - study included children, young people and adults but did not report findings separately
Anderson,B., Ho,J., Brackett,J., Finkelstein,D., Laffel,L., Parental involvement in diabetes management tasks: relationships to blood glucose monitoring adherence and metabolic control in young adolescents with insulin-dependent diabetes mellitus, <i>Journal of Pediatrics</i> , 130, 257-265, 1997	PICO not met - study reported goodness of fit statistics for multiple variables, one of which was frequency of self-monitoring of blood glucose, so no data specific to self-monitoring of blood glucose are available
Anderson,B.J., Vangsness,L., Connell,A., Butler,D., Goebel-Fabbri,A., Laffel,L.M., Family conflict, adherence, and glycaemic control in youth with short duration Type 1 diabetes, <i>Diabetic Medicine</i> , 19, 635-642, 2002	PICO not met - study reported goodness of fit statistics for multiple variables, one of which was frequency of self-monitoring of blood glucose, so no data specific to self-monitoring of blood glucose are available
Beck,R.W., Tamborlane,W.V., Bergenstal,R.M., Miller,K.M., DuBose,S.N., Hall,C.A., Clinic Network,D.Exchange, The T1D Exchange clinic registry, <i>Journal of Clinical Endocrinology and Metabolism</i> , 97, 4383-4389, 2012	Report is a descriptive analysis of the 'T1D Exchange' registry
Belmonte,M.M., Schiffrin,A., Dufresne,J., Suissa,S., Goldman,H., Polychronakos,C., Impact of SMBG on control of diabetes as measured by HbA1. 3-yr survey of a juvenile IDDM clinic, <i>Diabetes Care</i> , 11, 484-488, 1988	PICO not met - study does not report numerical data on the outcomes of interest
Brewer,K.W., Chase,H.P., Owen,S., Garg,S.K., Slicing the pie. Correlating HbA _{1c} -values with average blood glucose values in a pie chart form, <i>Diabetes Care</i> , 21, 209-212, 1998	PICO not met - study does not report the correlation between self-monitoring of blood glucose and glycaemic control
Cortina,S., Repaske,D.R., Hood,K.K., Sociodemographic and psychosocial factors associated with continuous subcutaneous insulin infusion in adolescents with type 1 diabetes, <i>Pediatric Diabetes</i> , 11, 337-344, 2010	PICO not met - study does not report the correlation between self-monitoring of blood glucose and glycaemic control
Derr,R., Garrett,E., Stacy,G.A., Saudek,C.D., Is HbA _{1c} affected by glycemic instability?, <i>Diabetes Care</i> , 26, 2728-2733, 2003	PICO not met - study did not include children or young people
Driscoll,K.A., Johnson,S.B., Tang,Y., Yang,F., Deeb,L.C., Silverstein,J.H., Does blood glucose monitoring increase prior to clinic visits in children with type 1 diabetes?, <i>Diabetes Care</i> , 34, 2170-2173, 2011	PICO not met - study does not report the correlation between self-monitoring of blood glucose and glycaemic control

Study	Reason for exclusion
Evans,J.M.M., Newton,R.W., Ruta,D.A., MacDonald,T.M., Stevenson,R.J., Morris,A.D., Frequency of blood glucose monitoring in relation to glycaemic control: Observational study with diabetes database, <i>British Medical Journal</i> , 318, 83-86, 1999	PICO not met - study included children, young people and adults but did not report findings separately
Faustino,E.V.S., Hirshberg,E.L., Bogue,C.W., Hypoglycemia in critically ill children, <i>Journal of Diabetes Science and Technology</i> , 6, 48-57, 2012	The study did not report number of finger pricks and information on glycaemic control
Formosa,N., Blood glucose monitoring in children and adolescents with Type 1 Diabetes Mellitus, <i>Malta Medical Journal</i> , 25, 31-35, 2013	Systematic review where only studies showing significant associations between self-monitoring of blood glucose and Hb1Ac were included; the majority of included studies have been identified separately in guideline review
Gomes,M.B., Cobas,R.A., Matheus,A.S., Tannus,L.R., Negrato,C.A., Rodacki,M., Braga,N., Cordeiro,M.M., Luescher,J.L., Berardo,R.S., Nery,M., Marques,M.A., Calliari,L.E., Noronha,R.M., Manna,T.D., Zajdenverg,L., Salvodelli,R., Penha,F.G., Foss,M.C., Foss-Freitas,M.C., Pires,A.C., Robles,F.C., Guedes,M., Dib,S.A., Dualib,P., Silva,S.C., Sepulveda,J., Almeida,H.G., Sampaio,E., Rea,R., Faria,A.C.R., Tschiedel,B., Lavigne,S., Cardozo,G.A., Azevedo,M.J., Canani,L.H., Zucatti,A.T., Coral,M.H.C., Pereira,D.A., Araujo,L.A., Tolentino,M., Pedrosa,H.C., Prado,F.A., Rassi,N., Araujo,L.B., Fonseca,R.M.C., Guedes,A.D., Matos,O.S., Faria,M., Azulay,R., Forti,A.C., Facanha,C., Montenegro,A.P., Montenegro,R., Melo,N.H., Rezende,K.F., Ramos,A., Felicio,J.S., Santos,F.M., Jezini,D.L., Cordeiro,M.M., Regional differences in clinical care among patients with type 1 diabetes in Brazil: Brazilian Type 1 Diabetes Study Group, <i>Diabetology and Metabolic Syndrome</i> , 4, -, 2012	Paper is in Portuguese
Gomes,M.B., Negrato,C.A., Cobas,R., Tannus,L.R.M., Goncalves,P.R., Da,SilvaP, Carneiro,J.R.I., Matheus,A.S.M., Dib,S.A., Azevedo,M.J., Nery,M., Rodacki,M., Zajdenverg,L., Montenegro,JuniorR, Sepulveda,J., Calliari,L.E., Jezini,D., Braga,N., Luescher,J.L., Berardo,R.S., ruda-Marques,M.C., Noronha,R.M., Manna,T.D., Salvodelli,R., Penha,F.G., Foss,M.C., Foss-Freitas,M.C., Pires,A.C., Robles,F.C., Guedes,M.D.F.S., Dualib,P., Silva,S.C., Sampaio,E., Rea,R., Faria,A.C.R., Tschiedel,B., Lavigne,S., Canani,L.H., Zucatti,A.T., Coral,M.H.C., Pereira,D.A., Araujo,L.A., Tolentino,M., Pedrosa,H.C., Prado,F.A., Rassi,N., Araujo,L.B., Fonseca,R.M.C., Guedes,A.D., Matos,O.S., Palma,C.C., Azulay,R., Forti,A.C., Facanha,C., Montenegro,A.P., Melo,N.H., Rezende,K.F., Ramos,A., Felicio,J.S., Santos,F.M., Determinants of intensive insulin therapeutic regimens in patients with type 1 diabetes: Data from a nationwide multicenter survey in Brazil, <i>Diabetology and Metabolic Syndrome</i> , 6, -, 2014	The study included an adult population
Gomes,M.B., Tannus,L.R., Cobas,R.A., Matheus,A.S., Dualib,P., Zucatti,A.T., Cani,C., Guedes,A.D., Santos,F.M., Sepulveda,J., Tolentino,M., Facanha,M.C., Faria,A.C., Lavigne,S., Montenegro,A.P., Rodacki,M., de Fatima,Guedes M., Szundy,R., Cordeiro,M.M., Santos,P.T., Negrato,C.A., Brazilian,Type, Determinants of self-monitoring of blood glucose in patients with Type 1 diabetes: a multi-centre study in Brazil, <i>Diabetic Medicine</i> , 30, 1255-1262, 2013	The study did not report frequency of finger-prick according to age group as included population was of mixed ages
Gordon,D., Semple,C.G., Paterson,K.R., Do different frequencies of self-monitoring of blood glucose influence control in type 1 diabetic patients?, <i>Diabetic Medicine</i> , 8, 679-682, 1991	PICO not met - both groups received 4 or fewer tests per day
Grady,M., Campbell,D., MacLeod,K., Srinivasan,A., Evaluation of a blood glucose monitoring system with automatic high- and low-pattern recognition software in insulin-using patients: Pattern detection and patient-reported insights, <i>Journal of Diabetes Science and Technology</i> , 7, 970-978, 2013	The study did not report different age groups as the population was of mixed ages
Grossi,S.A., Lottenberg,S.A., Lottenberg,A.M., Della,Manna T., Kuperman,H., Home blood glucose monitoring in type 1 diabetes mellitus, <i>Revista Latino-Americana de Enfermagem</i> , 17, 194-200, 2009	PICO not met - both groups performed fewer than 5 finger-prick tests per day
Haupt,E., Herrmann,R., ecke-Timp,A., Vogel,H., Haupt,A., Walter,C., The KID study IV: effects of inpatient rehabilitation on the frequency of glucose self-monitoring, quality of further primary care, on time being unable to work and on everyday	PICO not met - study included adults only

Study	Reason for exclusion
psychic strain of type I and type II diabetics--a one-year follow-up. Kissingen Diabetes Intervention Study, <i>Experimental and Clinical Endocrinology and Diabetes</i> , 105, 21-31, 1997	
Helgeson,V.S., Snyder,P.R., Seltman,H., Escobar,O., Becker,D., Siminerio,L., Brief report: trajectories of glycaemic control over early to middle adolescence, <i>Journal of Pediatric Psychology</i> , 35, 1161-1167, 2010	PICO not met - study examined factors associated with 'good' glycaemic control compared with 'poor' glycaemic control
Hershey,T., Bhargava,N., Sadler,M., White,N.H., Craft,S., Conventional versus intensive diabetes therapy in children with type 1 diabetes: effects on memory and motor speed, <i>Diabetes Care</i> , 22, 1318-1324, 1999	PICO not met - both randomised groups used 4 or fewer blood glucose tests per day
McGrady,M.E., Peugh,J.L., Hood,K.K., Illness representations predict adherence in adolescents and young adults with type 1 diabetes, <i>Psychology and Health</i> , 29, 985-998, 2014	No comparator group, and data were not reported according to age groups as study included mixed ages
Messer,L., Ruedy,K., Xing,D., Coffey,J., Englert,K., Caswell,K., Ives,B., Educating families on real time continuous glucose monitoring: the DirecNet navigator pilot study experience, <i>Diabetes Educator</i> , 35, 124-135, 2009	PICO not met - study examined education in use of a real-time continuous glucose monitoring device
Mortensen,H.B., Hougaard,P., Comparison of metabolic control in a cross-sectional study of 2,873 children and adolescents with IDDM from 18 countries. The Hvidovre Study Group on Childhood Diabetes, <i>Diabetes Care</i> , 20, 714-720, 1997	PICO not met - study does not report relationship between self-monitoring of blood glucose and glycaemic control
Olinder,A.L., Kernell,A., Smide,B., Missed bolus doses: devastating for metabolic control in CSII-treated adolescents with type 1 diabetes, <i>Pediatric Diabetes</i> , 10, 142-148, 2009	PICO not met - study does not report numerical data on the outcomes of interest
Radermecker,R.P., Fayolle,C., Brun,J.F., Bringer,J., Renard,E., Accuracy assessment of online glucose monitoring by a subcutaneous enzymatic glucose sensor during exercise in patients with type 1 diabetes treated by continuous subcutaneous insulin infusion, <i>Diabetes and Metabolism</i> , 39, 258-262, 2013	Adult population
Schiffrin,A., Belmonte,M., Multiple daily self-glucose monitoring: Its essential role in long-term glucose control in insulin-dependent diabetic patients treated with pump and multiple subcutaneous injections, <i>Diabetes Care</i> , 5, 479-484, 1982	PICO not met - non-randomised study comparing 2 tests per day with 4 or more tests per day
Service,F.J., O'Brien,P.C., Influence of glycaemic variables on hemoglobin A1c, <i>Endocrine Practice</i> , 13, 350-354, 2007	PICO not met - study does not report data on outcome of interest (correlation of self-monitoring of blood glucose and glycaemic control)
Svoren,B.M., Volkening,L.K., Butler,D.A., Moreland,E.C., Anderson,B.J., Laffel,L.M., Temporal trends in the treatment of pediatric type 1 diabetes and impact on acute outcomes, <i>Journal of Pediatrics</i> , 150, 279-285, 2007	PICO not met - study did not report the correlation between self-monitoring of blood glucose and glycaemic control
Timar,B., Serban,V., Lacatusu,A., Barna,L., Fiera,F., Vlad,A., The relationship between quality of self-monitoring and glycaemic control in Romanian children with type 1 diabetes mellitus, <i>Romanian Journal of Diabetes, Nutrition and Metabolic Diseases</i> , 19, 237-244, 2012	Duration of measurement of HbA1c not reported
Vanelli,M., Cerutti,F., Chiarelli,F., Lorini,R., Meschi,F., MCDC-Italy Group., Nationwide cross-sectional survey of 3560 children and adolescents with diabetes in Italy.[Erratum appears in <i>J Endocrinol Invest</i> . 2005 Oct;28(9):868], <i>Journal of Endocrinological Investigation</i> , 28, 692-699, 2005	PICO not met - study did not report numerical data on the outcomes of interest
Vervoort,T., Goubert,L., Vandenbossche,H., van,AkenS, Matthys,D., Crombez,G., Child's and parents' catastrophizing about pain is associated with procedural fear in children: A study in children with diabetes and their mothers, <i>Psychological Reports</i> , 109, 879-895, 2011	The study did not have a comparator group; the participants appeared to have 1 finger prick test only
Wing,R.R., Lamparski,D.M., Zaslow,S., Betschart,J., Siminerio,L., Becker,D., Frequency and accuracy of self-monitoring of blood glucose in children: relationship to glycaemic control, <i>Diabetes Care</i> , 8, 214-218, 1985	PICO not met - study did not report the correlation between self-monitoring of blood glucose and glycaemic control
Wyllie,H.R., McLaren,E.H., Self monitoring of blood glucose 'a walking stick and not a cane', <i>Practical Diabetes</i> , 11, 116-118, 1994	PICO not met - study includes both young people and adults but results not presented separately for both age groups
Wysocki,T., Green,L., Huxtable,K., Blood glucose monitoring by diabetic adolescents: compliance and metabolic control, <i>Health Psychology</i> , 8, 267-284, 1989	PICO not met - study examined incentives for self-monitoring of blood glucose, not different frequencies of self-monitoring
Yi-Frazier,J.P., Hood,K., Case,D., Waitzfelder,B., Anderson,A., Bloch,C.A., Naughton,M., Seid,M., Imperatore,G., Loots,B., Bell,R., Lawrence,J.M., SEARCH	PICO not met - study did not report the correlation between self-monitoring of blood glucose and glycaemic control

Study	Reason for exclusion
for Diabetes in Youth Study Group., Caregiver reports of provider recommended frequency of blood glucose monitoring and actual testing frequency for youth with type 1 diabetes, Diabetes Research and Clinical Practice, 95, 68-75, 2012	

What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?

Study	Reason for exclusion
Battelino,T., Conget,I., Olsen,B., Schutz-Fuhrmann,I., Hommel,E., Hoogma,R., Schierloh,U., Sulli,N., Bolinder,J., SWITCH Study Group., The use and efficacy of continuous glucose monitoring in type 1 diabetes treated with insulin pump therapy: a randomised controlled trial, Diabetologia, 55, 3155-3162, 2012	Separate paediatric data comparing treatment groups not available
Bergenstal,R.M., Tamborlane,W.V., Ahmann,A., Buse,J.B., Dailey,G., Davis,S.N., Joyce,C., Peoples,T., Perkins,B.A., Welsh,J.B., Willi,S.M., Wood,M.A., Study Group., Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes.[Erratum appears in N Engl J Med. 2010 Sep 9;363(11):1092]. New England Journal of Medicine, 363, 311-320, 2010	PICO not met: non-parallel comparison
Bode,B.W., Clinical utility of the continuous glucose monitoring system, Diabetes Technology and Therapeutics, 2 Suppl 1, S35-S41, 2000	Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (case study only)
Chase,H.P., Beck,R., Tamborlane,W., Buckingham,B., Mauras,N., Tsalikian,E., Wysocki,T., Weinzimer,S., Kollman,C., Ruedy,K., Xing,D., A randomized multicenter trial comparing the GlucoWatch Biographer with standard glucose monitoring in children with type 1 diabetes, Diabetes Care, 28, 1101-1106, 2005	GlucoWatch G2 Biographer has been withdrawn from the market
Chase,H.P., Beck,R.W., Xing,D., Tamborlane,W.V., Coffey,J., Fox,L.A., Ives,B., Keady,J., Kollman,C., Laffel,L., Ruedy,K.J., Continuous glucose monitoring in youth with type 1 diabetes: 12-month follow-up of the juvenile diabetes research foundation continuous glucose monitoring randomized trial, Diabetes Technology and Therapeutics, 12, 507-515, 2010	No comparative data between CGMS users and capillary blood glucose monitoring users
Chase,H.P., Kim,L.M., Owen,S.L., MacKenzie,T.A., Klingensmith,G.J., Murfeldt,R., Garg,S.K., Continuous subcutaneous glucose monitoring in children with type 1 diabetes, Pediatrics, 107, 222-226, 2001	Included in the Cochrane systematic review (Langendam 2012) - also included in the 2004 guideline review
Chase,H.P., Roberts,M.D., Wightman,C., Klingensmith,G., Garg,S.K., Van,Wyhe M., Desai,S., Harper,W., Lopatin,M., Bartkowiak,M., Tamada,J., Eastman,R.C., Use of the GlucoWatch biographer in children with type 1 diabetes, Pediatrics, 111, 790-794, 2003	The first generation GlucoWatch Biographer was withdrawn from the market in 2008
Chase,H.P., Roberts,M.D., Wightman,C., Klingensmith,G., Garg,S.K., Van,Wyhe M., Desai,S., Harper,W., Lopatin,M., Bartkowiak,M., Tamada,J., Eastman,R.C., Use of the GlucoWatch biographer in children with type 1 diabetes, Pediatrics, 111, 790-794, 2003	GlucoWatch G2 Biographer has been withdrawn from the market
Chetty,V.T., Almulla,A., Oduyungbo,A., Thabane,L., The effect of continuous subcutaneous glucose monitoring (CGMS) versus intermittent whole blood finger-stick glucose monitoring (SBGM) on hemoglobin A1c (HBA1c) levels in Type I diabetic patients: a systematic review, Diabetes Research and Clinical Practice, 81, 79-87, 2008	Superseded by more recent systematic reviews
Cobry,E., Chase,H.P., Burdick,P., McFann,K., Yetzer,H., Scrimgeour,L., Use of CoZmonitor in youth with type 1 diabetes, Pediatric Diabetes, 9, 148-151, 2008	PICO not met - study related to integration of capillary blood glucose monitoring and insulin pump therapy
Deiss,D., Hartmann,R., Schmidt,J., Kordonouri,O., Results of a randomised controlled cross-over trial on the effect of continuous subcutaneous glucose monitoring (CGMS) on glycaemic control in children and adolescents with type 1 diabetes, Experimental and Clinical Endocrinology and Diabetes, 114, 63-67, 2006	Included in the Cochrane systematic review (Langendam 2012)
Deiss,Dorothee, Bolinder,Jan, Riveline,Jean Pierre,	Included in the Cochrane systematic review (Langendam

Study	Reason for exclusion
Battelino,Tadej, Bosi,Emanuele, Tubiana-Rufi,Nadia, Kerr,David, Phillip,Moshe, Improved Glycemic Control in Poorly Controlled Patients with Type 1 Diabetes Using Real-Time Continuous Glucose Monitoring, <i>Diabetes Care</i> , 29, 2730-2732, 2006	2012)
Gandhi,G.Y., Kovalaske,M., Kudva,Y., Walsh,K., Elamin,M.B., Beers,M., Coyle,C., Goalen,M., Murad,M.S., Erwin,P.J., Corpus,J., Montori,V.M., Murad,M.H., Efficacy of continuous glucose monitoring in improving glycemic control and reducing hypoglycemia: a systematic review and meta-analysis of randomized trials, <i>Journal of Diabetes Science and Technology</i> , 5, 952-965, 2011	Individual studies checked for inclusion and all except for the GlucoWatch studies are included in the Cochrane systematic review (Langendam 2012)
Guelho,D., Paiva,I., Batista,C., Barros,L., Carrilho,F., A1c, glucose variability and hypoglycemia risk in patients with type 1 diabetes, <i>Minerva Endocrinologica</i> , 39, 127-133, 2014	The study was carried out among adults; retrospective in design, and made no comparison between finger-prick blood glucose testing and CGMS
Hirsch,I.B., Abelseith,J., Bode,B.W., Fischer,J.S., Kaufman,F.R., Mastrototaro,J., Parkin,C.G., Wolpert,H.A., Buckingham,B.A. Sensor-augmented insulin pump therapy: results of the first randomized treat-to-target study, <i>Diabetes Technology and Therapeutics</i> , 10, 377-383, 2008	Included in the Cochrane systematic review (Langendam 2012)
Hoeks,L.B., Greven,W.L., de Valk,H.W., Real-time continuous glucose monitoring system for treatment of diabetes: a systematic review, <i>Diabetic Medicine</i> , 28, 386-94, 2011	Superseded by more recent systematic reviews
Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Beck,R.W., Hirsch,I.B., Laffel,L., Tamborlane,W.V., Bode,B.W., Buckingham,B., Chase,P., Clemons,R., Fiallo-Scharer,R., Fox,L.A., Gilliam,L.K., Huang,E.S., Kollman,C., Kowalski,A.J., Lawrence,J.M., Lee,J., Mauras,N., O'Grady,M., Ruedy,K.J., Tansey,M., Tsalikian,E., Weinzimer,S.A., Wilson,D.M., Wolpert,H., Wysocki,T., Xing,D., The effect of continuous glucose monitoring in well-controlled type 1 diabetes, <i>Diabetes Care</i> , 32, 1378-1383, 2009	Included in the Cochrane systematic review (Langendam 2012)
Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Beck,R.W., Lawrence,J.M., Laffel,L., Wysocki,T., Xing,D., Huang,E.S., Ives,B., Kollman,C., Lee,J., Ruedy,K.J., Tamborlane,W.V., Quality-of-life measures in children and adults with type 1 diabetes: Juvenile Diabetes Research Foundation Continuous Glucose Monitoring randomized trial.[Erratum appears in <i>Diabetes Care</i> . 2010 Dec;33(12):2725], <i>Diabetes Care</i> , 33, 2175-2177, 2010	Included in the Cochrane systematic review (Langendam 2012)
Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Tamborlane,W.V., Beck,R.W., Bode,B.W., Buckingham,B., Chase,H.P., Clemons,R., Fiallo-Scharer,R., Fox,L.A., Gilliam,L.K., Hirsch,I.B., Huang,E.S., Kollman,C., Kowalski,A.J., Laffel,L., Lawrence,J.M., Lee,J., Mauras,N., O'Grady,M., Ruedy,K.J., Tansey,M., Tsalikian,E., Weinzimer,S., Wilson,D.M., Wolpert,H., Wysocki,T., Xing,D., Continuous glucose monitoring and intensive treatment of type 1 diabetes, <i>New England Journal of Medicine</i> , 359, 1464-1476, 2008	Included in the Cochrane systematic review (Langendam 2012)
Kaufman,F.R., Gibson,L.C., Halvorson,M., Carpenter,S., Fisher,L.K., Pitukcheewanont,P., A pilot study of the continuous glucose monitoring system: clinical decisions and glycemic control after its use in pediatric type 1 diabetic subjects, <i>Diabetes Care</i> , 24, 2030-2034, 2001	Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (not a randomised study)
Kordonouri,O., Hartmann,R., Pankowska,E., Rami,B., Kapellen,T., Coutant,R., Lange,K., Danne,T., Follow-up of patients with sensor-augmented pump therapy during the first year of diabetes-pediatric onset study, <i>Pediatric Diabetes</i> , 12, 29-, 2011	An abstract
Kordonouri,O., Hartmann,R., Pankowska,E., Rami,B., Kapellen,T., Coutant,R., Lange,K., Danne,T., Sensor augmented pump therapy from onset of type 1 diabetes: late follow-up results of the Pediatric Onset Study, <i>Pediatric Diabetes</i> , 13, 515-518, 2012	Secondary publication of an included study
Kordonouri,O., Hartmann,R., Pankowska,E., Rami,B., Kapellen,T., Coutant,R., Lange,K., Danne,T., Sensor augmented pump therapy from onset of type 1 diabetes: Late follow-up results of the Pediatric ONSET Study, <i>Diabetologia</i> , 54, S41-, 2011	An abstract
Kordonouri,O., Pankowska,E., Rami,B., Kapellen,T.,	Included in the Cochrane systematic review (Langendam

Study	Reason for exclusion
Coutant,R., Hartmann,R., Lange,K., Knip,M., Danne,T., Sensor-augmented pump therapy from the diagnosis of childhood type 1 diabetes: results of the Paediatric Onset Study (ONSET) after 12 months of treatment, <i>Diabetologia</i> , 53, 2487-2495, 2010	2012)
Lagarde,W.H., Barrows,F.P., Davenport,M.L., Kang,M., Guess,H.A., Calikoglu,A.S., Continuous subcutaneous glucose monitoring in children with type 1 diabetes mellitus: a single-blind, randomized, controlled trial, <i>Pediatric Diabetes</i> , 7, 159-164, 2006	Included in the Cochrane systematic review (Langendam 2012)
Lange,K., Coutant,R., Danne,T., Kapellen,T., Pankowska,E., Rami,B., Aschemeier,B., Blasig,S., Hartmann,R., Krug,N., Marquardt,E., Remus,K., Kordonouri,O., High quality of life in children and psychological wellbeing in mothers 12 month after diabetes onset: Results of the paediatric onset-trial of sensor-enhanced CSII, <i>Pediatric Diabetes</i> , 11, 101-, 2010	An abstract
Lawson,M.L., Bradley,B., McAssey,K., Clarson,C., Kirsch,S.E., Mahmud,F.H., Curtis,J.R., Richardson,C., Courtney,J., Cooper,T., Downie,C.J., Rajamannar,G., Barrowman,N., CGM TIME Trial Study Group, JDRF Canadian Clinical Trial Network CCTN, The JDRF CCTN CGM TIME Trial: Timing of Initiation of continuous glucose Monitoring in Established pediatric type 1 diabetes: study protocol, recruitment and baseline characteristics, <i>BMC Pediatrics</i> , 14, 183-, 2014	This is a protocol and only reports baseline characteristics of participants
Ludvigsson,J., Hanas,R., Continuous subcutaneous glucose monitoring improved metabolic control in pediatric patients with type 1 diabetes: a controlled crossover study, <i>Pediatrics</i> , 111, 933-938, 2003	Included in the Cochrane systematic review(Langendam 2012)
Ly,T.T., Hewitt,J., Davey,R.J., Lim,E.M., Davis,E.A., Jones,T.W., Improving epinephrine responses in hypoglycemia unawareness with real-time continuous glucose monitoring in adolescents with type 1 diabetes, <i>Diabetes Care</i> , 34, 50-52, 2011	Minimum length of follow-up not met and objective not pertinent to this review question
Markowitz,J.T., Pratt,K., Aggarwal,J., Volkening,L.K., Laffel,L.M., Psychosocial correlates of continuous glucose monitoring use in youth and adults with type 1 diabetes and parents of youth, <i>Diabetes Technology and Therapeutics</i> , 14, 523-526, 2012	The original study (Juvenile Diabetes Research Foundation (JDRF) trial) was included in the Cochrane systematic review (Langendam 2012)
McGahan,L., Continuous glucose monitoring in the management of diabetes mellitus, <i>Issues in Emerging Health Technologies</i> , 1-4, 2002	Included in 2004 guideline review - copy could not be obtained for consideration in 2015 update review
O'Connell,M.A., Donath,S., O'Neal,D.N., Colman,P.G., Ambler,G.R., Jones,T.W., Davis,E.A., Cameron,F.J., Glycaemic impact of patient-led use of sensor-guided pump therapy in type 1 diabetes: a randomised controlled trial, <i>Diabetologia</i> , 52, 1250-1257, 2009	Included in the Cochrane systematic review (Langendam 2012)
Pickup,J.C., Freeman,S.C., Sutton,A.J., Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data, <i>BMJ</i> , 343, d3805-, 2011	Not strictly a systematic review and superseded by more recent systematic reviews
Raccah,D., Sulmont,V., Reznik,Y., Guerci,B., Renard,E., Hanaire,H., Jeandier,N., Nicolino,M., Incremental value of continuous glucose monitoring when starting pump therapy in patients with poorly controlled type 1 diabetes: the RealTrend study, <i>Diabetes Care</i> , 32, 2245-2250, 2009	Included in the Cochrane systematic review (Langendam 2012)
Rami,B., Lange,K., Coutant,R., Danne,T., Aschemeier,B., Blasig,S., Hartmann,R., Marquardt,E., Walte,K., Krug,N., Kapellen,T., Pankowska,E., Kordonouri,O., Paediatric ONSET-Study: Impaired QoL in children and depressed mood in mothers at onset of diabetes mellitus type 1 in children, <i>Diabetologia</i> , 52, S28-, 2009	Objective is not relevant to the review question
Schiaffini,R., Ciampalini,P., Fierabracci,A., Spera,S., Borrelli,P., Bottazzo,G.F., Crino,A., The continuous glucose monitoring system (CGMS) in type 1 diabetic children is the way to reduce hypoglycemic risk, <i>Diabetes/metabolism research and reviews</i> , 18, 324-329, 2002	Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (cohort study only)
Sequeira,P.A., Montoya,L., Ruelas,V., Xing,D., Chen,V., Beck,R., Peters,A.L., Continuous glucose monitoring pilot in low-income type 1 diabetes patients, <i>Diabetes Technology and Therapeutics</i> , 15, 855-858, 2013	Age of participants was 18 years and over
Szypowska,A., Ramotowska,A., Dzygalo,K., Golicki,D., Beneficial effect of real-time continuous glucose monitoring	All the studies included are covered by the Cochrane systematic review (Langendam 2012)

Study	Reason for exclusion
system on glycem control in type 1 diabetic patients: systematic review and meta-analysis of randomized trials, European Journal of Endocrinology, 166, 567-574, 2012	
Tansey,M., Laffel,L., Cheng,J., Beck,R., Coffey,J., Huang,E., Kollman,C., Lawrence,J., Lee,J., Ruedy,K., Tamborlane,W., Wysocki,T., Xing,D., Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group., Satisfaction with continuous glucose monitoring in adults and youths with Type 1 diabetes, Diabetic Medicine, 28, 1118-1122, 2011	Outcome not compared between intervention and comparator groups
Wojciechowski,P., Rys,P., Lipowska,A., Gaweska,M., Malecki,M.T., Efficacy and safety comparison of continuous glucose monitoring and self-monitoring of blood glucose in type 1 diabetes: systematic review and meta-analysis, Polskie Archiwum Medycyny Wewnetrznej, 121, 333-343, 2011	All the studies included are covered by the Cochrane systematic review (Langendam 2012)
Yates,K., Hasnat,Milton A., Dear,K., Ambler,G., Continuous glucose monitoring-guided insulin adjustment in children and adolescents on near-physiological insulin regimens: a randomized controlled trial, Diabetes Care, 29, 1512-1517, 2006	Included in the Cochrane systematic review (Langendam 2012)
Yeh,H.C., Brown,T.T., Maruthur,N., Ranasinghe,P., Berger,Z., Suh,Y.D., Wilson,L.M., Haberl,E.B., Brick,J., Bass,E.B., Golden,S.H., Comparative effectiveness and safety of methods of insulin delivery and glucose monitoring for diabetes mellitus: a systematic review and meta-analysis, Annals of Internal Medicine, 157, 336-347, 2012	All relevant included studies are covered by the Cochrane systematic review (Langendam 2012)

What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?

Study	Reason for exclusion
Battelino,T., Bode,B.W., Continuous glucose monitoring in 2010, International Journal of Clinical Practice, Supplement, 10-15, 2011	Not a systematic review
Battelino,T., Conget,I., Olsen,B., Schutz-Fuhrmann,I., Hommel,E., Hoogma,R., Schierloh,U., Sulli,N., Bolinder,J., SWITCH Study Group., The use and efficacy of continuous glucose monitoring in type 1 diabetes treated with insulin pump therapy: a randomised controlled trial, Diabetologia, 55, 3155-3162, 2012	Paediatric data not reported separately by treatment group
Bergenstal,R.M., Tamborlane,W.V., Ahmann,A., Buse,J.B., Dailey,G., Davis,S.N., Joyce,C., Peoples,T., Perkins,B.A., Welsh,J.B., Willi,S.M., Wood,M.A., Study Group., Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes.[Erratum appears in N Engl J Med. 2010 Sep 9;363(11):1092], New England Journal of Medicine, 363, 311-320, 2010	Participants were randomly assigned to insulin pump therapy group or injection therapy group and then given a form of continuous glucose monitoring; unable to tell whether any differences in groups is due to the form of CGMS used or to the therapy received
Bode,B.W., Clinical utility of the continuous glucose monitoring system, Diabetes Technology and Therapeutics, 2 Suppl 1, S35-S41, 2000	Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (case study only)
Chase,H.P., Beck,R.W., Xing,D., Tamborlane,W.V., Coffey,J., Fox,L.A., Ives,B., Keady,J., Kollman,C., Laffel,L., Ruedy,K.J., Continuous glucose monitoring in youth with type 1 diabetes: 12-month follow-up of the juvenile diabetes research foundation continuous glucose monitoring randomized trial, Diabetes Technology and Therapeutics, 12, 507-515, 2010	A sub-study: the original study was excluded
Chetty,V.T., Almulla,A., Oduyungbo,A., Thabane,L., The effect of continuous subcutaneous glucose monitoring (CGMS) versus intermittent whole blood finger-stick glucose monitoring (SBGM) on hemoglobin A1c (HBA1c) levels in Type I diabetic patients: a systematic review. [34 refs], Diabetes Research and Clinical Practice, 81, 79-87, 2008	PICO not met: comparator was self-monitoring of blood glucose
Danne,T., Lange,K., Kordonouri,O., Real-time glucose sensors in children and adolescents with type-1 diabetes. [64 refs], Hormone Research, 70, 193-202, 2008	Not a systematic review
Deiss,D., Hartmann,R., Schmidt,J., Kordonouri,O., Results	PICO not met: outcome data not been presented as

Study	Reason for exclusion
of a randomised controlled cross-over trial on the effect of continuous subcutaneous glucose monitoring (CGMS) on glycaemic control in children and adolescents with type 1 diabetes, <i>Experimental and Clinical Endocrinology and Diabetes</i> , 114, 63-67, 2006	specified in the protocol
Edelman,S.V., Bailey,T.S., Continuous glucose monitoring health outcomes, <i>Diabetes Technology and Therapeutics</i> , 11 Suppl 1, S68-S74, 2009	Review article: individual studies checked for inclusion
Halvorson,M., Carpenter,S., Kaiserman,K., Kaufman,F.R., A pilot trial in pediatrics with the sensor-augmented pump: combining real-time continuous glucose monitoring with the insulin pump, <i>Journal of Pediatrics</i> , 150, 103-105, 2007	Not an RCT
Hoeks,L.B., Greven,W.L., de Valk,H.W., Real-time continuous glucose monitoring system for treatment of diabetes: a systematic review, <i>Diabetic Medicine</i> , 28, 386-94, 2011	Systematic review: individual studies checked for inclusion
Hovorka,R., Elleri,D., Thabit,H., Allen,J.M., Leelarathna,L., El-Khairi,R., Kumareswaran,K., Caldwell,K., Calhoun,P., Kollman,C., Murphy,H.R., Acerini,C.L., Wilinska,M.E., Nodale,M., Dunger,D.B., Overnight closed-loop insulin delivery in young people with type 1 diabetes: A free-living, randomized clinical trial, <i>Diabetes Care</i> , 37, 1204-1211, 2014	The intervention and comparator were not as specified in the protocol (real-time CGMS versus real-time CGMS closed loop)
Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Beck,R.W., Buckingham,B., Miller,K., Wolpert,H., Xing,D., Block,J.M., Chase,H.P., Hirsch,I., Kollman,C., Laffel,L., Lawrence,J.M., Milaszewski,K., Ruedy,K.J., Tamborlane,W.V., Factors predictive of use and of benefit from continuous glucose monitoring in type 1 diabetes, <i>Diabetes Care</i> , 32, 1947-1953, 2009	A secondary analysis of an RCT
Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Beck,R.W., Lawrence,J.M., Laffel,L., Wysocki,T., Xing,D., Huang,E.S., Ives,B., Kollman,C., Lee,J., Ruedy,K.J., Tamborlane,W.V., Quality-of-life measures in children and adults with type 1 diabetes: Juvenile Diabetes Research Foundation Continuous Glucose Monitoring randomized trial.[Erratum appears in <i>Diabetes Care</i> . 2010 Dec;33(12):2725], <i>Diabetes Care</i> , 33, 2175-2177, 2010	PICO not met: the comparator is self-monitoring of blood glucose only
Klonoff,D.C., Continuous glucose monitoring study does not demonstrate benefit in children and adolescents, <i>Journal of Pediatrics</i> , 154, 463-464, 2009	Not an RCT
Laffel,L.M., Hsu,W.C., McGill,J.B., Meneghini,L., Volkening,L.K., Continued use of an integrated meter with electronic logbook maintains improvements in glycemic control beyond a randomized, controlled trial, <i>Diabetes Technology and Therapeutics</i> , 9, 254-264, 2007	Paediatric data not reported separately; participants with type 1 diabetes and those with type 2 diabetes cannot be distinguished
Lagarde,W.H., Barrows,F.P., Davenport,M.L., Kang,M., Guess,H.A., Calikoglu,A.S., Continuous subcutaneous glucose monitoring in children with type 1 diabetes mellitus: a single-blind, randomized, controlled trial, <i>Pediatric Diabetes</i> , 7, 159-164, 2006	PICO not met: comparator was self-monitoring of blood glucose(although CGMS data were collected, they were not reported)
Langendam,M., Luijck,Y.M., Hooft,L., Devries,J.H., Mudde,A.H., Scholten,R.J., Continuous glucose monitoring systems for type 1 diabetes mellitus, <i>Cochrane Database of Systematic Reviews</i> , 1, CD008101-, 2012	Systematic review: individual articles checked for inclusion
Ludvigsson,J., Hanas,R., Continuous subcutaneous glucose monitoring improved metabolic control in pediatric patients with type 1 diabetes: a controlled crossover study, <i>Pediatrics</i> , 111, 933-938, 2003	PICO not met: comparator was self-monitoring of blood glucose(although CGMS data were collected they were not reported)
Ly,T.T., Hewitt,J., Davey,R.J., Lim,E.M., Davis,E.A., Jones,T.W., Improving epinephrine responses in hypoglycemia unawareness with real-time continuous glucose monitoring in adolescents with type 1 diabetes, <i>Diabetes Care</i> , 34, 50-52, 2011	PICO not met: comparator is 'standard therapy'- assumed that this refers to self-monitoring of blood glucose
Maahs,D.M., Calhoun,P., Buckingham,B.A., Chase,H.P., Hramiak,I., Lum,J., Cameron,F., Bequette,B.W., Aye,T., Paul,T., Slover,R., Wadwa,R.P., Wilson,D.M., Kollman,C., Beck,R.W., A randomized trial of a home system to reduce nocturnal hypoglycemia in type 1 diabetes, <i>Diabetes Care</i> , 37, 1885-1891, 2014	The trial included participants aged 15-45 years, but results were not stratified by age group
Mauras,N., Fox,L., Englert,K., Beck,R.W., Continuous glucose monitoring in type 1 diabetes, <i>Endocrine</i> , 43, 41-50,	Not a systematic review

Study	Reason for exclusion
2013	
Mauras,N., Beck,R., Xing,D., Ruedy,K., Buckingham,B., Tansey,M., White,N.H., Weinzimer,S.A., Tamborlane,W., Kollman,C., Diabetes Research in Children Network (DirecNet) Study Group., A randomized clinical trial to assess the efficacy and safety of real-time continuous glucose monitoring in the management of type 1 diabetes in young children aged 4 to <10 years, <i>Diabetes Care</i> , 35, 204-210, 2012	PICO not met: the comparator was self-monitoring of blood glucose only
McGahan,L., Continuous glucose monitoring in the management of diabetes mellitus, <i>Issues in Emerging Health Technologies</i> , 1-4, 2002	Included in 2004 guideline review - copy could not be obtained for consideration in 2015 update review
O'Connell,M.A., Donath,S., O'Neal,D.N., Colman,P.G., Ambler,G.R., Jones,T.W., Davis,E.A., Cameron,F.J., Glycaemic impact of patient-led use of sensor-guided pump therapy in type 1 diabetes: a randomised controlled trial, <i>Diabetologia</i> , 52, 1250-1257, 2009	PICO not met: the comparator was self-monitoring of blood glucose
Pickup,J.C., Freeman,S.C., Sutton,A.J., Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data, <i>BMJ</i> , 343, d3805-, 2011	PICO not met: meta-analysis of RCTs comparing CGMS against self-monitoring of blood glucose
Racah,D., Sulmont,V., Reznik,Y., Guerci,B., Renard,E., Hanaire,H., Jeandier,N., Nicolino,M., Incremental value of continuous glucose monitoring when starting pump therapy in patients with poorly controlled type 1 diabetes: the RealTrend study, <i>Diabetes Care</i> , 32, 2245-2250, 2009	Paediatric data not reported separately
Riveline,J.P., Schaepelynck,P., Chaillous,L., Renard,E., Sola-Gazagnes,A., Penformis,A., Tubiana-Rufi,N., Sulmont,V., Catargi,B., Lukas,C., Radermecker,R.P., Thivolet,C., Moreau,F., Benhamou,P.Y., Guerci,B., Leguerrier,A.M., Millot,L., Sachon,C., Charpentier,G., Hanaire,H., EVADIAC Sensor Study Group., Assessment of patient-led or physician-driven continuous glucose monitoring in patients with poorly controlled type 1 diabetes using basal-bolus insulin regimens: a 1-year multicenter study, <i>Diabetes Care</i> , 35, 965-971, 2012	PICO not met: the results were not stratified by age
Schiaffini,R., Ciampalini,P., Fierabracci,A., Spera,S., Borrelli,P., Bottazzo,G.F., Crino,A., The continuous glucose monitoring system (CGMS) in type 1 diabetic children is the way to reduce hypoglycemic risk, <i>Diabetes/metabolism research and reviews</i> , 18, 324-329, 2002	Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (cohort study only)
Soliman,A., DeSanctis,V., Yassin,M., Elalaily,R., Eldarsy,N.E., Continuous glucose monitoring system and new era of early diagnosis of diabetes in high risk groups, <i>Indian Journal of Endocrinology and Metabolism</i> , 18, 274-282, 2014	Discussion paper related to CGMS as a diagnostic tool
Tamborlane,W.V., Insulin pumps and continuous glucose monitoring in pediatric patients with type 1 diabetes mellitus, <i>Endocrine Practice</i> , 18, 13-16, 2012	Not a systematic review
Tansey,M., Laffel,L., Cheng,J., Beck,R., Coffey,J., Huang,E., Kollman,C., Lawrence,J., Lee,J., Ruedy,K., Tamborlane,W., Wysocki,T., Xing,D., Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group., Satisfaction with continuous glucose monitoring in adults and youths with Type 1 diabetes, <i>Diabetic Medicine</i> , 28, 1118-1122, 2011	A sub-study: the original study was excluded
Tsalikian,E., Fox,L., Weinzimer,S., Buckingham,B., White,N.H., Beck,R., Kollman,C., Xing,D., Ruedy,K., Diabetes Research in Children Network Study Group., Feasibility of prolonged continuous glucose monitoring in toddlers with type 1 diabetes, <i>Pediatric Diabetes</i> , 13, 301-307, 2012	Not an RCT
Weinzimer,S., Xing,D., Tansey,M., Fiallo-Scharer,R., Mauras,N., Wysocki,T., Beck,R., Tamborlane,W., Ruedy,K., Diabetes Research in Children Network (DirecNet) Study Group., FreeStyle navigator continuous glucose monitoring system use in children with type 1 diabetes using glargine-based multiple daily dose regimens: results of a pilot trial Diabetes Research in Children Network (DirecNet) Study Group, <i>Diabetes Care</i> , 31, 525-527, 2008	Not an RCT
Weinzimer,S.A., Continuous glucose monitoring in young children: Satisfaction without success?, <i>Diabetes Technology and Therapeutics</i> , 14, 753-755, 2012	Not a systematic review

H.8 Type 1 diabetes – blood ketone monitoring

Review question

What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis?

Study	Reason for exclusion
Bashford,J., Acerini,C.L., How to use near-patient capillary ketone meters, <i>Archives of Disease in Childhood Education and Practice</i> , 97, 217-221, 2012	Narrative review article. Only relevant study cited is already included in review (Laffel et al., 2006)
Bektas,F., Eray,O., Sari,R., Akbas,H., Point of care blood ketone testing of diabetic patients in the emergency department, <i>Endocrine Research</i> , 30, 395-402, 2004	Monitoring in hospital
Bismuth,E., Laffel,L., Can we prevent diabetic ketoacidosis in children?, <i>Pediatric Diabetes</i> , 8, 24-33, 2007	Not a systematic review
Charles,R.A., Bee,Y.M., Eng,P.H., Goh,S.Y., Point-of-care blood ketone testing: screening for diabetic ketoacidosis at the emergency department, <i>Singapore Medical Journal</i> , 48, 986-989, 2007	Monitoring in hospital
Chiari,G., Direct measurement of 3-B-hydroxybutyrate in the management of diabetic ketoacidosis in children: A cost effective enhancement in the management of diabetic ketoacidosis in children, <i>Diabetes Technology and Therapeutics</i> , 13, 178-179, 2011	Conference abstract
Donohoe,P.B., Kessler,R., Beattie,T.F., Exploring the clinical utility of blood ketone levels in the emergency department assessment of paediatric patients, <i>Emergency Medicine Journal</i> , 23, 783-787, 2006	Monitoring in hospital
Klocker,A.A., Phelan,H., Twigg,S.M., Craig,M.E., Blood beta-hydroxybutyrate vs. urine acetoacetate testing for the prevention and management of ketoacidosis in Type 1 diabetes: a systematic review, <i>Diabetic Medicine</i> , 30, 818-824, 2013	Systematic review. References checked - only relevant article is already included in this review (Laffel et al., 2006). Three other studies included in systematic review do not pertain to this question (all consider inpatient monitoring of ketones).
Lawrence,S.E., Diagnosis and treatment of diabetic ketoacidosis in children and adolescents, <i>Paediatrics and Child Health</i> , 10, 21-24, 2005	Review and recommendations (not a systematic review)
Meas,T., Taboulet,P., Sobngwi,E., Gautier,J.F., Is capillary ketone determination useful in clinical practice? In which circumstances?. [22 refs], <i>Diabetes and Metabolism</i> , 31, 299-303, 2005	Not a systematic review
Naunheim,R., Jang,T.J., Banet,G., Richmond,A., McGill,J., Point-of-care test identifies diabetic ketoacidosis at triage, <i>Academic Emergency Medicine</i> , 13, 683-685, 2006	Monitoring in hospital
Prisco,F., Picardi,A., Iafusco,D., Lorini,R., Minicucci,L., Martinucci,M.E., Toni,S., Cerutti,F., Rabbone,I., Buzzetti,R., Crino,A., Pozzilli,P., Blood ketone bodies in patients with recent-onset type 1 diabetes (a multicenter study), <i>Pediatric Diabetes</i> , 7, 223-228, 2006	Monitoring in hospital
Rewers,M., Pihoker,C., Donaghue,K., Hanas,R., Swift,P., Klingensmith,G.J., Assessment and monitoring of glycemic control in children and adolescents with diabetes. [94 refs], <i>Pediatric Diabetes</i> , 10 Suppl 12, 71-81, 2009	ISPAD Clinical Practice Consensus Guidelines 2009 Compendium
Taboulet,P., Deconinck,N., Thurel,A., Haas,L., Manamani,J., Porcher,R., Schmit,C., Fontaine,J.P., Gautier,J.F., Correlation between urine ketones (acetoacetate) and capillary blood ketones (3-beta-hydroxybutyrate) in hyperglycaemic patients, <i>Diabetes and Metabolism</i> , 33, 135-139, 2007	Monitoring in hospital
Turan,S., Omar,A., Bereket,A., Comparison of capillary blood ketone measurement by electrochemical method and urinary ketone in treatment of diabetic ketosis and ketoacidosis in children, <i>Acta Diabetologica</i> , 45, 83-85, 2008	Monitoring in hospital
Vanelli,M., Chiari,G., Capuano,C., Iovane,B., Bernardini,A., Giacalone,T., The direct measurement of 3-beta-hydroxy butyrate enhances the management of diabetic ketoacidosis in children and reduces time and costs of treatment, <i>Diabetes, Nutrition and Metabolism - Clinical and Experimental</i> , 16, 312-316, 2003	Monitoring in hospital

H.9 Type 1 diabetes – dietary advice

Review questions

What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?

Study	Reason for exclusion
Aguilar, Maria J., Garcia, Pedro A., Gonzalez, Emilio, Perez, Maria C., Padilla, Carlos A., A nursing educational intervention helped by One Touch UltraSmart improves monitoring and glycated haemoglobin levels in type I diabetic children, <i>Journal of Clinical Nursing</i> , 21, 1024-1032, 2012	Non-randomised study
Bell, K.J., Barclay, A.W., Petocz, P., Colagiuri, S., Brand-Miller, J.C., Efficacy of carbohydrate counting in type 1 diabetes: a systematic review and meta-analysis, <i>The Lancet Diabetes and Endocrinology</i> , 2, 133-140, 2014	Systematic review - only relevant paper included is Gilbertson et al., 2001
Bishop, F.K., Maahs, D.M., Spiegel, G., Owen, D., Klingensmith, G.J., Bortsov, A., Thomas, J., Mayer-Davis, E.J., The carbohydrate counting in adolescents with type 1 diabetes (CCAT) study, <i>Diabetes Spectrum</i> , 22, 56-62, 2009	Not an RCT. Only assesses ability of children and young people to count carbohydrates, not outcomes associated with carbohydrate counting
Blazik, M., Pankowska, E., The impact of the bolus and food calculator "Diabetics" on decreasing postprandial glucose variability in children with type 1 diabetes treated with insulin pump: The results of RCT, <i>Diabetologia</i> , 54, S401-, 2011	Conference abstract
Buccino, J., Murray, K., Farmer, S., Assor, E., Daneman, D., Systematic review of the dietary management of children with type 1 diabetes, <i>Canadian Journal of Diabetes</i> , 28, 219-225, 2004	Systematic review. No relevant papers identified
Cadario, F., Prodam, F., Pasqualicchio, S., Bellone, S., Bonsignori, I., Demarchi, I., Monzani, A., Bona, G., Lipid profile and nutritional intake in children and adolescents with Type 1 diabetes improve after a structured dietician training to a Mediterranean-style diet, <i>Journal of Endocrinological Investigation</i> , 35, 160-168, 2012	Non-randomised study
Forsander, G., Malmödin, B., Eklund, C., Persson, B., Relationship between dietary intake in children with diabetes mellitus type I, their management at diagnosis, social factors, anthropometry and glycaemic control, <i>Scandinavian Journal of Nutrition/Naringsforskning</i> , 47, 75-84, 2003	PICO (Population Intervention Comparator Outcomes) not met - study examines different diabetic care programmes
Gilbertson, H.R., Brand-Miller, J.C., Thorburn, A.W., Evans, S., Chondros, P., Werther, G.A., Erratum: The effect of flexible low glycemic index dietary advice versus measured carbohydrate exchange diets on glycaemic control in children with type 1 diabetes (<i>Diabetes Care</i> (2001) 24 (1137-1143)), <i>Diabetes Care</i> , 36, 1056-, 2013	Erratum for excluded study only
Gilbertson, H.R., Brand-Miller, J.C., Thorburn, A.W., Evans, S., Chondros, P., Werther, G.A., The effect of flexible low glycemic index dietary advice versus measured carbohydrate exchange diets on glycaemic control in children with type 1 diabetes, <i>Diabetes Care</i> , 24, 1137-1143, 2001	PICO not met - study did not examine carbohydrate counting
Goksen, D., Darcan, S., Buyukinan, M., Kose, T., Erermis, S., Coker, M., The effect of insulin glargine and nutritional model on metabolic control, quality of life and behavior in children and adolescents with type 1 diabetes mellitus, <i>Acta Diabetologica</i> , 45, 47-52, 2008	Non-randomised study
Goksen, D., Ozen, S., Atik, Altinok Y., Demir, G., Darcan, S., Effects of carbohydrate counting method on metabolic control in children with type 1 diabetes, <i>Pediatric Diabetes</i> , 13, 142-, 2012	Conference abstract only, therefore insufficient data for inclusion
Hayes, R.L., Garnett, S.P., Clarke, S.L., Harkin, N.M., Chan, A.K., Ambler, G.R., A flexible diet using an insulin to carbohydrate ratio for adolescents with type 1 diabetes - a pilot study, <i>Clinical Nutrition</i> , 31, 705-709, 2012	Longitudinal study, not an RCT
Kaufman, F.R., Halvorson, M., Carpenter, S., Use of a plastic insulin dosage guide to correct blood glucose levels out of the target range and for carbohydrate counting in subjects with type 1 diabetes, <i>Diabetes Care</i> , 22, 1252-1257, 1999	PICO not met - study examined two different methods of calculating insulin based on carbohydrate counting and both groups used carbohydrate counting
Kawamura, T., The importance of carbohydrate counting in the treatment of children with diabetes, <i>Pediatric Diabetes</i> , 8, 57-62, 2007	Narrative review of carbohydrate counting
Lowe, J., Linjawi, S., Mensch, M., James, K., Attia, J., Flexible	Non-randomised study

Study	Reason for exclusion
eating and flexible insulin dosing in patients with diabetes: Results of an intensive self-management course, <i>Diabetes Research and Clinical Practice</i> , 80, 439-443, 2008	
Maffei, C., Morandi, A., Ventura, E., Sabbion, A., Contreas, G., Tomasselli, F., Tommasi, M., Fasan, I., Costantini, S., Pinelli, L., Diet, physical, and biochemical characteristics of children and adolescents with type 1 diabetes: Relationship between dietary fat and glucose control, <i>Pediatric Diabetes</i> , 13, 137-146, 2012	Non-randomised study
Marigliano, M., Morandi, A., Maschio, M., Sabbion, A., Contreas, G., Tomasselli, F., Tommasi, M., Maffei, C., Nutritional education and carbohydrate counting in children with type 1 diabetes treated with continuous subcutaneous insulin infusion: the effects on dietary habits, body composition and glycometabolic control, <i>Acta Diabetologica</i> , 50, 959-964, 2013	Not an RCT - longitudinal study
Marquard, J., Stahl, A., Lerch, C., Wolters, M., Grotzke-Leweling, M., Mayatepek, E., Meissner, T., A prospective clinical pilot-trial comparing the effect of an optimized mixed diet versus a flexible low-glycemic index diet on nutrient intake and HbA1c levels in children with type 1 diabetes, <i>Journal of Pediatric Endocrinology and Metabolism</i> , 24, 441-447, 2011	PICO not met - study did not examine carbohydrate counting
Rabbone, I., Scaramuzza, A.E., Ignaccolo, M.G., Tinti, D., Sicignano, S., Redaelli, F., De Angelis, L., Bosetti, A., Zuccotti, G.V., Cerutti, F., Carbohydrate counting with an automated bolus calculator helps to improve glycaemic control in children with type 1 diabetes using multiple daily injection therapy: an 18-month observational study, <i>Diabetes Research and Clinical Practice</i> , 103, 388-394, 2014	Observational study
Riccardi, G., Giacco, R., Parillo, M., Turco, S., Rivellesse, A.A., Ventura, M.R., Contadini, S., Marra, G., Monteduro, M., Santeusano, F., Brunetti, P., Librenti, M.C., Pontiroli, A.E., Vedani, P., Pozza, G., Bergamini, L., Bianchi, C., Efficacy and safety of acarbose in the treatment of Type 1 diabetes mellitus: a placebo-controlled, double-blind, multicentre study, <i>Diabetic Medicine</i> , 16, 228-232, 1999	PICO not met - study only included adults (aged between 18 and 65 years)
Schmidt, S., Meldgaard, M., Serifovski, N., Storm, C., Christensen, T.M., Gade-Rasmussen, B., Norgaard, K., Use of an automated bolus calculator in MDI-treated type 1 diabetes: the BolusCal Study, a randomized controlled pilot study, <i>Diabetes Care</i> , 35, 984-990, 2012	All participants aged > 18 years
Spiegel, G., Bortsov, A., Bishop, F.K., Owen, D., Klingensmith, G.J., Mayer-Davis, E.J., Maahs, D.M., Randomized Nutrition Education Intervention to Improve Carbohydrate Counting in Adolescents with Type 1 Diabetes Study: Is More Intensive Education Needed?, <i>Journal of the Academy of Nutrition and Dietetics</i> , , 1736-1746, 2012	PICO not met - study examines carbohydrate counting in children and young people with poor carbohydrate counting accuracy
Waller, H., Eiser, C., Knowles, J., Rogers, N., Wharmby, S., Heller, S., Hall, C., Greenhalgh, S., Tinklin, T., Metcalfe, C., Millard, E., Parkin, V., Denial, M., Price, K., Pilot study of a novel educational programme for 11-16 year olds with type 1 diabetes mellitus: the KICK-OFF course, <i>Archives of Disease in Childhood</i> , 93, 927-931, 2008	Non-randomised pilot study for an RCT of carbohydrate counting and insulin dosage adjustment

What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?

Study	Reason for exclusion
Brand-Miller, J., Hayne, S., Petocz, P., Colagiuri, S., Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials, <i>Diabetes Care</i> , 26, 2261-2267, 2003	Meta-analysis of trials of low glycaemic index diets. Studies included predominantly adults. Two studies identified which relate to children: Gilbertson et al., Collier et al.
Buccino, J., Murray, K., Farmer, S., Assor, E., Daneman, D., Systematic review of the dietary management of children with type 1 diabetes, <i>Canadian Journal of Diabetes</i> , 28, 219-225, 2004	Systematic review that identifies no new studies
Forsander, G., Malmödin, B., Eklund, C., Persson, B.,	PICO (Population Intervention Comparator Outcomes) not

Relationship between dietary intake in children with diabetes mellitus type I, their management at diagnosis, social factors, anthropometry and glycaemic control, Scandinavian Journal of Nutrition/Naringsforskning, 47, 75-84, 2003	met - study examines different diabetic care programmes
Gilbertson,H.R., Thorburn,A.W., Brand-Miller,J.C., Chondros,P., Werther,G.A., Effect of low-glycemic-index dietary advice on dietary quality and food choice in children with type 1 diabetes, American Journal of Clinical Nutrition, 77, 83-90, 2003	Secondary publication of an included study (Gilbertson et al., 2001)
Marquard,J., Stahl,A., Lerch,C., Wolters,M., Grotzke-Leweling,M., Mayatepek,E., Meissner,T., A prospective clinical pilot-trial comparing the effect of an optimized mixed diet versus a flexible low-glycemic index diet on nutrient intake and HbA1c levels in children with type 1 diabetes, Journal of Pediatric Endocrinology and Metabolism, 24, 441-447, 2011	PICO not met - study does not measure outcomes at > 4 months
Nansel,T.R., Gellar,L., McGill,A., Effect of varying glycemic index meals on blood glucose control assessed with continuous glucose monitoring in youth with type 1 diabetes on basal-bolus insulin regimens, Diabetes Care, 31, 695-697, 2008	PICO not met - study does not measure outcomes at > 4 months
Nansel,T.R., Gellar,L., Zeitzoff,L., Acceptability of lower glycemic index foods in the diabetes camp setting, Journal of Nutrition Education and Behavior, 38, 143-150, 2006	PICO not met - study does not measure outcomes at > 4 months
Riccardi,G., Giacco,R., Parillo,M., Turco,S., Rivellese,A.A., Ventura,M.R., Contadini,S., Marra,G., Monteduro,M., Santeusano,F., Brunetti,P., Librenti,M.C., Pontiroli,A.E., Vedani,P., Pozza,G., Bergamini,L., Bianchi,C., Efficacy and safety of acarbose in the treatment of Type 1 diabetes mellitus: a placebo-controlled, double-blind, multicentre study, Diabetic Medicine, 16, 228-232, 1999	PICO not met - population aged between 18 and 65 years
Rovner,A.J., Nansel,T.R., Gellar,L., The effect of a low-glycemic diet vs a standard diet on blood glucose levels and macronutrient intake in children with type 1 diabetes, Journal of the American Dietetic Association, 109, 303-307, 2009	PICO not met - study does not measure outcomes at > 4 months
Ryan,R.L., King,B.R., Anderson,D.G., Attia,J.R., Collins,C.E., Smart,C.E., Influence of and optimal insulin therapy for a low-glycemic index meal in children with type 1 diabetes receiving intensive insulin therapy, Diabetes Care, 31, 1485-1490, 2008	PICO not met - study did not examine effectiveness of dietetic advice
Spiegel,G., Bortsov,A., Bishop,F.K., Owen,D., Klingensmith,G.J., Mayer-Davis,E.J., Maahs,D.M., Randomized Nutrition Education Intervention to Improve Carbohydrate Counting in Adolescents with Type 1 Diabetes Study: Is More Intensive Education Needed?, Journal of the Academy of Nutrition and Dietetics, , 1736-1746, 2012	PICO not met - study examines two forms of carbohydrate counting not glycaemic index

H.10 Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

Review question

What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?

Study	Reason for exclusion
Bashford,James, Acerini,Carlo L., How to use near-patient capillary ketone meters, Archives of disease in childhood - Education & practice edition, 97, 217-221, 2012	Review article.
Bektas,F., Eray,O., Sari,R., Akbas,H., Point of care blood ketone testing of diabetic patients in the emergency department, Endocrine Research, 30, 395-402, 2004	PICO not met - adult participants only.
Bilan,N., Behbahan,A.G., Khosroshahi,A.J., Validity of venous blood gas analysis for diagnosis of acid-base imbalance in children admitted to pediatric intensive care unit, World Journal of Pediatrics, 4, 114-117, 2008	PICO not met - assesses correlation of arterial and venous blood gas measurement, but no reference to diagnosing DKA

Charles,R.A., Bee,Y.M., Eng,P.H., Goh,S.Y., Point-of-care blood ketone testing: screening for diabetic ketoacidosis at the emergency department, Singapore Medical Journal, 48, 986-989, 2007	PICO not met - no age restriction, but median age 60 years.
Ham,M.R., Okada,P., White,P.C., Bedside ketone determination in diabetic children with hyperglycemia and ketosis in the acute care setting, Pediatric Diabetes, 5, 39-43, 2004	PICO not met - outcomes of interest not reported, and not able to be calculated from data provided. Article only describes positive and negative predictive values. Cannot define 2x2 table to calculate other measures of diagnostic test accuracy.
Harris,S., Ng,R., Syed,H., Hillson,R., Near patient blood ketone measurements and their utility in predicting diabetic ketoacidosis, Diabetic Medicine, 22, 221-224, 2005	PICO not met - no age inclusion criteria. Age range in study 16 to 93 years but results for those aged < 18 years not presented separately.
Hendey,G.W., Schwab,T., Soliz,T., Urine ketone dip test as a screen for ketonemia in diabetic ketoacidosis and ketosis in the emergency department, Annals of Emergency Medicine, 29, 735-738, 1997	PICO not met - participant mean age was 38 years, although range was 14 to 80 years. Number of participants under 18 years not reported. Results for participants under 18 years not reported separately.
Nadler,O.A., Finkelstein,M.J., Reid,S.R., How well does serum bicarbonate concentration predict the venous pH in children being evaluated for diabetic ketoacidosis?, Pediatric Emergency Care, 27, 907-910, 2011	PICO not met - outcomes of interest not reported, and not able to be calculated from data provided.
Naunheim,R., Jang,T.J., Banet,G., Richmond,A., McGill,J., Point-of-care test identifies diabetic ketoacidosis at triage, Academic Emergency Medicine, 13, 683-685, 2006	PICO not met - adult participants only.
Qiao,Y., Gao,Z., Liu,Y., Cheng,Y., Yu,M., Zhao,L., Duan,Y., Breath ketone testing: A new biomarker for diagnosis and therapeutic monitoring of diabetic ketosis, BioMed Research International, 2014, 2014. Article Number, -, 2014	PICO not met - age range in study 11 to 85 years but results for those aged < 18 years not presented separately.
Schwab,T.M., Hendey,G.W., Soliz,T.C., Screening for ketonemia in patients with diabetes, Annals of Emergency Medicine, 34, 342-346, 1999	PICO not met - adult participants only.

H.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions

What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?

Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:

- general observations (for example, heart and respiratory rate and blood pressure)
- body weight
- hydration status
- fluid balance
- neurological observations
- electrocardiographic (ECG) monitoring?

Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:

- blood glucose
- blood or urine ketones
- serum urea or electrolytes
- acid/base status?

These 3 questions were addressed through a single search and there is one combined list of excluded studies.

Study	Reason for exclusion
Fagan,M.J., Avner,J., Khine,H., Initial fluid resuscitation for patients with diabetic ketoacidosis: how dry are they?, <i>Clinical Pediatrics</i> , 47, 851-855, 2008	Not a comparative study
Felner,E.I., White,P.C., Improving management of diabetic ketoacidosis in children, <i>Pediatrics</i> , 108, 735-740, 2001	PICO not met - intervention (two different DKA management protocols) not of interest
Glaser,N.S., Ghetti,S., Casper,T.C., Dean,J.M., Kuppermann,N., Pediatric Emergency Care Applied Research Network (PECARN) DKA FLUID Study Group., Pediatric diabetic ketoacidosis, fluid therapy, and cerebral injury: the design of a factorial randomized controlled trial, <i>Pediatric Diabetes</i> , 14, 435-446, 2013	Not a comparative study
Harris,G.D., Fiordalisi,I., Physiologic management of diabetic ketoacidemia. A 5-year prospective pediatric experience in 231 episodes, <i>Archives of Pediatrics and Adolescent Medicine</i> , 148, 1046-1052, 1994	Not a comparative study
Harrower,A.D., Campbell,I.W., Ewing,D.J., Murray,A., Neilson,J.M., Clarke,B.F., The value of continuous ECG monitoring during treatment of diabetic ketoacidosis. A computer study, <i>Acta Diabetologica Latina</i> , 15, 88-94, 1978	PICO not met - population were mainly adults
Jahagirdar,R.R., Khadilkar,V.V., Khadilkar,A.V., Lalwani,S.K., Management of diabetic ketoacidosis in PICU, <i>Indian Journal of Pediatrics</i> , 74, 551-554, 2007	Not a comparative study
Klocker,A.A., Phelan,H., Twigg,S.M., Craig,M.E., Blood beta-hydroxybutyrate vs. urine acetoacetate testing for the prevention and management of ketoacidosis in Type 1 diabetes: a systematic review, <i>Diabetic Medicine</i> , 30, 818-824, 2013	Systematic review of blood versus urine ketone testing
Koves,I.H., Neutze,J., Donath,S., Lee,W., Werther,G.A., Barnett,P., Cameron,F.J., The accuracy of clinical assessment of dehydration during diabetic ketoacidosis in childhood, <i>Diabetes Care</i> , 27, 2485-2487, 2004	Not a comparative study
Ma,O.J., Rush,M.D., Godfrey,M.M., Gaddis,G., Arterial blood gas results rarely influence emergency physician management of patients with suspected diabetic ketoacidosis, <i>Academic Emergency Medicine</i> , 10, 836-841, 2003	Not a comparative study
McBride,M.E., Berkenbosch,J.W., Tobias,J.D., Transcutaneous carbon dioxide monitoring during diabetic ketoacidosis in children and adolescents, <i>Paediatric Anaesthesia</i> , 14, 167-171, 2004	PICO not met - interventions (different methods of carbon dioxide monitoring) not of interest
Naunheim,R., Jang,T.J., Banet,G., Richmond,A., McGill,J., Point-of-care test identifies diabetic ketoacidosis at triage, <i>Academic Emergency Medicine</i> , 13, 683-685, 2006	Not a comparative study
Rewers,A., McFann,K., Chase,H.P., Bedside monitoring of blood beta-hydroxybutyrate levels in the management of diabetic ketoacidosis in children, <i>Diabetes Technology and Therapeutics</i> , 8, 671-676, 2006	Not a comparative study
Sottosanti,M., Morrison,G.C., Singh,R.N., Sharma,A.P., Fraser,D.D., Alawi,K., Seabrook,J.A., Kornecki,A., Dehydration in children with diabetic ketoacidosis: a prospective study, <i>Archives of Disease in Childhood</i> , 97, 96-100, 2012	Not a comparative study
Turan,S., Omar,A., Bereket,A., Comparison of capillary blood ketone measurement by electrochemical method and urinary ketone in treatment of diabetic ketosis and ketoacidosis in children, <i>Acta Diabetologica</i> , 45, 83-85, 2008	PICO not met - outcomes of interest not reported
Wootton-Gorges,S.L., Buonocore,M.H., Kuppermann,N., Marcin,J., Dicarolo,J., Neely,E.K., Barnes,P.D., Glaser,N., Detection of cerebral {beta}-hydroxy butyrate, acetoacetate, and lactate on proton MR spectroscopy in children with diabetic ketoacidosis, <i>Ajnr: American Journal of Neuroradiology</i> , 26, 1286-1291, 2005	Not a comparative study

H.12 Type 1 and type 2 diabetes – diabetic ketoacidosis- fluids

Review questions

What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?

No articles were ordered for detailed consideration for this review question and so there is no excluded studies list.

At what rate should children and young people with diabetic ketoacidosis be rehydrated?

Study	Reason for exclusion
Carcillo,J.A., Intravenous fluid choices in critically ill children, Current Opinion in Critical Care, 20, 396-401, 2014	Discussion paper for reference checking. Relevant studies have been included in the guideline review.
Duck,S.C., Wyatt,D.T., Factors associated with brain herniation in the treatment of diabetic ketoacidosis, Journal of Pediatrics, 113, 10-14, 1988	Not a comparative study.
Hom,J., Sinert,R., Evidence-based emergency medicine/critically appraised topic. Is fluid therapy associated with cerebral edema in children with diabetic ketoacidosis?. [12 refs], Annals of Emergency Medicine, 52, 69-75, 2008	Systematic review which includes papers already identified in the guideline search results.
Mel,J.M., Werther,G.A., Incidence and outcome of diabetic cerebral oedema in childhood: are there predictors?, Journal of Paediatrics and Child Health, 31, 17-20, 1995	Assesses risk factors for, and survival after, cerebral oedema. No comparison of the different fluid protocols.

What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

Study	Reason for exclusion
Basnet,S., Venepalli,P.K., Andoh,J., Verhulst,S., Koirala,J., Effect of normal saline and half normal saline on serum electrolytes during recovery phase of diabetic ketoacidosis, Journal of Intensive Care Medicine, 29, 38-42, 2014	Normal saline was compared with half-normal saline; no additives of interest to the GDG were assessed.
Duck,S.C., Wyatt,D.T., Factors associated with brain herniation in the treatment of diabetic ketoacidosis, Journal of Pediatrics, 113, 10-14, 1988	Not a comparative study.
Hale,P.J., Crase,J., Natrass,M., Metabolic effects of bicarbonate in the treatment of diabetic ketoacidosis, British Medical Journal Clinical Research Ed., 289, 1035-1038, 1984	PICO not met: adult population, mean ages of 47 years and 41 years for each treatment group.
Krumlik,J.J., Ehrlich,R.M., Insulin and sodium bicarbonate treatment of diabetic acidosis: a retrospective review, Journal of Pediatrics, 83, 269-271, 1973	No comparative analysis of different fluid compositions.
Reddy,C.M., Orti,E., Crump,E.P., Treatment of diabetic ketoacidosis in children: A retrospective review, Clinical Research, 25, 68A-, 1977	Duplicate of previously weeded-out study with different title - abstract only.
Rother,K.I., Schwenk,W.F., Effect of rehydration fluid with 75 mmol/L of sodium on serum sodium concentration and serum osmolality in young patients with diabetic ketoacidosis, Mayo Clinic Proceedings, 69, 1149-1153, 1994	Not a comparative study.
Soler,N.G., Bennett,M.A., Dixon,K., Fitzgerald,M.G., Malins,J.M., Potassium balance during treatment of diabetic ketoacidosis with special reference to the use of bicarbonate, Lancet, 2, 665-667, 1972	PICO not met: adult population, age range 13 to 84 years. No subgroup analyses for age group of relevance in this guideline.
Thuzar,M., Malabu,U.H., Tisdell,B., Sangla,K.S., Use of a standardised diabetic ketoacidosis management protocol improved clinical outcomes, Diabetes Research and Clinical Practice, 104, E8-E11, 2014	Patients >= 16 years were included (mean age 30 years).
Toledo,J.D., Modesto,V., Peinador,M., Alvarez,P., Lopez-Prats,J.L., Sanchis,R., Vento,M., Sodium concentration in rehydration fluids for children with ketoacidotic diabetes: effect on serum sodium concentration, Journal of Pediatrics,	Not a comparative study. Regression analysis only.

Study	Reason for exclusion
154, 895-900, 2009	
White,P.C., Dickson,B.A., Low morbidity and mortality in children with diabetic ketoacidosis treated with isotonic fluids.[Erratum appears in J Pediatr. 2013 Sep;163(3):927], Journal of Pediatrics, 163, 761-766, 2013	The dextrose assessed in this study, which is a type of additive, was not included in the protocol.
Wilson,H.K., Keuer,S.P., Lea,A.S., Boyd,A.E.,III, Eknoyan,G., Phosphate therapy in diabetic ketoacidosis, Archives of Internal Medicine, 142, 517-520, 1982	PICO not met: adult population, mean age 26.8 years, range 14 to 58 years.

H.13 Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents

Review question

What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?

Study	Reason for exclusion
Treating diabetic ketoacidosis in children requires careful management of fluid, electrolytes and insulin, Drugs and Therapy Perspectives, 25, 14-17, 2009	Management article
Rosenbloom,A.L., Cerebral edema in diabetic ketoacidosis and other acute devastating complications: Recent observations, Pediatric Diabetes, 6, 41-49, 2005	A review of reports
Rosenbloom,A.L., Intracerebral crises during treatment of diabetic ketoacidosis, Diabetes Care, 13, 22-33, 1990	Review of unpublished case records and published reports
Sherry,N.A., Levitsky,L.L., Management of diabetic ketoacidosis in children and adolescents. [49 refs], Paediatric Drugs, 10, 209-215, 2008	Exclude since it is a management article (used for checking references)
Tasker,R.C., Burns,J., Hypertonic saline therapy for cerebral edema in diabetic ketoacidosis: no change yet, please, Pediatric Critical Care Medicine, 15, 284-285, 2014	For reference checking
White,P.C., Dickson,B.A., Low morbidity and mortality in children with diabetic ketoacidosis treated with isotonic fluids, Journal of Pediatrics, 163, 761-766, 2013	Case series
Wolfsdorf,J., Craig,M.E., Daneman,D., Dunger,D., Edge,J., Lee,W., Rosenbloom,A., Sperling,M., Hanas,R., Diabetic ketoacidosis in children and adolescents with diabetes, Pediatric Diabetes, 10, 118-133, 2009	Clinical practice consensus guidelines compendium

H.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

Review questions

When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?

All articles order for detailed consideration for this review question were included in the review and so there is no excluded studies list.

How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

All articles order for detailed consideration for this review question were included in the review and so there is no excluded studies list.

H.15 Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis

Review question

What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?

No articles were ordered for detailed consideration for this review question and so there is no excluded studies list.

H.16 Type 1 diabetes – retinopathy

Review question

What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?

Study	Reason for exclusion
When to screen for retinopathy in children with diabetes, <i>Consultant</i> , 38, 1320-, 1998	Summary of American Academy of Pediatrics guidelines only; no data reported
Progression of retinopathy with intensive versus conventional treatment in the Diabetes Control and Complications Trial. Diabetes Control and Complications Trial Research Group, <i>Ophthalmology</i> , 102, 647-661, 1995	Mean age 26.4 years; data on children and young people reported separately in an included study
Aiello, L.P., Diabetic retinopathy and other ocular findings in the diabetes control and complications trial/epidemiology of diabetes interventions and complications study, <i>Diabetes Care</i> , 37, 17-23, 2014	No stratification by age; full DCCT cohort, therefore, mean age > 18 years
Al-Fifi, S.H., Intensive insulin treatment versus conventional regimen for adolescents with type 1 diabetes, benefits and risks, <i>Saudi Medical Journal</i> , 24, 485-487, 2003	Population included 12 to 18 year-olds; no stratification of prevalence of retinopathy within this age range
Amutha, A., Datta, M., Unnikrishnan, R., Anjana, R.M., Mohan, V., Clinical profile and complications of childhood and adolescent-onset type 2 diabetes seen at a diabetes center in south India, <i>Diabetes Technology and Therapeutics</i> , 14, 497-504, 2012	No data on prevalence of retinopathy according to age or duration of diabetes
Betts, P.R., Logatchov, M., Volkov, I., Murphy, H., Dombrowskaya, N., Borzikh, S., Ivanova, I., Twyman, S., Vartan, J., An assessment of paediatric diabetes care in three centres in Russia and in Southampton, UK. The Paediatric Teams in Moscow, Tula, Tambov, Southampton, <i>Diabetic Medicine</i> , 16, 772-778, 1999	No stratification according to age or duration of diabetes; method of identifying retinopathy not reported
Bognetti, E., Calori, G., Meschi, F., Macellaro, P., Bonfanti, R., Chiumello, G., Prevalence and correlations of early microvascular complications in young type I diabetic patients: role of puberty, <i>Journal of Pediatric Endocrinology</i> , 10, 587-592, 1997	No stratification of prevalence according to age or duration of diabetes
Bonney, M., Hing, S.J., Fung, A.T., Stephens, M.M., Fairchild, J.M., Donaghue, K.C., Howard, N.J., Silink, M., Development and progression of diabetic retinopathy: adolescents at risk, <i>Diabetic Medicine</i> , 12, 967-973, 1995	Incidence data already included in Cheung 2008, and prevalence according to age already included in Cho 2011
Burger, W., Hovener, G., Dusterhus, R., Hartmann, R., Weber, B., Prevalence and development of retinopathy in children and adolescents with type 1 (insulin-dependent) diabetes mellitus. A longitudinal study, <i>Diabetologia</i> , 29, 17-22, 1986	Fluorescein angiography used to identify retinopathy
Cahill, M., Wallace, D., Travers, S., Lipinski, H., Aldington, S., Costigan, C., Mooney, D., Detection and prevalence of early diabetic retinopathy in juvenile diabetics with diabetes for 10 years or more, <i>Eye</i> , 14, 847-850, 2000	No stratification of retinopathy prevalence within age group (population age range 11.4 to 22.6 years)
Chiumello, G., Bognetti, E., Meschi, F., Carra, M., Balzano, E., Early diagnosis of subclinical complications in insulin dependent diabetic children and adolescents, <i>Journal of Endocrinological Investigation</i> , 12, 101-104, 1989	Prevalence of retinopathy not grouped according to age or duration of diabetes; method of identifying retinopathy not reported
Cobuz, M., Cobuz, C., Chronic complications of type 1 diabetes mellitus in children, <i>Romanian Journal of Diabetes, Nutrition and Metabolic Diseases</i> , 19, 301-309, 2012	Ophthalmoscopy used to identify retinopathy; no stratification of prevalence according to age or duration of diabetes

Study	Reason for exclusion
Danne,T., Kordonouri,O., Casani,A., Tumini,S., Chiarelli,F., Recent advances on the pathogenesis and management of both diabetic retinopathy and nephropathy with particular reference to children and adolescents with Type 1 diabetes. [87 refs], Diabetes, Nutrition and Metabolism - Clinical and Experimental, 12, 136-144, 1999	Narrative review
Dart,A.B., Martens,P.J., Rigatto,C., Brownell,M.D., Dean,H.J., Sellers,E.A., Earlier onset of complications in youth with type 2 diabetes, Diabetes Care, 37, 436-443, 2014	No stratification by age
Demirel,F., Tepe,D., Kara,O., Esen,I., Microvascular complications in adolescents with type 1 diabetes mellitus, JCRPE Journal of Clinical Research in Pediatric Endocrinology, 5, 145-149, 2013	No stratification by age or duration of diabetes
Donaghue,K.C., Chiarelli,F., Trotta,D., Allgrove,J., hl-Jorgensen,K., Microvascular and macrovascular complications associated with diabetes in children and adolescents, Pediatric Diabetes, 10, 195-203, 2009	Clinical guideline, no primary data
Donaghue,K.C., Craig,M.E., Chan,A.K., Fairchild,J.M., Cusumano,J.M., Verge,C.F., Crock,P.A., Hing,S.J., Howard,N.J., Silink,M., Prevalence of diabetes complications 6 years after diagnosis in an incident cohort of childhood diabetes, Diabetic Medicine, 22, 711-718, 2005	Prevalence of retinopathy recorded according to age, but data only provided graphically therefore unable to determine exact numbers
Donaghue,K.C., Fairchild,J.M., Craig,M.E., Chan,A.K., Hing,S., Cutler,L.R., Howard,N.J., Silink,M., Do all prepubertal years of diabetes duration contribute equally to diabetes complications?, Diabetes Care, 26, 1224-1229, 2003	No data on prevalence stratified by age or duration of diabetes
Donaghue,K.C., Fung,A.T., Hing,S., Fairchild,J., King,J., Chan,A., Howard,N.J., Silink,M., The effect of prepubertal diabetes duration on diabetes. Microvascular complications in early and late adolescence, Diabetes Care, 20, 77-80, 1997	No stratification of prevalence according to age or duration of diabetes
Donaghue,K.C., Fairchild,J.M., Chan,A., Hing,S.J., King,J., Howard,N.J., Silink,M., Diabetes microvascular complications in prepubertal children, Journal of Pediatric Endocrinology, 10, 579-585, 1997	Background population identical to that used in Donaghue et 1999
Downie,E., Craig,M.E., Hing,S., Cusumano,J., Chan,A.K., Donaghue,K.C., Continued reduction in the prevalence of retinopathy in adolescents with type 1 diabetes: role of insulin therapy and glycaemic control, Diabetes Care, 34, 2368-2373, 2011	No data on prevalence of retinopathy according to age or duration of diabetes
El,AsrarM, Adly,A.A., El,HadidyE, Abdelwahab,M.A., D-dimer levels in type 1 and type 2 diabetic children and adolescents; Relation to microvascular complications and dyslipidemia "own data and review", Pediatric endocrinology reviews : PER, 9, 657-668, 2012	Ophthalmoscopy used to identify retinopathy; no stratification of prevalence according to age or duration of diabetes
Eppens,M.C., Craig,M.E., Cusumano,J., Hing,S., Chan,A.K., Howard,N.J., Silink,M., Donaghue,K.C., Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes, Diabetes Care, 29, 1300-1306, 2006	No assessment of prevalence of retinopathy according to age or duration of diabetes
Fairchild,J.M., Hing,S.J., Donaghue,K.C., Bonney,M.A., Fung,A.T., Stephens,M.M., Mitchell,P., Howard,N.J., Silink,M., Prevalence and risk factors for retinopathy in adolescents with type 1 diabetes, Medical Journal of Australia, 160, 757-762, 1994	No assessment of prevalence according to age or duration of diabetes
Falck,A.A., Kaar,M.L., Laatikainen,L.T., Prevalence and risk factors of retinopathy in children with diabetes. A population-based study on Finnish children, Acta Ophthalmologica, 71, 801-809, 1993	Data already included in Falck 1996
Florkowski,C.M., Scott,R.S., Coope,P.A., Graham,P.J., Moir,C.L., Age at diagnosis, glycaemic control and the development of retinopathy in a population-based cohort of Type 1 diabetic subjects in Canterbury, New Zealand, Diabetes Research and Clinical Practice, 52, 125-131, 2001	Ophthalmoscopy used to identify retinopathy; no assessment of prevalence according to age or duration of diabetes
Frank,R.N., Hoffman,W.H., Podgor,M.J., Joondeph,H.C., Lewis,R.A., Margherio,R.R., Nachazel,D.P., Jr., Weiss,H., Christopherson,K.W., Cronin,M.A., Retinopathy in juvenile-onset diabetes of short duration, Ophthalmology, 87, 1-9, 1980	Data already included in Frank 1982
Gallego,P.H., Craig,M.E., Hing,S., Donaghue,K.C., Role of blood pressure in development of early retinopathy in adolescents with type 1 diabetes: Prospective cohort study, BMJ, 337, 497-500, 2008	No stratification of prevalence according to age or duration of diabetes

Study	Reason for exclusion
Hammes,H.P., Kerner,W., Hofer,S., Kordonouri,O., Raile,K., Holl,R.W., DPV-Wiss Study Group., Diabetic retinopathy in type 1 diabetes-a contemporary analysis of 8,784 patients, <i>Diabetologia</i> , 54, 1977-1984, 2011	Ophthalmoscopy used to identify retinopathy; no stratification according to age or prevalence of diabetes
Holl,R.W., Lang,G.E., Grabert,M., Heinze,E., Lang,G.K., Debatin,K.M., Diabetic retinopathy in pediatric patients with type-1 diabetes: effect of diabetes duration, prepubertal and pubertal onset of diabetes, and metabolic control, <i>Journal of Pediatrics</i> , 132, 790-794, 1998	No assessment of prevalence of retinopathy according to age or duration of diabetes; data presented only graphically
Huo,B., Steffen,A.T., Swan,K., Sikes,K., Weinzimer,S.A., Tamborlane,W.V., Clinical outcomes and cost-effectiveness of retinopathy screening in youth with type 1 diabetes, <i>Diabetes Care</i> , 30, 362-363, 2007	Ophthalmoscopy used to identify retinopathy; no data on prevalence of retinopathy according to age or duration of diabetes
itez-Aguirre,P., Craig,M.E., Sasongko,M.B., Jenkins,A.J., Wong,T.Y., Wang,J.J., Cheung,N., Donaghue,K.C., Retinal vascular geometry predicts incident retinopathy in young people with type 1 diabetes: a prospective cohort study from adolescence, <i>Diabetes Care</i> , 34, 1622-1627, 2011	No stratification according to age or duration of diabetes
Izumi,K., Hoshi,M., Kuno,S., Okuno,G., Yamazaki,Y., Isshiki,G., Sasaki,A., Glycemic control, growth and complications in children with insulin-dependent diabetes mellitus--a study of children enrolled in a Summer camp program for diabetics in Kinki district, Japan, <i>Diabetes Research and Clinical Practice</i> , 28, 185-190, 1995	Method of assessment of retinopathy not reported; no assessment of prevalence according to age or duration of diabetes
Jackson,R.L., Ide,C.H., Guthrie,R.A., James,R.D., Retinopathy in adolescents and young adults with onset of insulin-dependent diabetes in childhood, <i>Ophthalmology</i> , 89, 7-13, 1982	No assessment of prevalence of retinopathy according to age or duration of diabetes
Johnson,B., Elliott,J., Scott,A., Heller,S., Eiser,C., Medical and psychological outcomes for young adults with Type 1 diabetes: No improvement despite recent advances in diabetes care, <i>Diabetic Medicine</i> , 31, 227-231, 2014	Mean age 18.1 years; no stratification by age group
Kalter-Leibovici,O., Leibovici,L., Loya,N., Kremer,I., xer-Siegel,R., Karp,M., Laron,Z., The development and progression of diabetic retinopathy in type I diabetic patients: a cohort study, <i>Diabetic Medicine</i> , 14, 858-866, 1997	Retinal photography only obtained when fundoscopy suggested abnormalities; prevalence not stratified by age or duration of diabetes
Kanematsu,S., Maruyama,H., Ishiba,S., Uchigata,Y., Otani,T., Kasahara,T., Yao,K., Kameyama,K., Omori,Y., Fukuyama,Y., Hirata,Y., Onset and prevalence of retinopathy in insulin-dependent diabetic Japanese children, Current status of prevention and treatment of diabetic complications: proceedings of the Third International Symposium on treatment of Diabetes Mellitus, 501-505, 1990	All participants > 20 years old at time of examination
Klein,B.E., Moss,S.E., Klein,R., Is menarche associated with diabetic retinopathy?, <i>Diabetes Care</i> , 13, 1034-1038, 1990	No stratification of prevalence of retinopathy according to age or duration of diabetes
Klein,R., Klein,B.E., Moss,S.E., Davis,M.D., DeMets,D.L., Retinopathy in young-onset diabetic patients, <i>Diabetes Care</i> , 8, 311-315, 1985	Data were obtained from same background population as Klein 1984, therefore already included in guideline review via that article
Kong,A., Donath,S., Harper,C.A., Werther,G.A., Cameron,F.J., Rates of diabetes mellitus-related complications in a contemporary adolescent cohort, <i>Journal of Pediatric Endocrinology</i> , 18, 247-255, 2005	Slit lamp examination/ophthalmoscopy only used to identify retinopathy
Kostraba,J.N., Dorman,J.S., Orchard,T.J., Becker,D.J., Ohki,Y., Ellis,D., Doft,B.H., Lobes,L.A., LaPorte,R.E., Drash,A.L., Contribution of diabetes duration before puberty to development of microvascular complications in IDDM subjects, <i>Diabetes Care</i> , 12, 686-693, 1989	No assessment of prevalence of retinopathy according to age or duration of diabetes, only according to puberty
Kovacs,M., Mukerji,P., Drash,A., Iyengar,S., Biomedical and psychiatric risk factors for retinopathy among children with IDDM, <i>Diabetes Care</i> , 18, 1592-1599, 1995	No stratification of prevalence of retinopathy according to age or duration of diabetes
Kubin,M., Tossavainen,P., Hannula,V., Lahti,S., Hautala,N., Falck,A., Prevalence of retinopathy in Finnish children and adolescents with type 1 diabetes: a cross-sectional population-based retrospective study, <i>Archives of Disease in Childhood</i> , 96, 963-968, 2011	No assessment of prevalence according to age or duration of diabetes
Lecaire,T., Palta,M., Zhang,H., Allen,C., Klein,R., D'Alessio,D., Lower-than-expected prevalence and severity of retinopathy in an incident cohort followed during the first 4-14 years of type 1 diabetes: the Wisconsin Diabetes Registry Study, <i>American Journal of Epidemiology</i> , 164, 143-150, 2006	Data on prevalence of retinopathy according to age and duration of diabetes reported only in graphical form
Levy-Shraga,Y., Lerner-Geva,L., Boyko,V., Graph-Barel,C., Mazor-Aronovitch,K., Modan-Moses,D., Pinhas-Hamiel,O.,	No assessment of prevalence according to age or duration of diabetes; method of identifying retinopathy not reported

Diagnosis and management of type 1 diabetes in children and young people
Excluded studies

Study	Reason for exclusion
Type 1 diabetes in pre-school children--long-term metabolic control, associated autoimmunity and complications, <i>Diabetic Medicine</i> , 29, 1291-1296, 2012	
Lievre,M., Marre,M., Robert,J.J., Charpentier,G., Iannascoli,F., Passa,P., Cross-sectional study of care, socio-economic status and complications in young French patients with type 1 diabetes mellitus, <i>Diabetes and Metabolism</i> , 31, 41-46, 2005	Method of identifying retinopathy not reported; no assessment of prevalence according to age or duration of diabetes
Lim,S.W., Cheung,N., Wang,J.J., Donaghue,K.C., Liew,G., Islam,F.M., Jenkins,A.J., Wong,T.Y., Retinal vascular fractal dimension and risk of early diabetic retinopathy: A prospective study of children and adolescents with type 1 diabetes, <i>Diabetes Care</i> , 32, 2081-2083, 2009	No stratification according to age or duration of diabetes
Lueder,G.T., Pradhan,S., White,N.H., Risk of retinopathy in children with type 1 diabetes mellitus before 2 years of age, <i>American Journal of Ophthalmology</i> , 140, 930-931, 2005	Retinopathy identified with ophthalmoscopy
Maguire,A., Chan,A., Cusumano,J., Hing,S., Craig,M., Silink,M., Howard,N., Donaghue,K., The case for biennial retinopathy screening in children and adolescents.[Erratum appears in <i>Diabetes Care</i> . 2007 Apr;30(4):1035], <i>Diabetes Care</i> , 28, 509-513, 2005	Duplication of data already included in Donaghue 1999
Malone,J.I., Grizzard,S., Espinoza,L.R., Achenbach,K.E., Van Cader,T.C., Risk factors for diabetic retinopathy in youth, <i>Pediatrics</i> , 73, 756-761, 1984	Fluorescein angiography used to identify retinopathy; no assessment of prevalence according to age or duration of diabetes
Mayer-Davis,E.J., Davis,C., Saadine,J., D'Agostino,R.B., Jr., Dabelea,D., Dolan,L., Garg,S., Lawrence,J.M., Pihoker,C., Rodriguez,B.L., Klein,B.E., Klein,R., SEARCH for Diabetes in Youth Study Group., Diabetic retinopathy in the SEARCH for Diabetes in Youth Cohort: a pilot study, <i>Diabetic Medicine</i> , 29, 1148-1152, 2012	Age of participants not reported; prevalence of retinopathy not reported according to age or duration of diabetes
Minuto,N., Emmanuele,V., Vannati,M., Russo,C., Reboria,C., Panarello,S., Pistorio,A., Lorini,R., d'Annunzio,G., Retinopathy screening in patients with type 1 diabetes diagnosed in young age using a non-mydratric digital stereoscopic retinal imaging, <i>Journal of Endocrinological Investigation</i> , 35, 389-394, 2012	No stratification of results according to age or duration of diabetes
Mohsin,F., Craig,M.E., Cusumano,J., Chan,A.K., Hing,S., Lee,J.W., Silink,M., Howard,N.J., Donaghue,K.C., Discordant trends in microvascular complications in adolescents with type 1 diabetes from 1990 to 2002, <i>Diabetes Care</i> , 28, 1974-1980, 2005	No stratification of prevalence of retinopathy according to age or duration of diabetes
Nicoloff,G., Baydanoff,S., Stanimirova,N., Petrova,C., Christova,P., Relationship between anti-elastin IgG subclasses and the development of microvascular complications - A three-year follow-up study in children with Type 1 (insulin-dependent) diabetes mellitus, <i>Central-European Journal of Immunology</i> , 26, 12-16, 2001	No assessment of prevalence according to age or duration of diabetes
Nicoloff,G., Baydanoff,S., Stanimirova,N., Petrova,Ch, Christova,P., An association of anti-elastin IgA antibodies with development of retinopathy in diabetic children, <i>General Pharmacology: The Vascular System</i> , 35, 83-87, 2000	Method of assessing retinopathy not reported; no assessment of prevalence according to age or duration of diabetes
North,R.V., Farrell,U., Banford,D., Jones,C., Gregory,J.W., Butler,G., Owens,D.R., Visual function in young IDDM patients over 8 years of age. A 4-year longitudinal study, <i>Diabetes Care</i> , 20, 1724-1730, 1997	Includes longitudinal data only but 13.5% of participants had retinopathy at baseline, and new incidence not reported; cannot assume new incidence for 4 years' follow up due to the potential for regression of retinopathy
Olsen,B.S., Johannesen,J., Sjolie,A.K., Borch-Johnsen,K., Hougaardss,P., Thorsteinsson,B., Prammingss,S., Marinelli,K., Mortensen,H.B., Metabolic control and prevalence of microvascular complications in young Danish patients with Type 1 diabetes mellitus. Danish Study Group of Diabetes in Childhood, <i>Diabetic Medicine</i> , 16, 79-85, 1999	Data on prevalence of retinopathy according to duration of diabetes presented only graphically; no data on prevalence stratified according to age
Owen,D.R., Farrell,U., Jones,C., North,R., Screening for diabetic retinopathy in young insulin-dependent diabetics (Type I), <i>Pediatric Reviews and Communications</i> , 8, 50-55, 1994	Data on prevalence of retinopathy at different ages reported only graphically; no data on prevalence after different durations of diabetes
Palmberg,P., Smith,M., Waltman,S., Krupin,T., Singer,P., Burgess,D., Wendtland,T., Achtenberg,J., Cryer,P., Santiago,J., White,N., Kilo,C., Daughaday,W., The natural history of retinopathy in insulin-dependent juvenile-onset diabetes, <i>Ophthalmology</i> , 88, 613-618, 1981	Age of participants not reported; no assessment of prevalence according to age or duration of diabetes
Papali'i-Curtin,A.T., Dalziel,D.M., Prevalence of diabetic retinopathy and maculopathy in Northland, New Zealand: 2011-2012, <i>New Zealand Medical Journal</i> , 126, 20-28, 2013	Mean age 62.7 years
Raman,V., Campbell,F., Holland,P., Chapman,T., Dabbs,T.,	No assessment of prevalence according to age or duration

Study	Reason for exclusion
Bodansky,H.J., O'Neill,D.P., Retinopathy screening in children and adolescents with diabetes, Annals of the New York Academy of Sciences, 958, 387-389, 2002	of diabetes
Rogers,D.G., White,N.H., Shalwitz,R.A., Palmberg,P., Smith,M.E., Santiago,J.V., The effect of puberty on the development of early diabetic microvascular disease in insulin-dependent diabetes, Diabetes Research and Clinical Practice, 3, 39-44, 1987	No assessment of prevalence according to age; although all participants had 5 to 7 years' duration of diabetes, the study did not include participants in puberty, or early post-pubertal stage therefore not representative of entire population of children and young people with type 1 diabetes
Salardi,S., Rubbi,F., Puglioli,R., Brancaloni,A., Bacchi-Reggiani,L., Ragni,L., Cacciari,E., Diabetic retinopathy in childhood: long-term follow-up by fluorescein angiography beginning in the first months of disease, Journal of Pediatric Endocrinology, 14, 507-515, 2001	Fluoroscein angiography used to identify retinopathy; no assessment of prevalence according to age or duration of diabetes
Shamoon,H., Duffy,H., Fleischer,N., Engel,S., Saenger,P., Strelzyn,M., Litwak,M., Wylie-Rosett,J., Farkash,A., Geiger,D., Engel,H., Fleischman,J., Pompei,D., Ginsberg,N., Glover,M., Brisman,M., Walker,E., Thomasunis,A., Gonzalez,J., The effect of intensive diabetes treatment on the progression of diabetic retinopathy in insulin-dependent diabetes mellitus: The diabetes control and complications trial, Archives of Ophthalmology, 113, 36-51, 1995	Mean age 26.5 years
Shamoon,H., Duffy,H., Fleischer,N., Engel,S., Saenger,P., Strelzyn,M., Litwak,M., Wylie-Rosett,J., Farkash,A., Geiger,D., Engel,H., Fleischman,J., Pompei,D., Ginsberg,N., Glover,M., Brisman,M., Walker,E., Thomashunis,A., Gonzalez,J., The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus, New England Journal of Medicine, 329, 977-986, 1993	Mean age for entire group was 26 +/- 8 years (conventional treatment group) and 27 +/- 7 years (intensive treatment group); data for age range of interest not reported separately
Verougstraete,C., Toussaint,D., De,Schepper,J, Haentjens,M., Dorchy,H., First microangiographic abnormalities in childhood diabetes - Types of lesions, Graefe's Archive for Clinical and Experimental Ophthalmology, 229, 24-32, 1991	Fluoroscein angiography used to identify retinopathy; no assessment of prevalence according to age or duration of diabetes
Wan Nazaimoon,W.M., Letchuman,R., Noraini,N., Ropilah,A.R., Zainal,M., Ismail,I.S., Wan Mohamad,W.B., Faridah,I., Singaraveloo,M., Sheriff,I.H., Khalid,B.A., Systolic hypertension and duration of diabetes mellitus are important determinants of retinopathy and microalbuminuria in young diabetics, Diabetes Research and Clinical Practice, 46, 213-221, 1999	Retinopathy assessed by ophthalmoscopy; mean age of participants 26.9 years
White,N.H., Cleary,P.A., Dahms,W., Goldstein,D., Malone,J., Tamborlane,W.V., Diabetes Control and Complications Trial (DCCT), Beneficial effects of intensive therapy of diabetes during adolescence: outcomes after the conclusion of the Diabetes Control and Complications Trial (DCCT), Journal of Pediatrics, 139, 804-812, 2001	No stratification of prevalence according to age or duration of diabetes
Wiltshire,E.J., Mohsin,F., Chan,A., Donaghue,K.C., Methylenetetrahydrofolate reductase and methionine synthase reductase gene polymorphisms and protection from microvascular complications in adolescents with type 1 diabetes, Pediatric Diabetes, 9, 348-353, 2008	No stratification of prevalence according to age or duration of diabetes

H.17 Type 1 diabetes – nephropathy

Review question

What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?

Study	Reason for exclusion
Al-Agha,A.E., Ocheltree,A., Hakeem,A., Occurrence of microalbuminuria among children and adolescents with insulin-dependent diabetes mellitus, Saudi Journal of Kidney Diseases and Transplantation, 24, 1180-1188, 2013	Study from Saudi Arabia
Allen,T.J., Cooper,M.E., Gilbert,R.E., Winikoff,J., Skinni,S.L., Jerums,G., Serum total renin is increased before microalbuminuria in diabetes, Kidney International, 50, 902-907, 1996	Study involving adults
Alleyn,C.R., Volkening,L.K., Wolfson,J., Rodriguez-	The threshold (ACR > 20 microg/mg)for confirmation of

Study	Reason for exclusion
Ventura,A., Wood,J.R., Laffel,L.M., Occurrence of microalbuminuria in young people with Type 1 diabetes: importance of age and diabetes duration, <i>Diabetic Medicine</i> , 27, 532-537, 2010	microalbuminuria used in the study corresponds to an ACR of > 2.26 mg/mmol, which is lower than the UK standard of 2.5 mg/mmol for males and 3.5 mg/mmol for females
Amin,R., Bahu,T.K., Widmer,B., Dalton,R.N., Dunger,D.B., Longitudinal relation between limited joint mobility, height, insulin-like growth factor 1 levels, and risk of developing microalbuminuria: The Oxford Regional Prospective Study, <i>Archives of Disease in Childhood</i> , 90, 1039-1044, 2005	Only the numbers of microalbuminuria participants under or above 11 years were reported; no information about the population size in each age group and, therefore, prevalence cannot be calculated
Amin,R., Turner,C., Van,Aken S., Bahu,T.K., Watts,A., Lindsell,D.R., Dalton,R.N., Dunger,D.B., The relationship between microalbuminuria and glomerular filtration rate in young type 1 diabetic subjects: The Oxford Regional Prospective Study, <i>Kidney International</i> , 68, 1740-1749, 2005	Children and young people under 16 years diagnosed with type 1 diabetes were included; at 5 years' duration, when microalbuminuria was measured, some of them were already over 18 years
Amin,R., Widmer,B., Dalton,R.N., Dunger,D.B., Unchanged incidence of microalbuminuria in children with type 1 diabetes since 1986: a UK based inception cohort, <i>Archives of Disease in Childhood</i> , 94, 258-262, 2009	No cumulative prevalence before the age of 18 years was reported; prevalence by diabetes duration was reported in Kaplan-Meier graph only
Amin,R., Widmer,B., Prevost,A.T., Schwarze,P., Cooper,J., Edge,J., Marcovecchio,L., Neil,A., Dalton,R.N., Dunger,D.B., Risk of microalbuminuria and progression to macroalbuminuria in a cohort with childhood onset type 1 diabetes: prospective observational study, <i>BMJ</i> , 336, 697-701, 2008	Prevalence by age for all types of microalbuminuria(including intermittent and persistent) were reported together
Bakman,M., Yuksel,B., Topaloglu,A.K., Mungan,N.O., Ozer,G., Risk factors for microalbuminuria in children and adolescents with insulin dependent diabetes mellitus, <i>Annals of Medical Sciences</i> , 10, 156-159, 2001	Just an overall prevalence for all participants was reported, no stratification according to age
Barkai,L., Vamosi,I., Lukacs,K., Enhanced progression of urinary albumin excretion in IDDM during puberty, <i>Diabetes Care</i> , 21, 1019-1023, 1998	Just an overall prevalence was reported, no stratification according to age
Basiratnia,M., Abadi,S.F., Amirhakimi,G.H., Karamizadeh,Z., Karamifar,H., Ambulatory blood pressure monitoring in children and adolescents with type-1 diabetes mellitus and its relation to diabetic control and microalbuminuria, <i>Saudi Journal of Kidney Diseases and Transplantation</i> , 23, 311-315, 2012	Just an overall prevalence was reported, no stratification according to age
Bertalan,R., Gregory,J.W., Detecting diabetes complications in children, <i>Practical Diabetes</i> , 28, 352-357a, 2011	Background reading
Bojestig,M., Arnqvist,H.J., Karlberg,B.E., Ludvigsson,J., Unchanged incidence of severe retinopathy in a population of Type 1 diabetic patients with marked reduction of nephropathy, <i>Diabetic Medicine</i> , 15, 863-869, 1998	Only a cumulative incidence of nephropathy after 20 years' follow-up was reported
Bojestig,M., Arnqvist,H.J., Karlberg,B.E., Ludvigsson,J., Glycemic control and prognosis in type I diabetic patients with microalbuminuria, <i>Diabetes Care</i> , 19, 313-317, 1996	Just an overall prevalence was reported, no stratification according to age
Bruno,G., Pagano,G., Low prevalence of microalbuminuria in young Italian insulin-dependent diabetic patients with short duration of disease: a population-based study. Piedmont Study Group for Diabetes Epidemiology, <i>Diabetic Medicine</i> , 13, 889-893, 1996	Microalbuminuria was tested on 1 overnight urine sample only
Campbell,F.M., Microalbuminuria and nephropathy in insulin dependent diabetes mellitus, <i>Archives of Disease in Childhood</i> , 73, 4-7, 1995	Background reading
Chiarelli,F., Verrotti,A., Morgese,G., Glomerular hyperfiltration increases the risk of developing microalbuminuria in diabetic children, <i>Pediatric Nephrology</i> , 9, 154-158, 1995	Only participants with hyperfiltration > 140 ml/minute per 1.73 square metres were included in the study to assess the development of microalbuminuria
Cizmecioglu,F.M., Noyes,K., Bath,L., Kelnar,C., Audit of microalbumin excretion in children with type I diabetes, <i>Journal of clinical research in pediatric endocrinology</i> , 1, 136-143, 2009	Just an overall prevalence for the age group 10 to 16 years was reported, no further stratification
Cobas,R.A., Santos,B., Da,SilvaP, Neves,R., Gomes,M.B., Progression to microalbuminuria in patients with type 1 diabetes: A seven-year prospective study, <i>Diabetology and metabolic syndrome</i> , 3, -, 2011	Study subjects included those who were older than 18 years
Cobuz,M., Cobuz,C., Chronic complications of type 1 diabetes mellitus in children, <i>Romanian Journal of Diabetes, Nutrition and Metabolic Diseases</i> , 19, 301-309, 2012	Just an overall prevalence was reported, no stratification according to age
Constantino,M.I., Molyneaux,L., Limacher-Gisler,F., Al-Saeed,A., Luo,C., Wu,T., Twigg,S.M., Yue,D.K., Wong,J., Long-term complications and mortality in young-onset diabetes: type 2 diabetes is more hazardous and lethal than	Study involving adults

Study	Reason for exclusion
type 1 diabetes, <i>Diabetes Care</i> , 36, 3863-3869, 2013	
Couper,J.J., Staples,A.J., Cocciolone,R., Nairn,J., Badcock,N., Henning,P., Relationship of smoking and albuminuria in children with insulin-dependent diabetes, <i>Diabetic Medicine</i> , 11, 666-669, 1994	Just the number of microalbuminuria participants was reported, prevalence cannot be calculated
Dahlquist,G., Rudberg,S., The prevalence of microalbuminuria in diabetic children and adolescents and its relation to puberty, <i>Acta Paediatrica Scandinavica</i> , 76, 795-800, 1987	AER was tested on 1 urine sample only, not in line with the UK standard (at least 2 out of 3 consecutive urine collections over a period of 3 to 4 months)
Dahlquist,G., Stattin,E.L., Rudberg,S., Urinary albumin excretion rate and glomerular filtration rate in the prediction of diabetic nephropathy; a long-term follow-up study of childhood onset type-1 diabetic patients, <i>Nephrology Dialysis Transplantation</i> , 16, 1382-1386, 2001	Only an overall prevalence for all participants after 8 years' follow-up was reported
D'Antonio,J.A., Ellis,D., Doft,B.H., Becker,D.J., Drash,A.L., Kuller,L.H., Orchard,T.J., Diabetes complications and glycemic control. The Pittsburgh Prospective Insulin-Dependent Diabetes Cohort Study Status Report after 5 yr of IDDM, <i>Diabetes Care</i> , 12, 694-70, 1989	Microalbuminuria was tested on a 24-hour urine collection only
Demirel,F., Tepe,D., Kara,O., Esen,I., Microvascular complications in adolescents with type 1 diabetes mellitus, <i>JCRPE Journal of Clinical Research in Pediatric Endocrinology</i> , 5, 145-149, 2013	Only an overall prevalence for the duration between 2 and 15 years was reported; no data stratified by age
Doggen,K., Debacker,N., Beckers,D., Casteels,K., Coeckelberghs,M., Dooms,L., Dorchy,H., Lebrethon,M., Logghe,K., Maes,M., Massa,G., Mouraux,T., Rooman,R., Thirty-Counson,G., Van,Aken S., Vanbesien,J., Van,Casteren,V., Care delivery and outcomes among Belgian children and adolescents with type 1 diabetes, <i>European Journal of Pediatrics</i> , 171, 1679-1685, 2012	Just an overall prevalence for all participants was reported, no stratification according to age
Donaghue,K.C., Craig,M.E., Chan,A.K., Fairchild,J.M., Cusumano,J.M., Verge,C.F., Crock,P.A., Hing,S.J., Howard,N.J., Silink,M., Prevalence of diabetes complications 6 years after diagnosis in an incident cohort of childhood diabetes, <i>Diabetic Medicine</i> , 22, 711-718, 2005	Just an overall prevalence for all participants was reported; for prevalence by age group, just the numbers of microalbuminuric children and young people in each group reported, prevalence cannot be calculated
Donaghue,K.C., Fairchild,J.M., Chan,A., Hing,S.J., King,J., Howard,N.J., Silink,M., Diabetes microvascular complications in prepubertal children, <i>Journal of Pediatric Endocrinology</i> , 10, 579-585, 1997	The threshold (AER > 15 microg/minute) used for confirmation of microalbuminuria in the study corresponds to ACR > 2.65mg/mmol for males or 2.96 mg/mmol for females, the threshold for females was lower than that of the UK standards (2.5 mg/mmol for males and 3.5 mg/mmol for females)
Donaghue,K.C., Fairchild,J.M., Craig,M.E., Chan,A.K., Hing,S., Cutler,L.R., Howard,N.J., Silink,M., Do all prepubertal years of diabetes duration contribute equally to diabetes complications?, <i>Diabetes Care</i> , 26, 1224-1229, 2003	Longitudinal study, data analysed were from the latest assessment when selected participants were already older than 18 years
Dost,A., Klinkert,C., Kapellen,T., Lemmer,A., Naeke,A., Grabert,M., Kreuder,J., Holl,R.W., DPV,Science,I, Arterial hypertension determined by ambulatory blood pressure profiles: contribution to microalbuminuria risk in a multicenter investigation in 2,105 children and adolescents with type 1 diabetes, <i>Diabetes Care</i> , 31, 720-725, 2008	Just an overall prevalence was reported, no stratification according to age
Ebeling,P., Koivisto,V.A., Occurrence and interrelationships of complications in insulin-dependent diabetes in Finland, <i>Acta Diabetologica</i> , 34, 33-38, 1997	The youngest age group assessed ranged from 15 to 27 years
Elamin,A., li Omer,M.I., Ismail,B., Tuvemo,T., Microalbuminuria in young Sudanese patients with type 1 diabetes, <i>Annals of Saudi Medicine</i> , 13, 493-497, 1993	The study was undertaken in Sudan
Gorman,D., Sochett,E., Daneman,D., The natural history of microalbuminuria in adolescents with type 1 diabetes, <i>Journal of Pediatrics</i> , 134, 333-337, 1999	Just an overall prevalence was reported, no stratification according to age
Harvey,J.N., Allagoa,B., The long-term renal and retinal outcome of childhood-onset Type 1 diabetes, <i>Diabetic Medicine</i> , 21, 26-31, 2004	Mean AER values by age at onset of diabetes rather than microalbuminuria prevalence by age were reported
Holl,R.W., Grabert,M., Thon,A., Heinze,E., Urinary excretion of albumin in adolescents with type 1 diabetes: persistent versus intermittent microalbuminuria and relationship to duration of diabetes, sex, and metabolic control, <i>Diabetes Care</i> , 22, 1555-1560, 1999	Just numbers of microalbuminuria patients by age were reported, no prevalence or incidence can be calculated
Ishikawa,K., Nagayoshi,M., Higa,S., Murakami,K., Kono,Y., Jinnouchi,T., Mimura,G., Frequency of diabetic nephropathy in childhood diabetics in southern districts of Kyusyu, <i>Journal of Diabetic Complications</i> , 5, 134-Sep, 1991	Available in abstract form only
Izumi,K., Hoshi,M., Kuno,S., Okuno,G., Yamazaki,Y.,	Just an overall prevalence for all participants was reported,

Study	Reason for exclusion
Isshiki,G., Sasaki,A., Glycemic control, growth and complications in children with insulin-dependent diabetes mellitus--a study of children enrolled in a Summer camp program for diabetics in Kinki district, Japan, <i>Diabetes Research and Clinical Practice</i> , 28, 185-190, 1995	no stratification according to age
Janner,M., Knill,S.E., Diem,P., Zuppinger,K.A., Mullis,P.E., Persistent microalbuminuria in adolescents with type I (insulin-dependent) diabetes mellitus is associated to early rather than late puberty. Results of a prospective longitudinal study, <i>European Journal of Pediatrics</i> , 153, 403-408, 1994	Just an overall prevalence for all participants was reported, no stratification according to age
Joner,G., Brinchmann-Hansen,O., Torres,C.G., Hanssen,K.F., A nationwide cross-sectional study of retinopathy and microalbuminuria in young Norwegian type 1 (insulin-dependent) diabetic patients, <i>Diabetologia</i> , 35, 1049-1054, 1992	Cut-off point for microalbuminuria was set at AER > 15 microg/minute, which corresponds to ACR >= 2.65 mg/mmol for males or >= 2.96 mg/mmol for females, the threshold for females was lower than that of the UK standards (2.5 mg/mmol for males and 3.5 mg/mmol for females)
Jones,C.A., Francis,M.E., Eberhardt,M.S., Chavers,B., Coresh,J., Engelgau,M., Kusek,J.W., Byrd-Holt,D., Narayan,K.M., Herman,W.H., Jones,C.P., Salive,M., Agodoa,L.Y., Microalbuminuria in the US population: third National Health and Nutrition Examination Survey, <i>American Journal of Kidney Diseases</i> , 39, 445-459, 2002	Microalbuminuria prevalence was stratified by age band, but the youngest group's age range was 6 to 19 years
Jones,C.A., Leese,G.P., Kerr,S., Bestwick,K., Isherwood,D.I., Vora,J.P., Hughes,D.A., Smith,C., Development and progression of microalbuminuria in a clinic sample of patients with insulin dependent diabetes mellitus, <i>Archives of Disease in Childhood</i> , 78, 518-523, 1998	Prevalence by age for all types of microalbuminuria(including intermittent and persistent) was reported
Karavanaki,K., Baum,J.D., Coexistence of impaired indices of autonomic neuropathy and diabetic nephropathy in a cohort of children with type 1 diabetes mellitus, <i>Journal of Pediatric Endocrinology</i> , 16, 79-90, 2003	Just the number of persistent microalbuminuria participants was reported, no population size of age groups and no prevalence can be calculated
Kim,N.H., Pavkov,M.E., Knowler,W.C., Hanson,R.L., Weil,E.J., Curtis,J.M., Bennett,P.H., Nelson,R.G., Predictive value of albuminuria in American Indian youth with or without type 2 diabetes, <i>Pediatrics</i> , 125, e844-e851, 2010	Study involving adults > 18 years
Laborde,K., Levy-Marchal,C., Kindermans,C., Dechaux,M., Czernichow,P., Sachs,C., Glomerular function and microalbuminuria in children with insulin-dependent diabetes, <i>Pediatric Nephrology</i> , 4, 39-43, 1990	Microalbuminuria was determined by 1 urine sample in the morning only
Lee,T.H., Han,S.H., The prevalence of complications in Korean diabetic subjects, <i>Tohoku Journal of Experimental Medicine</i> , 141 Suppl, 361-365, 1983	The youngest group started from 19 years of age, and just the number of microalbuminuria participants was reported
Lee,T.H., Ryu,H.J., Chung,P.W., Lim,W.S., Chung,M.Y., The prevalence of diabetic complications in Korea, <i>Korean Journal of Internal Medicine</i> , 2, 42-47, 1987	The youngest age group started from 19 years
Levy-Shraga,Y., Lerner-Geva,L., Boyko,V., Graph-Barel,C., Mazor-Aronovitch,K., Modan-Moses,D., Pinhas-Hamiel,O., Type 1 diabetes in pre-school children--long-term metabolic control, associated autoimmunity and complications, <i>Diabetic Medicine</i> , 29, 1291-1296, 2012	Complications were grouped together and cumulative incidence of all complications was reported in a graph
Lievre,M., Marre,M., Robert,J.J., Charpentier,G., Iannascoli,F., Passa,P., Diabetes,therapeutic Strategies and COmplications (DISCO) investigators., Cross-sectional study of care, socio-economic status and complications in young French patients with type 1 diabetes mellitus, <i>Diabetes and Metabolism</i> , 31, 41-46, 2005	Just an overall prevalence for all participants was reported, no stratification according to age
Likitmaskul,S., Wacharasindhu,S., Rawdaree,P., Ngarmukos,C., Deerochanawong,C., Suwanwalaikorn,S., Chetthakul,T., Bunnag,P., Kosachunhanun,N., Plengvidhaya,N., Leelawatana,R., Krittiyawong,S., Benjasuratwong,Y., Pratipanawatr,T., Thailand Diabetes Registry Project: Type of diabetes, glycemic control and prevalence of microvascular complications in children and adolescents with diabetes, <i>Journal of the Medical Association of Thailand</i> , 89, S10-S16, 2006	No microalbuminuria prevalence was reported
Maahs,D.M., Snively,B.M., Beyer,J., Imperatore,G., Bell,R., Mayer-Davis,E.J., Dolan,L.M., Pettitt,D.J., Hirsch,I., Rodriguez,B., Dabelea,D., Birth weight [corrected] and elevated albumin to creatinine ratio in youth with diabetes: the SEARCH for Diabetes in Youth study.[Erratum appears in <i>Pediatr Nephrol</i> . 2009 Jan;24(1):221], <i>Pediatric Nephrology</i> , 23, 2255-2260, 2008	Just an overall prevalence was reported, no stratification according to age
Majaliwa,E.S., Munubhi,E., Ramaiya,K., Mpembeni,R., Sanyiwa,A., Mohn,A., Chiarelli,F., Survey on acute and chronic complications in children and adolescents with type	Just the numbers of microalbuminuric participants by age group were reported, no prevalence can be calculated

Study	Reason for exclusion
1 diabetes at Muhimbili National Hospital in Dar es Salaam, Tanzania, <i>Diabetes Care</i> , 30, 2187-2192, 2007	
Marcovecchio, M.L., Dalton, R.N., Chiarelli, F., Dunger, D.B., A1C variability as an independent risk factor for microalbuminuria in young people with type 1 diabetes, <i>Diabetes Care</i> , 34, 1011-1013, 2011	Just an overall prevalence was reported, no stratification according to age
Marshall, S.M., Hackett, A., Court, S., Parkin, M., Alberti, K.G., Albumin excretion in children and adolescents with insulin-dependent diabetes, <i>Diabetes Research</i> , 3, 345-348, 1986	Only an overall prevalence was reported, no stratification according to age
Mathiesen, E.R., Saurbrey, N., Hommel, E., Parving, H.H., Prevalence of microalbuminuria in children with type 1 (insulin-dependent) diabetes mellitus, <i>Diabetologia</i> , 29, 640-643, 1986	Cut-off point for microalbuminuria was set at AER >14 microg/min, which corresponds to ACR \geq 2.48mg/mmol for males or \geq 2.71mg/mmol for females (lower than the UK standards)
Matyka, K., Microalbuminuria in childhood diabetes, <i>Journal of the Royal College of Physicians of Edinburgh</i> , 39, 233-235, 2009	Not a primary study; summary of previous relevant publications
McVean, J.J., Eickhoff, J.C., MacDonald, M.J., Prevalence of early microalbuminuria in children with type 1 diabetes mellitus, <i>Journal of Pediatric Endocrinology</i> , 21, 469-471, 2008	ACR was tested on at least 1 random urine collection, including single urine sample
Midyett, L.K., Grunt, J., Simon, S.D., Noninvasive radial artery tonometry augmentation index and urinary albumin/creatinine levels in early adolescents with type 1 diabetes mellitus, <i>Journal of Pediatric Endocrinology and Metabolism</i> , 22, 531-537, 2009	ACRs by age and diabetes duration were only reported graphically
Moayeri, H., Dalili, H., Prevalence of microalbuminuria in children and adolescents with diabetes mellitus type I, <i>Acta Medica Iranica</i> , 44, 105-110, 2006	Just the number of microalbuminuria participants was reported, no prevalence by age can be calculated
Mogensen, C.E., Christensen, C.K., Predicting diabetic nephropathy in insulin-dependent patients, <i>New England Journal of Medicine</i> , 311, 89-93, 1984	Just an overall prevalence was reported, no stratification according to age
Mohsin, F., Craig, M.E., Cusumano, J., Chan, A.K., Hing, S., Lee, J.W., Silink, M., Howard, N.J., Donaghue, K.C., Discordant trends in microvascular complications in adolescents with type 1 diabetes from 1990 to 2002, <i>Diabetes Care</i> , 28, 1974-1980, 2005	Just an overall prevalence was reported, no stratification according to age
Moore, T.H., Shield, J.P., Prevalence of abnormal urinary albumin excretion in adolescents and children with insulin dependent diabetes: the MIDAC study. Microalbuminuria in Diabetic Adolescents and Children (MIDAC) research group, <i>Archives of Disease in Childhood</i> , 83, 239-243, 2000	Microalbuminuria prevalence was stratified by puberty status (which was not defined by age) rather than by age
Moore, T.H., Shield, J.P., Microalbuminuria in diabetic adolescents and children—feasibility phase of a national cross-sectional study. MIDAC Research Group, <i>Journal of Diabetes and its Complications</i> , 13, 122-128, 1999	Just an overall prevalence for all participants was reported, not stratified by age
Morgese, G., Chiarelli, F., LaPenna G., Verrotti, A., Early detection of nephropathy in juvenile diabetes, <i>Journal of Endocrinological Investigation</i> , 12, 139-140, 1989	Just an overall prevalence for all participants was reported, no stratification according to age
Mortensen, H.B., Epidemiology of microalbuminuria among children with and without diabetes. Danish Study Group of Diabetes in Childhood, <i>Journal of Diabetes and its Complications</i> , 8, 164-165, 1994	Only an overall prevalence was reported, no stratification according to age
Mortensen, H.B., Hougaard, P., Ibsen, K.K., Parving, H.H., Petersen, K., Nerup, J., Marner, B., Holsteen, V., Haase, H., Saurbrey, N., Klinge, I., Bille, T., Kreutzfeldt, J., Lund, H.I., Pedersen, I.L., MacIntyre, B., Rasmussen, S.W., Hobolth, N., Brems, M., Relationship between blood pressure and urinary albumin excretion rate in young Danish Type 1 diabetic patients: Comparison to non-diabetic children, <i>Diabetic Medicine</i> , 11, 155-161, 1994	Just the numbers of microalbuminuria participants for different age groups were reported, no prevalence can be calculated
Mortensen, H.B., Marinelli, K., Norgaard, K., Main, K., Kastrop, K.W., Ibsen, K.K., Villumsen, J., Parving, H.H., A nation-wide cross-sectional study of urinary albumin excretion rate, arterial blood pressure and blood glucose control in Danish children with type 1 diabetes mellitus, <i>Diabetic Medicine</i> , 7, 887-897, 1990	Prevalence stratified by age and duration was only reported only graphically
Mullis, P., Kochli, H.P., Zuppinger, K., Schwarz, H.P., Intermittent microalbuminuria in children with type 1 diabetes mellitus without clinical evidence of nephropathy, <i>European Journal of Pediatrics</i> , 147, 385-388, 1988	The threshold (AER >15 microg/min) used for confirmation of microalbuminuria in the study corresponds to ACR > 2.65mg/mmol for males or 2.96 mg/mmol for females, the threshold for females was lower than that of the UK standards (2.5mg/mmol for males and 3.5mg/mmol for females)
Nazim, J., Dziatkowiak, H., Sztefko, K., Six-year observation of adolescents with type 1 diabetes and microalbuminuria,	Age of participants ranged from 2.2 to 24 years

Study	Reason for exclusion
Diabetologia Polska, 7, 166-170, 2000	
Nicoloff,G., Baydanoff,S., Stanimirova,N., Petrova,C., Christova,P., Detection of serum collagen type IV in children with type 1 (insulin-dependent) diabetes mellitus--a longitudinal study, <i>Pediatric Diabetes</i> , 2, 184-190, 2001	Only an overall prevalence for a wide age range (5 to 13 years) was reported
Okpere,A.N., Anochie,I.C., Eke,F.U., Prevalence of microalbuminuria among secondary school children, <i>African Health Sciences</i> , 12, 140-147, 2012	Study carried out in Nigeria
Quattrin,T., Waz,W.R., Duffy,L.C., Sheldon,M.W., Campos,S.P., Albin,C.H., Feld,L.G., Microalbuminuria in an adolescent cohort with insulin-dependent diabetes mellitus, <i>Clinical Pediatrics</i> , 34, 12-17, 1995	Just an overall prevalence for all participants was reported, no stratification according to age
Raile,K., Galler,A., Hofer,S., Herbst,A., Dunstheimer,D., Busch,P., Holl,R.W., Diabetic nephropathy in 27,805 children, adolescents, and adults with type 1 diabetes: effect of diabetes duration, A1C, hypertension, dyslipidemia, diabetes onset, and sex, <i>Diabetes Care</i> , 30, 2523-2528, 2007	Just an overall prevalence was reported, no stratification according to age
Rowe,D.J.F., Hayward,M., Bagga,H., Betts,P., Effect of glycaemic control and duration of disease on overnight albumin excretion in diabetic children, <i>British Medical Journal</i> , 289, 957-959, 1984	Just the number of microalbuminuria participants > 12 years was reported, no prevalence can be calculated
Roy,M.S., Affouf,M., Roy,A., Six-year incidence of proteinuria in type 1 diabetic African Americans, <i>Diabetes Care</i> , 30, 1807-1812, 2007	The study was carried out only among African Americans in the USA
Salardi,S., Cacciari,E., Pascucci,M.G., Giambiasi,E., Tacconi,M., Tazzari,R., Cicognani,A., Boriani,F., Puglioli,R., Mantovani,W., Microalbuminuria in diabetic children and adolescents. Relationship with puberty and growth hormone, <i>Acta Paediatrica Scandinavica</i> , 79, 437-443, 1990	Cut-off point for microalbuminuria used in the study was 25mg/24h, which corresponds to ACR \geq 3.06mg/mmol in males and \geq 3.19 mg/mmol in females, the threshold for females was lower than that of the UK standards (2.5mg/mmol for males and 3.5mg/mmol for females)
Salgado,P.P., Silva,I.N., Vieira,E.C., Simoes e Silva A.C., Risk factors for early onset of diabetic nephropathy in pediatric type 1 diabetes, <i>Journal of Pediatric Endocrinology</i> , 23, 1311-1320, 2010	Just an overall prevalence was reported, no stratification according to age
Santilli,F., Spagnoli,A., Mohn,A., Tumini,S., Verrotti,A., Cipollone,F., Mezzetti,A., Chiarelli,F., Increased vascular endothelial growth factor serum concentrations may help to identify patients with onset of type 1 diabetes during childhood at risk for developing persistent microalbuminuria, <i>Journal of Clinical Endocrinology and Metabolism</i> , 86, 3871-3876, 2001	Just an overall prevalence was reported after 8 years' follow-up, no stratification by age and participants' attained age could have reached more than 18 years
Schultz,C.J., Konopelska-Bahu,T., Dalton,R.N., Carroll,T.A., Stratton,I., Gale,E.A., Neil,A., Dunger,D.B., Microalbuminuria prevalence varies with age, sex, and puberty in children with type 1 diabetes followed from diagnosis in a longitudinal study. Oxford Regional Prospective Study Group, <i>Diabetes Care</i> , 22, 495-502, 1999	Only the number of microalbuminuria participants aged < 11 years was reported without the whole number of this age group, prevalence cannot be calculated
Schultz,C.J., Neil,H.A., Dalton,R.N., Konopelska,Bahu T., Dunger,D.B., Oxford Regional Prospective Study Group., Blood pressure does not rise before the onset of microalbuminuria in children followed from diagnosis of type 1 diabetes. Oxford Regional Prospective Study Group, <i>Diabetes Care</i> , 24, 555-560, 2001	Just an overall prevalence was reported, no stratification according to age
Scott,A.R., Toomath,R., Bouchier,D., Bruce,R., Crook,N., Carroll,D., Cutfield,R., Dixon,P., Doran,J., Dunn,P., Hotu,C., Khant,M., Lonsdale,M., Lunt,H., Wiltshire,E., Wu,D., First national audit of the outcomes of care in young people with diabetes in New Zealand: High prevalence of nephropathy in Maori and Pacific Islanders, <i>New Zealand Medical Journal</i> , 119, -, 2006	Just an overall prevalence for participants aged between 12 and 26 years was reported
Sellers,E.A.C., Blydt-Hansen,T.D., Dean,H.J., Gibson,I.W., Birk,P.E., Ogborn,M., Macroalbuminuria and renal pathology in first nation youth with type 2 diabetes, <i>Diabetes Care</i> , 32, 786-790, 2009	Just an overall prevalence was reported, no stratification according to age
Sen,A., Buyukgebiz,A., Albumin excretion rate, serum insulin-like growth factor-I and glomerular filtration rate in type I diabetes mellitus at puberty, <i>Journal of Pediatric Endocrinology</i> , 10, 209-215, 1997	Mean values of AER for age groups such as 10 to 12 years, and 13 to 14 years, were reported, but prevalence cannot be calculated
Shield,J.P.H., Hunt,L.P., Karachaliou,F., Karavanaki,K., Baum,J.D., Is microalbuminuria progressive?, <i>Archives of Disease in Childhood</i> , 73, 512-514, 1995	Just an overall prevalence was reported, no stratification according to age
Simsek,D.G., Aycan,Z., Ozen,S., Cetinkaya,S., Kara,C., Abali,S., Demir,K., Tunc,O., Ucakturk,A., Asar,G., Bas,F., Cetinkaya,E., Aydin,M., Karaguzel,G., Orbak,Z., Siklar,Z.,	Only an overall prevalence was reported, no stratification by age or diabetes duration

Study	Reason for exclusion
Altincik,A., Okten,A., Ozkan,B., Ocal,G., Semiz,S., Arslanoglu,I., Evliyaoglu,O., Bundak,R., Darcan,S., Diabetes care, glycemic control, complications, and concomitant autoimmune diseases in children with type 1 diabetes in Turkey: a multicenter study, <i>Journal of clinical research in pediatric endocrinology</i> , 5, 20-26, 2013	
Stone,M.L., Craig,M.E., Chan,A.K., Lee,J.W., Verge,C.F., Donaghue,K.C., Natural history and risk factors for microalbuminuria in adolescents with type 1 diabetes: a longitudinal study, <i>Diabetes Care</i> , 29, 2072-2077, 2006	Just an overall prevalence was reported, no stratification according to age
Svensson,M., Eriksson,J.W., Dahlquist,G., Early glycemic control, age at onset, and development of microvascular complications in childhood-onset type 1 diabetes: a population-based study in northern Sweden, <i>Diabetes Care</i> , 27, 955-962, 2004	Just an overall prevalence was reported, no stratification according to age
Tan,S.H., Lee,B.W., Low,P.S., Lee,C.P., Assessment of complications in children with insulin-dependent diabetes mellitus, <i>Annals of the Academy of Medicine, Singapore</i> , 14, 266-271, 1985	Participants' age ranged from 1 to 20 years (small sample size of 19 participants only)
Tsai,C.W., Kuo,C.C., Wu,C.F., Chien,K.L., Wu,V.C., Chen,M.F., Sung,F.C., Su,T.C., Associations of renal vascular resistance with albuminuria in adolescents and young adults, <i>Nephrology Dialysis Transplantation</i> , 26, 3943-3949, 2011	The overall prevalence was reported when participants had attained 21 years of age
Tuomilehto,J., Borch-Johnsen,K., Molarius,A., Jormanainen,V., Lounamaa,R., Gronhagen-Riska,C., Reunanen,A., Sarti,C., The unchanging incidence of hospitalization for diabetic nephropathy in a population-based cohort of IDDM patients in Finland.[Erratum appears in <i>Diabetes Care</i> 1997 Nov;20(11):1802], <i>Diabetes Care</i> , 20, 1081-1086, 1997	Nephropathy was identified by ICD codes of diabetic nephropathy diagnosis on hospital discharge records rather than by AER or ACR
Wan Nazaimoon,W.M., Letchuman,R., Noraini,N., Ropilah,A.R., Zainal,M., Ismail,I.S., Wan Mohamad,W.B., Faridah,I., Singaraveloo,M., Sheriff,I.H., Khalid,B.A., Systolic hypertension and duration of diabetes mellitus are important determinants of retinopathy and microalbuminuria in young diabetics, <i>Diabetes Research and Clinical Practice</i> , 46, 213-221, 1999	Study on young adults older than 18 years
Yokoyama,H., Uchigata,Y., Otani,T., Maruyama,A., Yano-Aoki,K., Kanematsu,S., Kasahara,T., Matsuura,N., Omori,Y., Development of diabetic nephropathy in Japanese patients with insulin-dependent diabetes mellitus: Tokyo Women's Medical College epidemiologic study, <i>Journal of Diabetes and its Complications</i> , 8, 7-12, 1994	Participants included those who were older than 18 years

H.18 Type 2 diabetes – education

Review question

What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?

Study	Reason for exclusion
Armour,T.A., Norris,S.L., Jack,L.,Jr., Zhang,X., Fisher,L., The effectiveness of family interventions in people with diabetes mellitus: a systematic review. [47 refs], <i>Diabetic Medicine</i> , 22, 1295-1305, 2005	PICO not met - no studies included children or young people with type 2 diabetes. Interventions were generally behavioural in nature.
Atak,N., Gurkan,T., Kose,K., The effect of education on knowledge, self management behaviours and self efficacy of patients with type 2 diabetes, <i>Australian Journal of Advanced Nursing</i> , 26, 66-74, 2008	PICO not met - adult participants only
Avdal,Elif, Kizilci,Sevgi, Demirel,Neslihan, The effects of Web-based diabetes education on diabetes care results: a randomized control study, <i>CIN: Computers, Informatics, Nursing</i> , 29, TC29-TC34, 2011	PICO not met - adult participants only.
Babamoto,K.S., Sey,K.A., Camilleri,A.J., Karlan,V.J., Catalasan,J., Morisky,D.E., Improving diabetes care and health measures among hispanics using community health	PICO not met - adult participants only.

Study	Reason for exclusion
workers: results from a randomized controlled trial, Health Education and Behavior, 36, 113-126, 2009	
Borgermans,Liesbeth, Goderis,Geert, Carine, Verbeke,Geert, Carbonez,An, Ivanova,Anna, Mathieu,Chantal, Heyrman,Jan, Patients' experiences with patient-centred care are associated with documented outcome of care indicators for diabetes: findings from the Leuven Diabetes Project, International Journal of Care Pathways, 15, 65-75, 2011	PICO not met - although age not explicitly stated as an inclusion criterion, mean age of participants was 68 years (-12 years).
Brown,S.J., Lieberman,D.A., Gemeny,B.A., Fan,Y.C., Wilson,D.M., Pasta,D.J., Educational video game for juvenile diabetes: Results of a controlled trial, Medical Informatics, 22, 77-89, 1997	PICO not met - participants with type 1 diabetes only
Campbell,E.M., Redman,S., Moffitt,P.S., Sanson-Fisher,R.W., The relative effectiveness of educational and behavioral instruction programs for patients with NIDDM: a randomized trial, Diabetes Educator, 22, 379-386, 1996	PICO not met. Although inclusion criteria only state < 80 years, mean age of participants was 58.3 years
Charron-Prochownik,D., Sereika,S.M., Becker,D., White,N.H., Schmitt,P., Powell,A.B.,III, Diaz,A.M., Jones,J., Herman,W.H., Fischl,A.F., McEwen,L., DiNardo,M., Guo,F., Downs,J., Long-term effects of the booster-enhanced READY-Girls preconception counseling program on intentions and behaviors for family planning in teens with diabetes, Diabetes Care, 36, 3870-3874, 2013	No outcomes of interest. Only considers preconception counselling and outcomes relevant to this.
Colquhoun,E., Drury,Michael I., Cregan,Deirdre, Keenan,Patricia, Group work with diabetic adolescents, Irish Journal of Psychological Medicine, 5, 37-40, 1988	PICO not met - participants with type 1 diabetes, psychosocial intervention.
DaniÅ“le,Pacaud, Helen,Kelley, Angela,M., Mike,Chiasson, Successful Delivery of Diabetes Self-Care Education and Follow-Up through eHealth Media, Canadian Journal of Diabetes, 36, 257-262, 2012	PICO not met - adult participants only
Delamater,Alan M., Smith,Jeffrey A., Bubb,Jeanne, Davis,Susan Green, Gamble,Thomas, White,Neil H., Santiago,Julio V., Family-based behavior therapy for diabetic adolescents, Johnson, James H [Ed]; Johnson, Suzanne Bennett [Ed], , 293-306, 1991	PICO not met - type of diabetes not described (but likely type 1) and behavioural intervention, not educational.
Flamm,M., Panisch,S., Winkler,H., Johansson,T., Weitgasser,R., Sonnichsen,A.C., Effectiveness of the Austrian disease management programme "Therapie Aktiv" for type 2 diabetes regarding the improvement of metabolic control, risk profile and guideline adherence: 2 years of follow up, Wiener Klinische Wochenschrift, 124, 639-646, 2012	PICO not met - adult participants only
Gage,H., Hampson,S., Skinner,T.C., Hart,J., Storey,L., Foxcroft,D., Kimber,A., Cradock,S., McEvelly,E.A., Educational and psychosocial programmes for adolescents with diabetes: Approaches, outcomes and cost-effectiveness, Patient Education and Counseling, 53, 333-346, 2004	PICO not met - participants with type 1 diabetes only.
Heinrich,E., Schaper,N.C., de Vries,N.K., Self-management interventions for type 2 diabetes: a systematic review, European Diabetes Nursing, 7, 71-76, 2010	PICO not met - only adult studies included
Jeffreys,H.L., Hemoglobin A1C value for evaluating a community diabetes education series, Internet Journal of Advanced Nursing Practice, 9, -6p, 2008	PICO not met - not an RCT, and adult participants only
Johnson,S.T., Newton,A.S., Chopra,M., Buckingham,J., Huang,T.T.K., Franks,P.W., Jetha,M.M., Ball,G.D.C., In search of quality evidence for lifestyle management and glycemc control in children and adolescents with type 2 diabetes: a systematic review (Structured abstract), BMC Pediatrics, 10, 2010	Systematic review. Only includes one article which considers dietary modification rather than an educational intervention.
Keeratiyutawong,P., Hanucharumkul,S., Melkus,G.D.E., Panpakdee,O., Vorapongsathorn,T., Effectiveness of a self-management program for Thais with type 2 diabetes, Thai Journal of Nursing Research, 10, 85-97, 2006	PICO not met - adult participants only
LEE,Haejung, KIM,Myoung Soo, PARK,Kyung Yeon, PARK,Hyoung Sook, KIM,In Joo, Effects of a problem-solving counseling program to facilitate intensified walking on Koreans with type 2 diabetes, Japan Journal of Nursing Science, 8, 129-139, 2011	PICO not met - adult participants only (> 50 years), and not randomised

Study	Reason for exclusion
McIlhenny,C.,V, Guzik,B., Knee,D., Demuth,B., Roberts,J., Using technology to deliver healthcare education to rural patients, <i>Rural and Remote Health</i> , 11, 1-11, 2011	PICO not met - adult participants only
Moriyama,M., Nakano,M., Kuroe,Y., Nin,K., Niitani,M., Nakaya,T., Efficacy of a self-management education program for people with type 2 diabetes: results of a 12 month trial, <i>Japan Journal of Nursing Science</i> , 6, 51-63, 2009	No age restriction to enter study, but control and intervention groups had a mean age of 65.2 years (\pm 8.5 years) and 66.4 years (\pm 9.2 years), respectively.
Nichols,P.J., Norris,S.L., A systematic literature review of the effectiveness of diabetes education of school personnel, <i>The Diabetes Educator</i> , 28, 405-414, 2002	Systematic review that considers education of school teachers only. No reference to type 2 diabetes.
Norris,S.L., Nichols,P.J., Caspersen,C.J., Glasgow,R.E., Engelgau,M.M., Jack,Jr, Snyder,S.R., Carande-Kulis,V.G., Isham,G., Garfield,S., Briss,P., McCulloch,D., Increasing diabetes self-management education in community settings: A systematic review, <i>American Journal of Preventive Medicine</i> , 22, 39-66, 2002	PICO not met - 11 studies included young people but all had type 1 diabetes. One study looked at education of school personnel (type of diabetes not specified).
Norris,S.L., Engelgau,M.M., Narayan,K.M.V., Effectiveness of self management training in type 2 diabetes: a systematic review of randomized controlled trials, <i>Diabetes Care</i> , 24, 561-587, 2001	Only includes subjects > 18 years of age.
Norris,S.L., Nichols,P.J., Caspersen,P.J., Glasgow,R.E., Engelgau,M.M., Jack,L., Snyder, S.R., Carande-Kulis,V.G., Isham,G., Garfield,S., Briss,P., McCulloch,D., Increasing diabetes self-management education in community settings: a systematic review, <i>American Journal of Preventive Medicine</i> , 22, 39-66, 2002	Systematic review, predominantly considers educational interventions for adults or children and young people with type 1 diabetes. References checked and no relevant papers identified for children and young people with type 2 diabetes.
Pieter,Agema, Diana,Sherifali, Determining the impact of an intervention to increase problem-solving skills in diabetes self-management: The Diabetes Problem-Solving Passport Pilot Study, <i>Canadian Journal of Diabetes</i> , 36, 199-203, 2012	PICO not met - adult participants only.
Rothman,R.L., Malone,R., Bryant,B., Shintani,A.K., Crigler,B., Dewalt,D.A., Dittus,R.S., Weinberger,M., Pignone,M.P., A randomized trial of a primary care-based disease management program to improve cardiovascular risk factors and glycated hemoglobin levels in patients with diabetes, <i>The American journal of medicine</i> , 118, 276-284, 2005	PICO not met - adult participants only
Sturt,J., One-to-one structured education using the Diabetes Manual: evidence of effectiveness, <i>Journal of Diabetes Nursing</i> , 12, 368-70, 372, 374, 2008	PICO not met - adult participants only
Sutcliffe,Paul, Martin,Steven, Sturt,Jackie, Powell,John, Griffiths,Frances, Adams,Ann, Dale,Jeremy, Systematic review of communication technologies to promote access and engagement of young people with diabetes into healthcare, <i>BMC Endocrine Disorders</i> , 11, 1-, 2011	PICO not met - studies included use of IT to communicate advice on diabetes management, rather than educational tools. Only one educational Internet site included, and this study was not an RCT.
Tjam,E.Y., Sherifali,D., Steinacher,N., Hett,S., Physiological outcomes of an Internet disease management program vs. in-person counselling: a randomized, controlled trial, <i>Canadian Journal of Diabetes</i> , 30, 397-405, 2006	PICO not met - adults with type 1 or type 2 diabetes only
TODAY Study Group, A Clinical Trial to Maintain Glycemic Control in Youth with Type 2 Diabetes, <i>New England Journal of Medicine</i> <i>Engl J Med</i> , 366, 2247-2256, 2012	PICO not met - behavioural intervention, not education
TODAY Study Group, Zeitler,P., Epstein,L., Grey,M., Hirst,K., Kaufman,F., Tamborlane,W., Wilfley,D., Treatment options for type 2 diabetes in adolescents and youth: a study of the comparative efficacy of metformin alone or in combination with rosiglitazone or lifestyle intervention in adolescents with type 2 diabetes, <i>Pediatric Diabetes</i> , 8, 74-87, 2007	Protocol for study - no results included.
Tshiananga,J.K.T., Kocher,S., Weber,C., Eerny-Albrecht,K., Berndt,K., Neeser,K., The effect of nurse-led diabetes self-management education on glycosylated hemoglobin and cardiovascular risk factors: a meta-analysis, <i>The Diabetes Educator</i> , 38, 108-123, 2012	Mean age of participants 52.8 years.
Tshiananga,Jacques Kande Tshiang, Kocher,Serge, Weber,Christian, Eerny-Albrecht,Katrina, Berndt,Karsten, Neeser,Kurt, The Effect of Nurse-led Diabetes Self-	PICO not met - includes articles with either adult participants or children and young people with type 1 diabetes

Study	Reason for exclusion
management Education on Glycosylated Hemoglobin and Cardiovascular Risk Factors: A Meta-analysis, The Diabetes Educator, 38, 108-123, 2012	

H.19 Type 2 diabetes – behavioural interventions

Review questions

What is the effectiveness of behavioural interventions to promote engagement with clinical services in children and young people with type 2 diabetes?

What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 2 diabetes?

These 2 questions were addressed through a single search and there is one combined list of excluded studies.

Study	Reason for exclusion
Boost glycemic control in teen diabetics through 'family focused teamwork', Disease Management Advisor, 9, 120-122, 117, 2003	Editorial for a study which assessed interventions in type 1 diabetes.
Armour,T.A., Norris,S.L., Jack,L.,Jr., Zhang,X., Fisher,L., The effectiveness of family interventions in people with diabetes mellitus: a systematic review. [47 refs], Diabetic Medicine, 22, 1295-1305, 2005	PICO not met: adults with type 2 diabetes and children, young people and adults with type 1 diabetes.
Bradshaw,B., The role of the family in managing therapy in minority children with type 2 diabetes mellitus, Journal of Pediatric Endocrinology, 15 Suppl 1, 547-551, 2002	Intervention not behavioural. Focused on administering care such as diet supervision.
Calhoun,D., Brod,R., Kirlin,K., Howard,B.V., Schulberg,D., Fiore,C., Effectiveness of motivational interviewing for improving self-care among Northern Plains Indians with type 2 diabetes, Diabetes Spectrum, 23, 107-114, 2010	PICO not met: adult population only. Mean age 54 years.
Campbell,E.M., Redman,S., Moffitt,P.S., Sanson-Fisher,R.W., The relative effectiveness of educational and behavioral instruction programs for patients with NIDDM: a randomized trial, Diabetes Educator, 22, 379-386, 1996	PICO not met: adult population.
Delamater,A.M., Jacobson,A.M., Anderson,B., Cox,D., Fisher,L., Lustman,P., Rubin,R., Wysocki,T., Psychosocial Therapies Working Group., Psychosocial therapies in diabetes: report of the Psychosocial Therapies Working Group. [111 refs], Diabetes Care, 24, 1286-1292, 2001	Not a systematic review; general literature review only with no data.
Ellis,D.A., Naar-King,S., Chen,X., Moltz,K., Cunningham,P.B., Idalski-Carcone,A., Multisystemic therapy compared to telephone support for youth with poorly controlled diabetes: findings from a randomized controlled trial, Annals of Behavioral Medicine, 44, 207-215, 2012	Type 1 versus type 2 entered together as a confounding variable in a linear model. No analysis of the effect of the intervention on type 2 children and young people only.
Grey,M., Boland,E.A., Davidson,M., Yu,C., Sullivan-Bolyai,S., Tamborlane,W.V., Short-term effects of coping skills training as adjunct to intensive therapy in adolescents, Diabetes Care, 21, 902-908, 1998	PICO not met: participants had type 1 diabetes only.
Harris,M.A., Freeman,K.A., Beers,M., Family therapy for adolescents with poorly controlled diabetes: initial test of clinical significance, Journal of Pediatric Psychology, 34, 1097-1107, 2009	PICO not met: only 2 of 16 participants had type 2 diabetes.
Henry,J.L., Wilson,P.H., Bruce,D.G., Chisholm,D.J., Rawling,P.J., Cognitive-behavioural stress management for patients with non-insulin dependent diabetes mellitus, Psychology, Health and Medicine, 2, 109-118, 1997	PICO not met: adult population. Mean age 59.8 years.
Keeratiyutawong,P., Hanucharumkul,S., Melkus,G.D.E., Panpakdee,O., Vorapongsathorn,T., Effectiveness of a self-management program for Thais with type 2 diabetes, Thai Journal of Nursing Research, 10, 85-97, 2006	PICO not met: adult population. Age range of 21 to 60 years.
Keogh,K.M., White,P., Smith,S.M., McGilloway,S., O'Dowd,T., Gibney,J., Changing illness perceptions in	PICO not met: participants > 18 years of age.

Study	Reason for exclusion
patients with poorly controlled type 2 diabetes, a randomised controlled trial of a family-based intervention: protocol and pilot study, <i>BMC Family Practice</i> , 8, 36-, 2007	
LEE,Haejung, KIM,Myoung Soo, PARK,Kyung Yeon, PARK,Hyoung Sook, KIM,In Joo, Effects of a problem-solving counseling program to facilitate intensified walking on Koreans with type 2 diabetes, <i>Japan Journal of Nursing Science</i> , 8, 129-139, 2011	PICO not met: adult population > 50 years.
Lou,V.W.Q., Zhang,Y., Evaluating the effectiveness of a participatory empowerment group for Chinese type 2 diabetes patients, <i>Research on Social Work Practice</i> , 16, 491-499, 2006	PICO not met: adult population. Mean ages of 57.3 years and 56.8 years in each group.
Moriyama,M., Nakano,M., Kuroe,Y., Nin,K., Niitani,M., Nakaya,T., Efficacy of a self-management education program for people with type 2 diabetes: results of a 12 month trial, <i>Japan Journal of Nursing Science</i> , 6, 51-63, 2009	PICO not met: adult population. Mean ages of 66.4 years and 65.2 years in each group.
Partiprajak,Suphamas, Hanucharurnkul,Somchit, Piaseu,Noppawan, Brooten,Dorothy, Nityasuddhi,Dechavudh, Outcomes of an advanced practice nurse-led type-2 diabetes support group, <i>Pacific Rim International Journal of Nursing Research</i> , 15, 288-304, 2011	PICO not met: adult population. Age range 44 to 80 years.
Sabourin,Brigitte, Vallis,T., Currie,Shannon, Development and pilot-testing of a brief psychosocial group intervention protocol for type 2 diabetes self-management, <i>Canadian Journal of Diabetes</i> , 35, 287-294, 2011	PICO not met: adult population. Age range 59 to 78 years.
Satin,Wendy, la Greca,Annette M., Zigo,Marjorie A., Skyler,Jay S., Diabetes in adolescence: Effects of multifamily group intervention and parent simulation of diabetes, <i>Journal of Pediatric Psychology</i> , 14, 259-275, 1989	PICO not met: type 1 diabetes only.
Smith,S., Paul,G., Kelly,A., Whitford,D., O'Shea,E., O'Dowd,T., Peer support for patients with type 2 diabetes: cluster randomised controlled trial, <i>BMJ: British Medical Journal (Overseas and Retired Doctors Edition)</i> , 342, 482-482, 2011	PICO not met: adult population. Mean age ranges between 62.7 years and 66.1 years for each group.
Tjam,E.Y., Sherifali,D., Steinacher,N., Hett,S., Physiological outcomes of an Internet disease management program vs. in-person counselling: a randomized, controlled trial, <i>Canadian Journal of Diabetes</i> , 30, 397-405, 2006	PICO not met: adult population; 77% of participants > 40 years.

H.20 Type 2 diabetes – dietary advice

Review question

What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?

Study	Reason for exclusion
Albarracin,C.A., Fuqua,B.C., Evans,J.L., Goldfine,I.D., Chromium picolinate and biotin combination improves glucose metabolism in treated, uncontrolled overweight to obese patients with type 2 diabetes, <i>Diabetes/Metabolism Research Reviews</i> , 24, 41-51, 2008	PICO not met: excluded people aged < 18 years
Bantle,J.P., Laine,D.C., Thomas,J.W., Metabolic effects of dietary fructose and sucrose in types I and II diabetic subjects, <i>JAMA</i> , 256, 3241-3246, 1986	PICO not met: adults only for type 2 diabetes (36-80 years)
Brunner,S., Holub,I., Theis,S., Gostner,A., Melcher,R., Wolf,P., mann-Gassner,U., Scheppach,W., Hauner,H., Metabolic effects of replacing sucrose by isomaltulose in subjects with type 2 diabetes: a randomized double-blind trial, <i>Diabetes Care</i> , 35, 1249-1251, 2012	PICO not met: adult population only
Gellar,L., Nansel,T.R., High and low glycemic index mixed meals and blood glucose in youth with type 2 diabetes or impaired glucose tolerance.[Erratum appears in <i>J Pediatr</i> . 2009 Jun;154(6):937], <i>Journal of Pediatrics</i> , 154, 455-458, 2009	24 hour study only - meal not diet

Study	Reason for exclusion
Johnson,S.T., Newton,A.S., Chopra,M., Buckingham,J., Huang,T.T., Franks,P.W., Jetha,M.M., Ball,G.D., In search of quality evidence for lifestyle management and glycemic control in children and adolescents with type 2 diabetes: A systematic review, BMC Pediatrics, 10, 97-, 2010	Systematic review of non-RCT data; not included in evidence as the one study reviewed was identified in the non-RCT search
Kinmonth,A.L., Angus,R.M., Jenkins,P.A., Whole foods and increased dietary fibre improve blood glucose control in diabetic children, Archives of Disease in Childhood, 57, 187-194, 1982	Diabetes type not stated, appears to be type 1 based on background section
Kwak,J.H., Lee,J.H., Ahn,C.W., Park,S.H., Shim,S.T., Song,Y.D., Han,E.N., Lee,K.H., Chae,J.S., Black soy peptide supplementation improves glucose control in subjects with prediabetes and newly diagnosed type 2 diabetes mellitus, Journal of Medicinal Food, 13, 1307-1312, 2010	PICO not met: excluded people aged < 18 years
MacLean,C.H., Mojica,W.A., Morton,S.C., Pencharz,J., Hasenfeld,Garland R., Tu,W., Newberry,S.J., Jungvig,L.K., Grossman,J., Khanna,P., Rhodes,S., Shekelle,P., Effects of omega-3 fatty acids on lipids and glycemic control in type II diabetes and the metabolic syndrome and on inflammatory bowel disease, rheumatoid arthritis, renal disease, systemic lupus erythematosus, and osteoporosis, Evidence Report: Technology Assessment (Summary), 1-4, 2004	Short-term effects and insufficient follow-up of included studies
McCargar,L.J., Innis,S.M., Bowron,E., Leichter,J., Dawson,K., Toth,E., Wall,K., Effect of enteral nutritional products differing in carbohydrate and fat on indices of carbohydrate and lipid metabolism in patients with NIDDM, Molecular and Cellular Biochemistry, 188, 81-89, 1998	PICO not met: excluded people aged <18 years
Nansel,T.R., Gellar,L., Zeitzoff,L., Acceptability of lower glycemic index foods in the diabetes camp setting, Journal of Nutrition Education and Behavior, 38, 143-150, 2006	Type 1 and type 2 diabetes analysed together
Ooi,Peng Cheow, Loke,Cheong Seng, Sweet potato for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2012	PICO not met: adult population only, mean age > 55 years
Ooi,Peng Cheow, Yassin,Zaitun, Hamid,TengkuAizan, Momordica charantia for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2012	PICO not met: people aged <18 years excluded
Sonksen,P.H., Lowy,C., Perkins,J.R., Lim,H.S., Non-insulin-dependent diabetes: 10-year outcome in relation to initial response to diet and subsequent sulfonylurea therapy, Diabetes Care, Vol.7 Suppl 1, pp.59-66, 1984 May-Jun., -66, 1984	PICO not met: people aged < 18 years excluded
Thomas,Diana, Elliott,Elizabeth J., Low glycaemic index, or low glycaemic load, diets for diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2009	PICO not met: all but one paper involved adult populations and the other paper did not state which type of diabetes was studied
Vivian,E.M., Type 2 diabetes in children and adolescents--the next epidemic?, Current Medical Research and Opinion, 22, 297-306, 2006	Review not systematic
Voss,A.C., Maki,K.C., Garvey,W.T., Hustead,D.S., Alish,C., Fix,B., Mustad,V.A., Effect of two carbohydrate-modified tube-feeding formulas on metabolic responses in patients with type 2 diabetes, Nutrition, 24, 990-997, 2008	PICO not met: people aged < 18 years excluded

H.21 Type 2 diabetes – weight loss

Review question

Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?

Study	Reason for exclusion
Bohdjalian,A., Prager,G., Rosak,C., Weiner,R., Jung,R., Schramm,M., Aviv,R., Schindler,K., Haddad,W., Rosenthal,N., Ludvik,B., Improvement in glycemic control in morbidly obese type 2 diabetic subjects by gastric stimulation, Obesity Surgery, 19, 1221-1227, 2009	PICO not met: adults only
Copeland,K.C., Higgins,J., El,GhormliL, Delahanty,L., Grey,M., Kriska,A.M., Lipman,T.H., Pyle,L., Shepherd,J., Hirst,K., Treatment effects on measures of body composition in the TODAY clinical trial, Diabetes Care, 36, 1742-1748,	No specific weight loss intervention; no assessment of correlation between weight loss and glycaemic indices

Study	Reason for exclusion
2013	
Garanty-Bogacka,B., Syrenicz,M., Goral,J., Krupa,B., Syrenicz,J., Walczak,M., Syrenicz,A., Changes in inflammatory biomarkers after successful lifestyle intervention in obese children, <i>Endokrynologia Polska</i> , 62, 499-505, 2011	PICO not met: proportion of participants with type 2 diabetes not reported
Gidding,S.S., Lima,J., Pyle,L., Payan,M., Hirst,K., Katz,L.E.L., Bacha,F., McKay,S., Relationship of LV mass, LA diameter, and LV geometry to cardiovascular risk factors in the today cohort of adolescents with type 2 diabetes (T2D), <i>Circulation</i> , 126, -, 2012	PICO not met: outcomes not of interest
Grinstein,G., Muzumdar,R., Aponte,L., Vuguin,P., Saenger,P., Martino-Nardi,J., Presentation and 5-year follow-up of type 2 diabetes mellitus in African-American and Caribbean-Hispanic adolescents, <i>Hormone Research</i> , 60, 121-126, 2003	Outcomes for participants with type 1 diabetes and type 2 diabetes not presented separately
Himpens,J., Verbrugghe,A., Cadiere,G.B., Everaerts,W., Greve,J.W., Long-term results of laparoscopic Roux-en-Y Gastric bypass: evaluation after 9 years, <i>Obesity Surgery</i> , 22, 1586-1593, 2012	PICO not met: adults only
Horowitz,M., Flint,A., Jones,K.L., Hindsberger,C., Rasmussen,M.F., Kapitza,C., Doran,S., Jax,T., Zdravkovic,M., Chapman,I.M., Effect of the once-daily human GLP-1 analogue liraglutide on appetite, energy intake, energy expenditure and gastric emptying in type 2 diabetes, <i>Diabetes Research and Clinical Practice</i> , 97, 258-266, 2012	PICO not met: adults only
Inge,T.H., Miyano,G., Bean,J., Helmrath,M., Courcoulas,A., Harmon,C.M., Chen,M.K., Wilson,K., Daniels,S.R., Garcia,V.F., Brandt,M.L., Dolan,L.M., Reversal of type 2 diabetes mellitus and improvements in cardiovascular risk factors after surgical weight loss in adolescents, <i>Pediatrics</i> , 123, 214-222, 2009	An observational study with no correlation analysis between weight loss and glycaemic control
Jesudason,D.R., Pedersen,E., Clifton,P.M., Weight-loss diets in people with type 2 diabetes and renal disease: A randomized controlled trial of the effect of different dietary protein amounts, <i>American Journal of Clinical Nutrition</i> , 98, 494-501, 2013	All participants aged over 18 years
Kim,S., Richards,W.O., Long-term follow-up of the metabolic profiles in obese patients with type 2 diabetes mellitus after Roux-en-Y gastric bypass, <i>Annals of Surgery</i> , 251, 1049-1055, 2010	PICO not met: adults only
Kopelman,P., Groot,Gde H., Rissanen,A., Rossner,S., Toubro,S., Palmer,R., Hallam,R., Bryson,A., Hickling,R.I., Weight loss, HbA1c reduction, and tolerability of cetilistat in a randomized, placebo-controlled phase 2 trial in obese diabetics: comparison with orlistat (Xenical), <i>Obesity</i> , 18, 108-115, 2010	PICO not met: adults only
Korner,A., Wiegand,S., Hungele,A., Tuschy,S., Otto,K.P., l'Allemand-Jander,D., Widhalm,K., Kiess,W., Holl,R.W., APV,initiative, German Competence,Net Obesity, Longitudinal multicenter analysis on the course of glucose metabolism in obese children, <i>International Journal of Obesity</i> , 37, 931-936, 2013	No data specifically on children and young people with type 2 diabetes; population of obese people, 1.1% of whom had type 2 diabetes
Lawrence,J.M., Liese,A.D., Liu,L., Dabelea,D., Anderson,A., Imperatore,G., Bell,R., Weight-loss practices and weight-related issues among youth with type 1 or type 2 diabetes, <i>Diabetes Care</i> , 31, 2251-2257, 2008	PICO not met: no outcomes of interest
Lee,W.J., Chong,K., Ser,K.H., Chen,J.C., Lee,Y.C., Chen,S.C., Su,Y.H., Tsai,M.H., C-peptide predicts the remission of type 2 diabetes after bariatric surgery, <i>Obesity Surgery</i> , 22, 293-298, 2012	PICO not met: adults only
Leslie,D.B., Dorman,R.B., Serrot,F.J., Swan,T.W., Kellogg,T.A., Torres-Villalobos,G., Buchwald,H., Slusarek,B.M., Sampson,B.K., Bantle,J.P., Ikramuddin,S., Efficacy of the Roux-en-Y gastric bypass compared to medically managed controls in meeting the American Diabetes Association composite end point goals for management of type 2 diabetes mellitus, <i>Obesity Surgery</i> , 22, 367-374, 2012	PICO not met: adults only
Manning,R.M., Jung,R.T., Leese,G.P., Newton,R.W., The comparison of four weight reduction strategies aimed at overweight diabetic patients, <i>Diabetic Medicine</i> , 12, 409-415, 1995	Paediatric data not reported separately

Study	Reason for exclusion
Marinari,G.M., Papadia,F.S., Briatore,L., Adami,G., Scopinaro,N., Type 2 diabetes and weight loss following biliopancreatic diversion for obesity, <i>Obesity Surgery</i> , 16, 1440-1444, 2006	PICO not met: adults only
Narasimhan,S., Weinstock,R.S., Youth-onset type 2 diabetes mellitus: lessons learned from the TODAY study, <i>Mayo Clinic Proceedings</i> , 89, 806-816, 2014	This is a review of the TODAY RCT already included in the review
Pearson,E.R., Treating type 2 diabetes in youth: a depressing picture, <i>Journal of the Royal College of Physicians of Edinburgh</i> , 42, 228-, 2012	Expert opinion
Ramos,A.C., Galvao Neto,M.P., de Souza,Y.M., Galvao,M., Murakami,A.H., Silva,A.C., Canseco,E.G., Santamaria,R., Zambrano,T.A., Laparoscopic duodenal-jejunal exclusion in the treatment of type 2 diabetes mellitus in patients with BMI<30 kg/m2 (LBMI), <i>Obesity Surgery</i> , 19, 307-312, 2009	PICO not met: adults only
Reis,C.E., varez-Leite,J.I., Bressan,J., Alfenas,R.C., Role of bariatric-metabolic surgery in the treatment of obese type 2 diabetes with body mass index <35 kg/m2: a literature review, <i>Diabetes Technology and Therapeutics</i> , 14, 365-372, 2012	PICO not met: adults only
Scheen,A.J., Finer,N., Hollander,P., Jensen,M.D., Van Gaal,L.F., RIO-Diabetes Study Group., Efficacy and tolerability of rimonabant in overweight or obese patients with type 2 diabetes: a randomised controlled study.[Erratum appears in <i>Lancet</i> . 2006 Nov 11;368(9548):1650], <i>Lancet</i> , 368, 1660-1672, 2006	PICO not met: adults only
Shi,Y.F., Pan,C.Y., Hill,J., Gao,Y., Orlistat in the treatment of overweight or obese Chinese patients with newly diagnosed Type 2 diabetes, <i>Diabetic Medicine</i> , 22, 1737-1743, 2005	PICO not met: adults only
TODAY Study Group., Safety and Tolerability of the Treatment of Youth-Onset Type 2 Diabetes: The TODAY experience, <i>Diabetes Care</i> , 36, 1765-1771, 2013	PICO not met: outcomes not of interest
Tong,P.C., Lee,Z.S., Sea,M.M., Chow,C.C., Ko,G.T., Chan,W.B., So,W.Y., Ma,R.C., Ozaki,R., Woo,J., Cockram,C.S., Chan,J.C., The effect of orlistat-induced weight loss, without concomitant hypocaloric diet, on cardiovascular risk factors and insulin sensitivity in young obese Chinese subjects with or without type 2 diabetes, <i>Archives of Internal Medicine</i> , 162, 2428-2435, 2002	PICO not met: adults only
Toolabi,K., Arefanian,S., Golzarand,M., Arefanian,H., Effects of laparoscopic Roux-en-Y gastric bypass (LRYGB) on weight loss and biomarker parameters in morbidly obese patients: A 12-month follow-up, <i>Obesity Surgery</i> , 21, 1834-1842, 2011	PICO not met: predominantly adults
Varaschim,M., Nassif,P.A., Moreira,L.B., do Nascimento,M.M., Vieira,G.M., Garcia,R.F., Sue,K.M., Cruz,M.A., Changes in clinical and laboratory parameters in obese patients with type 2 diabetes mellitus submitted to Roux-en-y gastrojejunal bypass without ring, <i>Revista do Colegio Brasileiro de Cirurgioes</i> , 39, 178-182, 2012	PICO not met: adults only

H.22 Type 2 diabetes – metformin

Review question

What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?

Study	Reason for exclusion
Metformin. Useful for some children with type 2 diabetes, <i>Prescrire International</i> , 16, 50-52, 2007	Study criteria not met - overview of metformin in children and young people with type 2 diabetes
Al-Shareef,M.A., Sanneh,A.F., Aljoudi,A.S., Clinical effect of Metformin in children and adolescents with type 2 diabetes mellitus: a systematic review and meta-analysis, <i>Journal of Family and Community Medicine</i> , 19, 68-73, 2012	Systematic review of trials including metformin; 3 trials in the meta-analysis, 1 already included in the evidence summary (Jones et al., 2002). Remaining 2 trials excluded as do not compare metformin to placebo
Bernardita,PradoA, Veronica,GaeteP, Francisca,CoronaH, Eldreth,PeraltaV, Paula,DonosoA, Ximena,RaimannT, Metabolic effect of metformin in obese adolescents at risk of diabetes mellitus type 2Efecto metabolico de la metformina	PICO (Patient Intervention Comparator Outcome) criteria not met - population did not have type 2 diabetes

Study	Reason for exclusion
en adolescentes obesas con riesgo de diabetes mellitus tipo 2, Revista Chilena de Pediatría, 83, 48-57, 2012	
Burgert,T.S., Duran,E.J., Goldberg-Gell,R., Dziura,J., Yeckel,C.W., Katz,S., Tamborlane,W.V., Caprio,S., Short-term metabolic and cardiovascular effects of metformin in markedly obese adolescents with normal glucose tolerance, Pediatric Diabetes, 9, 567-576, 2008	PICO criteria not met - population did not have type 2 diabetes
Centre for Reviews and Dissemination., Efficacy of metformin in the treatment of NIDDM: meta-analysis (;Structured abstract);, Database of Abstracts of Reviews of Effects, -, 2012	Abstract of a published review
Centre for Reviews and Dissemination., Efficacy of metformin in the treatment of NIDDM: meta-analysis (Structured abstract), Database of Abstracts of Reviews of Effects, -, 2014	No information in abstract
Clarson,C.L., Mahmud,F.H., Baker,J.E., Clark,H.E., McKay,W.M., Schauteet,V.D., Hill,D.J., Metformin in combination with structured lifestyle intervention improved body mass index in obese adolescents, but did not improve insulin resistance, Endocrine, 36, 141-146, 2009	PICO criteria not met - population did not have type 2 diabetes
Freemark,M., Liver dysfunction in paediatric obesity: a randomized, controlled trial of metformin, Acta Paediatrica, 96, 1326-1332, 2007	PICO criteria not met - population did not have type 2 diabetes
Freemark,M., Bursey,D., A therapeutic trial of metformin in obese adolescents predisposed to type 2 diabetes mellitus, Pediatric Research, 47, 128A, 2000-, 2000	PICO criteria not met - population did not have type 2 diabetes
Freemark,M., Bursey,D., The effects of metformin on body mass index and glucose tolerance in obese adolescents with fasting hyperinsulinemia and a family history of type 2 diabetes, Pediatrics, 107, E55-, 2001	PICO criteria not met - population did not have type 2 diabetes
Gemmill,J.A.L., Brown,R.J., Nandagopal,R., Rodriguez,L.M., Rother,K.I., Clinical trials in youth with type 2 diabetes, Pediatric Diabetes, 12, 50-57, 2011	Systematic review of trials in children and young people with type 2 diabetes
Gottschalk,M., Danne,T., Vlainic,A., Cara,J.F., Glimepiride versus metformin as monotherapy in pediatric patients with type 2 diabetes: a randomized, single-blind comparative study, Diabetes Care, 30, 790-794, 2007	PICO not met - comparator was not placebo
Hess,A.M., Sullivan,D.L., Metformin for prevention of type 2 diabetes, Annals of Pharmacotherapy, 38, 1283-1285, 2004	PICO criteria not met - population did not have type 2 diabetes
Johansen,K., Efficacy of metformin in the treatment of NIDDM. Meta-analysis, Diabetes Care, 22, 33-37, 1999	No data reported for children or young people with type 2 diabetes
Kane,M.P., bu-Baker,A., Busch,R.S., The utility of oral diabetes medications in type 2 diabetes of the young. [58 refs], Current Diabetes Reviews, 1, 83-92, 2005	Study criteria not met - overview of medications for type 2 diabetes
Kay,J.P., Alemzadeh,R., Langley,G., D'Angelo,L., Smith,P., Holshouser,S., Beneficial effects of metformin in normoglycemic morbidly obese adolescents, Metabolism: Clinical and Experimental, 50, 1457-1461, 2001	PICO criteria not met - population did not have type 2 diabetes
List,J.F., Woo,V., Morales,E., Tang,W., Fiedorek,F.T., Sodium-glucose cotransport inhibition with dapagliflozin in type 2 diabetes, Diabetes Care, 32, 650-657, 2009	PICO criteria not met - population aged 18-79 years
Narasimhan,S., Weinstock,R.S., Youth-onset type 2 diabetes mellitus: lessons learned from the TODAY study, Mayo Clinic Proceedings, 89, 806-816, 2014	This is a review of the TODAY study
Saenz,Antonio, FernandezEsteban,Inmaculada, Mataix,Angel, usejo Segura,Monica, Figuls,Marta, Moher,David, Metformin monotherapy for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2013	Participants aged over 18 years
Saenz,Antonio, Fernandez-Esteban,Inmaculada, Mataix,Angel, usejo Segura,Monica, Figuls,Marta, Moher,David, Metformin monotherapy for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2009	Systematic review of metformin versus placebo in adults with type 2 diabetes
Srinivasan,S., Ambler,G.R., Baur,L.A., Garnett,S.P., Tepsa,M., Yap,F., Ward,G.M., Cowell,C.T., Randomized, controlled trial of metformin for obesity and insulin resistance in children and adolescents: improvement in body composition and fasting insulin, Journal of Clinical Endocrinology and Metabolism, 91, 2074-2080, 2006	PICO criteria not met - population did not have type 2 diabetes
TODAY Study Group, Zeitler,P., Hirst,K., Pyle,L., Linder,B., Copeland,K., Arslanian,S., Cuttler,L., Nathan,D.M., Tollefsen,S., Wilfley,D., Kaufman,F., A clinical trial to maintain glycemic control in youth with type 2 diabetes, New England Journal of Medicine, 366, 2247-2256, 2012	PICO criteria not met - participants in all groups received metformin

H.23 Type 2 diabetes – HbA1c targets

Review question

What is the optimal HbA1c target for children and young people with type 2 diabetes?

Study	Reason for exclusion
Bailey,C.J., Bagdonas,A., Rubes,J., McMorn,S.O., Donaldson,J., Biswas,N., Stewart,M.W., Rosiglitazone/metformin fixed-dose combination compared with uptitrated metformin alone in type 2 diabetes mellitus: a 24-week, multicenter, randomized, double-blind, parallel-group study, <i>Clinical Therapeutics</i> , 27, 1548-1561, 2005	PICO not met: excluded patients aged < 18 years
Chou,H.S., Palmer,J.P., Jones,A.R., Waterhouse,B., Ferreira-Cornwell,C., Krebs,J., Goldstein,B.J., Initial treatment with fixed-dose combination rosiglitazone/glimepiride in patients with previously untreated type 2 diabetes, <i>Diabetes, Obesity and Metabolism</i> , 10, 626-637, 2008	PICO not met: excluded patients aged <18 years
Derosa,G., Maffioli,P., D'Angelo,A., Salvadeo,S.A., Ferrari,I., Fogari,E., Mereu,R., Gravina,A., Palumbo,I., Randazzo,S., Cicero,A.F., Effects of insulin therapy with continuous subcutaneous insulin infusion (CSII) in diabetic patients: comparison with multi-daily insulin injections therapy (MDI), <i>Endocrine Journal</i> , 56, 571-578, 2009	PICO not met: excluded patients aged <18 years
Dorchy,H., Roggemans,M.P., Willems,D., Glycated hemoglobin and related factors in diabetic children and adolescents under 18 years of age: a Belgian experience, <i>Diabetes Care</i> , 20, 2-6, 1997	PICO not met: type 1 diabetes only.
hl-Jorgensen,K., Near-normoglycemia and late diabetic complications. The Oslo Study, <i>Acta Endocrinologica, Supplementum</i> . 284, 1-38, 1987	PICO not met: type 1 diabetes only.
Jones,K.L., Arslanian,S., Peterokova,V.A., Park,J.S., Tomlinson,M.J., Effect of metformin in pediatric patients with type 2 diabetes: a randomized controlled trial, <i>Diabetes Care</i> , 25, 89-94, 2002	Intervention not relevant - not treat to target
Rosenstock,J., Rood,J., Cobitz,A., Biswas,N., Chou,H., Garber,A., Initial treatment with rosiglitazone/metformin fixed-dose combination therapy compared with monotherapy with either rosiglitazone or metformin in patients with uncontrolled type 2 diabetes, <i>Diabetes, Obesity and Metabolism</i> , 8, 650-660, 2006	PICO not met: excluded patients aged < 18 years.
Saenz,Antonio, FernandezEsteban,Inmaculada, Mataix,Angel, usejo Segura,Monica, Figuls,Marta, Moher,David, Metformin monotherapy for type 2 diabetes mellitus, <i>Cochrane Database of Systematic Reviews</i> , -, 2009	PICO not met: excluded patients aged < 18 years.
Sellers,E.A., Dean,H.J., Short-term insulin therapy in adolescents with type 2 diabetes mellitus, <i>Journal of Pediatric Endocrinology</i> , 17, 1561-1564, 2004	No comparator.
Tong,P.C., Ko,G.T., So,W.Y., Chiang,S.C., Yang,X., Kong,A.P., Ozaki,R., Ma,R.C., Cockram,C.S., Chow,C.C., Chan,J.C., Use of anti-diabetic drugs and glycaemic control in type 2 diabetes-tThe Hong Kong Diabetes Registry, <i>Diabetes Research and Clinical Practice</i> , 82, 346-352, 2008	Children and young people were included in the study but no separate analyses were reported.

H.24 Type 2 diabetes – hypertension

Review question

What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Study	Reason for exclusion
Al-Agha,A.E., Ocheltree,A., Shata,N., Prevalence of	Prevalence estimates (measurements of blood pressure and

Study	Reason for exclusion
hyperinsulinism, type 2 diabetes mellitus and metabolic syndrome among Saudi overweight and obese pediatric patients, <i>Minerva Pediatrica</i> , 64, 623-631, 2012	lipids) are not provided with respect to a specific time since diagnosis - only mean age at diagnosis is provided with a wide age range
Bacha,F., Gidding,S.S., Caprio,S., Weinstock,R., Lynch,J., Hirst,K., High prevalence and rapid increase of cardiovascular disease risk factors in youth with type 2 diabetes: The today study group, <i>Circulation</i> , 127, -, 2013	Abstract only
Miller,J., Silverstein,J., How prevalent are diabetes-related complications in patients with youth-onset type 2 diabetes mellitus?, <i>Nature Clinical Practice Endocrinology and Metabolism</i> , 3, 12-13, 2007	Commentary on a study weeded out as it compared type 2 diabetes with type 1 diabetes
Schober,E., Holl,R.W., Grabert,M., Thon,A., Rami,B., Kapellen,T., Seewi,O., Reinehr,T., Diabetes mellitus type 2 in childhood and adolescence in Germany and parts of Austria, <i>European Journal of Pediatrics</i> , 164, 705-707, 2005	Data not presented at specific timepoints since diagnosis (all cases are grouped together regardless of age or time since diagnosis)
Scott,C.R., Smith,J.M., Craddock,M.M., Pihoker,C., Characteristics of youth-onset noninsulin-dependent diabetes mellitus and insulin-dependent diabetes mellitus at diagnosis, <i>Pediatrics</i> , 100, 84-91, 1997	Data not reported according to time since diagnosis or by age group. Mean age and range are reported - range is very wide (8 to 19 years)
Urakami,T., Suzuki,J., Yoshida,A., Saito,H., Wada,M., Takahashi,S., Mugishima,H., Frequencies of factors of metabolic syndrome at diagnosis in children with T2DM, <i>Pediatrics International</i> , 51, 435-437, 2009	The same population was used by another included study. Methods are not clear about measurements taken pre-1990 (the included study states that blood pressure and lipids were not measured pre-1990)
Zdravkovic,V., Daneman,D., Hamilton,J., Presentation and course of Type 2 diabetes in youth in a large multi-ethnic city, <i>Diabetic Medicine</i> , 21, 1144-1148, 2004	Wide age range (8.8 to 17.5 years) with data not reported according to time since diagnosis

H.25 Type 2 diabetes – dyslipidaemia

Review question

What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Study	Reason for exclusion
Al-Agha,A.E., Ocheltree,A., Shata,N., Prevalence of hyperinsulinism, type 2 diabetes mellitus and metabolic syndrome among Saudi overweight and obese pediatric patients, <i>Minerva Pediatrica</i> , 64, 623-631, 2012	Prevalence estimates (measurements of blood pressure and lipids) are not provided with respect to a specific time since diagnosis - only mean age at diagnosis is provided with a wide age range
Alavudeen,S.S., Dhanapal,C.K., Khan,N.A., Al,AkhaliK, Paulliah,S.D., Prevalence and control of cardiovascular risk factors among type 2 diabetes mellitus patients in southern region of Saudi Arabia, <i>Journal of Young Pharmacists</i> , 5, 144-147, 2013	Adult population only. Mean age 53.9 /- 10.02 years
Albers,J.J., Marcovina,S.M., Imperatore,G., Snively,B.M., Stafford,J., Fujimoto,W.Y., Mayer-Davis,E.J., Pettitt,D.B., Pihoker,C., Dolan,L., Dabelea,D.M., Prevalence and determinants of elevated apolipoprotein B and dense low-density lipoprotein in youths with type 1 and type 2 diabetes, <i>Journal of Clinical Endocrinology and Metabolism</i> , 93, 735-742, 2008	Data are not presented according to specific time points since diagnosis
Bacha,F., Gidding,S.S., Caprio,S., Weinstock,R., Lynch,J., Hirst,K., High prevalence and rapid increase of cardiovascular disease risk factors in youth with type 2 diabetes: The today study group, <i>Circulation</i> , 127, -, 2013	Abstract only
Kershner,A.K., Daniels,S.R., Imperatore,G., Palla,S.L., Pettitt,D.B., Pettitt,D.J., Marcovina,S., Dolan,L.M., Hamman,R.F., Liese,A.D., Pihoker,C., Rodriguez,B.L., Lipid abnormalities are prevalent in youth with type 1 and type 2 diabetes: the SEARCH for Diabetes in Youth Study, <i>Journal of Pediatrics</i> , 149, 314-319, 2006	Data presented as > 10 years of age only which captures the entire type 2 diabetes population. Results are not presented according to time since diagnosis or age groups
Levitsky,L., Burden of comorbidities in youth in the TODAY trial, <i>Pediatric Diabetes</i> , 13, 11-, 2012	Abstract only
Newfield,R.S., Dewan,A.K., Jain,S., Dyslipidemia in children with type 2 diabetes vs. obesity, <i>Pediatric Diabetes</i> , 9, 115-121, 2008	Data are not presented at specific time points and are grouped together across different time points
Schober,E., Holl,R.W., Grabert,M., Thon,A., Rami,B., Kapellen,T., Seewi,O., Reinehr,T., Diabetes mellitus type 2 in childhood and adolescence in Germany and parts of	Data not presented at specific timepoints since diagnosis (all cases are grouped together regardless of age or time since diagnosis)

Study	Reason for exclusion
Austria, European Journal of Pediatrics, 164, 705-707, 2005	
Sellers,E.A.C., Yung,G., Dean,H.J., Dyslipidemia and other cardiovascular risk factors in a Canadian First Nation pediatric population with type 2 diabetes mellitus, Pediatric Diabetes, 8, 384-390, 2007	Data not analysed by specific time points since diagnosis. Only mean age at diagnosis and mean age when study performed are reported and data for all participants are reported together
Sulehria,S.B., Awan,A.K., Comparison of pattern of dyslipidemia in type 1 & type 2 diabetes mellitus, Pakistan Journal of Medical and Health Sciences, 7, 911-912, 2013	Age range 13 to 85 years. No subgroup analyses
White,N.H., Pyle,L., Tamborlane,W.V., Geffner,M.E., Guandalini,C., Clinical characteristics and co-morbidities in a large cohort of youth with type 2 diabetes mellitus (T2DM) screened for the treatment options for type 2 diabetes in adolescents and youth (TODAY) study, Diabetes, 58, 2009. Date of Publication, -, 2009	Abstract only. One data table is provided but only mean values, not prevalences, are reported

H.26 Type 2 diabetes – retinopathy

Review question

What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?

Study	Reason for exclusion
Amutha,A., Datta,M., Unnikrishnan,R., Anjana,R.M., Mohan,V., Clinical profile and complications of childhood- and adolescent-onset type 2 diabetes seen at a diabetes center in south India, Diabetes Technology and Therapeutics, 14, 497-504, 2012	Mean age at screening for retinopathy 22.2 years (/- 9.7 years). Prevalence of retinopathy stratified by duration of diabetes (< 5, 5-10, 10-15 and > 15 years) but not by age.
Boussageon,R., Bejan-Angoulvant,T., Saadatian-Elahi,M., Lafont,S., Bergeonneay,C., Kassai,B., Erpeldinger,S., Wright, J.M., Gueyfflier,F., Cornu,C., Effect of intensive glucose lowering treatment on all cause mortality, cardiovascular death, and microvascular events in type 2 diabetes: meta-analysis of randomised controlled trials, BMJ, 343, d4169, 2011	All participants aged > 18 years.
Danne,T., Kordonouri,O., Casani,A., Chiarelli,F., Diabetic retinopathy in childhood and adolescents, Diabetes, Nutrition and Metabolism - Clinical and Experimental, 12, 136-144, 1999	Narrative review article
Dart,A.B., Martens,P.J., Rigatto,C., Brownell,M.D., Dean,H.J., Sellers,E.A., Earlier onset of complications in youth with type 2 diabetes, Diabetes Care, 37, 436-443, 2014	No stratification by age.
Donaghue,K.C., Chiarelli,F., Trotta,D., Allgrove,J., hl-Jorgensen,K., Microvascular and macrovascular complications associated with diabetes in children and adolescents, Pediatric Diabetes, 10, 195-203, 2009	Narrative review article.
Donaghue,K.C., Craig,M.E., Chan,A.K., Fairchild,J.M., Cusumano,J.M., Verge,C.F., Crock,P.A., Hing,S.J., Howard,N.J., Silink,M., Prevalence of diabetes complications 6 years after diagnosis in an incident cohort of childhood diabetes, Diabetic Medicine, 22, 711-718, 2005	Type 1 diabetes.
Donaghue,K.C., Fairchild,J.M., Craig,M.E., Chan,A.K., Hing,S., Cutler,L.R., Howard,N.J., Silink,M., Do all prepubertal years of diabetes duration contribute equally to diabetes complications?, Diabetes Care, 26, 1224-1229, 2003	Type 1 diabetes. Data on prevalence of retinopathy stratified by age or duration of diabetes not reported. Data reported as survival analysis only.
El,AsrarM, Adly,A.A., El,HadidyE, Abdelwahab,M.A., D-dimer levels in type 1 and type 2 diabetic children and adolescents; Relation to microvascular complications and dyslipidemia "own data and review", Pediatric endocrinology reviews : PER, 9, 657-668, 2012	Ophthalmoscopy used for identification of retinopathy. No stratification of prevalence according to age or duration of diabetes.
Eppens,M.C., Craig,M.E., Cusumano,J., Hing,S., Chan,A.K., Howard,N.J., Silink,M., Donaghue,K.C., Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes, Diabetes Care, 29, 1300-1306, 2006	Prevalence of retinopathy not stratified by age or duration of diabetes. Age range for participants with type 2 diabetes not reported.

Study	Reason for exclusion
Farah,S.E., Wals,K.T., Friedman,I.B., Pisacano,M.A., Martino-Nardi,J., Prevalence of retinopathy and microalbuminuria in pediatric type 2 diabetes mellitus, Journal of Pediatric Endocrinology, 19, 937-942, 2006	Ophthalmoscopy only used to identify retinopathy.
Forster,A.S., Forbes,A., Dodhia,H., Connor,C., Du,CheminA, Sivaprasad,S., Mann,S., Gulliford,M.C., Changes in detection of retinopathy in type 2 diabetes in the first 4 years of a population-based diabetic eye screening program: Retrospective cohort study, Diabetes Care, 36, 2663-2669, 2013	Outcome not stratified by age. Population mean age not described, but likely to include adults as well as children and young people.
Jialal,I., Welsh,N.H., Joubert,S.M., Rajput,M.C., Vascular complications in non-insulin-dependent diabetes in the young, South African Medical Journal, Suid-Afrikaanse Tydskrif Vir Geneeskunde. 62, 155-157, 1982	Age of participants not fully reported, but age of participants with retinopathy reported as 24 to 52 years, therefore likely to be inappropriate age group.
Mayer-Davis,E.J., Davis,C., Saadine,J., D'Agostino,R.B.,Jr., Dabelea,D., Dolan,L., Garg,S., Lawrence,J.M., Pihoker,C., Rodriguez,B.L., Klein,B.E., Klein,R., SEARCH for Diabetes in Youth Study Group., Diabetic retinopathy in the SEARCH for Diabetes in Youth Cohort: a pilot study, Diabetic Medicine, 29, 1148-1152, 2012	Mean age of participants with type 2 diabetes reported as 21.1 years (SD 2.8 years). Prevalence not stratified by age or duration of diabetes.
Papali'i-Curtin,A.T., Dalziel,D.M., Prevalence of diabetic retinopathy and maculopathy in Northland, New Zealand: 2011-2012, New Zealand Medical Journal, 126, 20-28, 2013	Mean age 62.7 years.
Raman,V., Campbell,F., Holland,P., Chapman,T., Dabbs,T., Bodansky,H.J., O'Neill,D.P., Retinopathy screening in children and adolescents with diabetes, Annals of the New York Academy of Sciences, 958, 387-389, 2002	Type 1 diabetes. No stratification by age or duration of diabetes. Detection of retinopathy was either by fundus photography or by slit lamp examination.
Verougstraete,C., Toussaint,D., De,SchepperJ, Haentjens,M., Dorchy,H., First microangiographic abnormalities in childhood diabetes - Types of lesions, Graefe's Archive for Clinical and Experimental Ophthalmology, 229, 24-32, 1991	Type 1 diabetes. Intervention not relevant - fluorescein angiography used to detect retinopathy.
Wan Nazaimoon,W.M., Letchuman,R., Noraini,N., Ropilah,A.R., Zainal,M., Ismail,I.S., Wan Mohamad,W.B., Faridah,I., Singaraveloo,M., Sheriff,I.H., Khalid,B.A., Systolic hypertension and duration of diabetes mellitus are important determinants of retinopathy and microalbuminuria in young diabetics, Diabetes Research and Clinical Practice, 46, 213-221, 1999	No description of prevalence of retinopathy for children and young people aged under 18.

H.27 Type 2 diabetes – nephropathy

Review question

What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

Study	Reason for exclusion
Copeland,K.C., Zeitler,P., Geffner,M., Guandalini,C., Higgins,J., Hirst,K., Kaufman,F.R., Linder,B., Marcovina,S., McGuigan,P., Pyle,L., Tamborlane,W., Willi,S., Characteristics of adolescents and youth with recent-onset type 2 diabetes: The TODAY cohort at baseline, Journal of Clinical Endocrinology and Metabolism, 96, 159-167, 2011	The reported microalbuminuria prevalence was tested on one urine sample only rather than on two out of three as reported. (This was clarified by the Today Cohort Study Group in correspondence with NCC-WCH)
Ettinger,L.M., Freeman,K., Martino-Nardi,J.R., Flynn,J.T., Microalbuminuria and abnormal ambulatory blood pressure in adolescents with type 2 diabetes mellitus, Journal of Pediatrics, 147, 67-73, 2005	Just an overall prevalence was reported, no stratification according to age.
Kim,N.H., Pavkov,M.E., Knowler,W.C., Hanson,R.L., Weil,E.J., Curtis,J.M., Bennett,P.H., Nelson,R.G., Predictive value of albuminuria in American Indian youth with or without type 2 diabetes, Pediatrics, 125, e844-e851, 2010	The incidence of microalbuminuria by age was only reported only in a graph.
Krakoff,J., Lindsay,R.S., Looker,H.C., Nelson,R.G., Hanson,R.L., Knowler,W.C., Incidence of retinopathy and nephropathy in youth-onset compared with adult-onset type 2 diabetes, Diabetes Care, 26, 76-81, 2003	The incidence rate by age (10 to 15 years) was only reported in a graph.

Study	Reason for exclusion
Maahs,D.M., Snively,B.M., Bell,R.A., Dolan,L., Hirsch,I., Imperatore,G., Linder,B., Marcovina,S.M., Mayer-Davis,E.J., Pettitt,D.J., Rodriguez,B.L., Dabelea,D., Higher prevalence of elevated albumin excretion in youth with type 2 than type 1 diabetes: the SEARCH for Diabetes in Youth study, <i>Diabetes Care</i> , 30, 2593-2598, 2007	Just an overall prevalence was reported, no stratification according to age.
Shield,J.P.H., Lynn,R., Wan,K.C., Haines,L., Barrett,T.G., Management and 1 year outcome for UK children with type 2 diabetes, <i>Archives of Disease in Childhood</i> , 94, 206-209, 2009	Just an overall prevalence was reported, no stratification according to age.
TODAY Study Group., Rapid rise in hypertension and nephropathy in youth with type 2 diabetes: the TODAY clinical trial.[Erratum appears in <i>Diabetes Care</i> . 2013 Aug;36(8):2448], <i>Diabetes Care</i> , 36, 1735-1741, 2013	Publication with error corrected on the TODAY clinical trial, relevant data to this review(which remain intact) have been extracted from the original publication.

H.28 Health economics

Study	Reason for exclusion
Anderson,D.G., Multiple daily injections in young patients using the ezy-BICC bolus insulin calculation card, compared to mixed insulin and CSII, <i>Pediatric Diabetes</i> , 10, 304-309, 2009	Right comparator, but no costs included
Blair,J., Gregory,J.W., Peak,M., Insulin delivery by multiple daily injections or continuous subcutaneous insulin infusion in childhood: Addressing the evidence gap, <i>Practical Diabetes</i> , 29, 47-48, 2012	Commentary; no cost effectiveness
Centre for Reviews and Dissemination, The cost-effectiveness of continuous glucose monitoring in type 1 diabetes (Provisional abstract), <i>NHS Economic Evaluation Database (NHSEED)</i> , -, 2010	Cost utility analysis (CUA) conducted only in adult cohort
Centre for Reviews and Dissemination, Continuous subcutaneous insulin infusion versus multiple daily injections of insulin: economic comparison in adult and adolescent Type 1 diabetes mellitus in Australia (Structured abstract), <i>NHS Economic Evaluation Database (NHSEED)</i> , -, 2007	CSII was not included in the 2015 update scope
Chiari,G., Direct measurement of 3-B-hydroxybutyrate in the management of diabetic ketoacidosis in children: A cost effective enhancement in the management of diabetic ketoacidosis in children, <i>Diabetes Technology and Therapeutics</i> , 13, 178-179, 2011	Same study/data as Vanelli 2003: no economic evaluation, only limited information on clinical cost (test, ICU)
Couch,R., Jetha,M., Dryden,D.M., Hooton,N., Liang,Y., Durec,T., Sumamo,E., Spooner,C., Milne,A., Gorman,K., Klassen,T.P., Diabetes education for children with type 1 diabetes mellitus and their families (Structured abstract), <i>Health Technology Assessment Database</i> , -, 2013	No cost effectiveness model; comparator not clear
Gage,H., Hampson,S., Skinner,T.C., Hart,J., Storey,L., Foxcroft,D., Kimber,A., Cradock,S., McEvilly,E.A., Educational and psychosocial programmes for adolescents with diabetes: approaches, outcomes and cost-effectiveness. [122 refs], <i>Patient Education and Counseling</i> , 53, 333-346, 2004	No cost effectiveness model for structured education versus usual care
Hampson,S.E., Skinner,T.C., Hart,J., Storey,L., Gage,H., Foxcroft,D., Kimber,A., Shaw,K., Walker,J., Effects of educational and psychosocial interventions for adolescents with diabetes mellitus: a systematic review. [148 refs], <i>Health Technology Assessment (Winchester, England)</i> , 5, 1-79, 2001	No information on structured education programmes reported
Health,Technology Assessment, Randomised controlled trial of continuous subcutaneous insulin infusion compared to multiple daily injection regimens in children and young people at diagnosis of type 1 diabetes mellitus (Project record), <i>Health Technology Assessment Database</i> , -, 2013	CSII was not included in the 2015 update scope
Health,Technology Assessment, Maximising engagement, motivation and long term change in a structured intensive education programme in diabetes for children, young people and their families: child and adolescent structured competencies approach to diabetes education (Project record), <i>Health Technology Assessment Database</i> , -, 2013	Not reporting results
Huang,E.S., O'Grady,M., Basu,A., Winn,A., John,P., Lee,J., Meltzer,D., Kollman,C., Laffel,L., Tamborlane,W.,	CUA conducted only in adult cohort

Study	Reason for exclusion
Weinzimer,S., Wysocki,T., Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group., The cost-effectiveness of continuous glucose monitoring in type 1 diabetes.[Erratum appears in Diabetes Care. 2010 Sep;33(9):2129], Diabetes Care, 33, 1269-1274, 2010	
Huang,E.S., O'Grady,M., Basu,A., Winn,A., John,P., Lee,J., Meltzer,D., Kollman,C., Laffel,L., Tamborlane,W., Weinzimer,S., Wysocki,T., Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group., The cost-effectiveness of continuous glucose monitoring in type 1 diabetes.[Erratum appears in Diabetes Care. 2010 Sep;33(9):2129], Diabetes Care, 33, 1269-1274, 2010	Adult population
Laffel,L.M., Wentzell,K., Loughlin,C., Tovar,A., Moltz,K., Brink,S., Sick day management using blood 3-hydroxybutyrate (3-OHB) compared with urine ketone monitoring reduces hospital visits in young people with T1DM: a randomized clinical trial, Diabetic Medicine, 23, 278-284, 2006	Right comparator, but no costs or cost effectiveness model
Meltzer,D., Egleston,B., Stoffel,D., Dasbach,E., Effect of future costs on cost-effectiveness of medical interventions among young adults: the example of intensive therapy for type 1 diabetes mellitus, Medical Care, 38, 679-685, 2000	DCCT model included participants aged 13 to 39 years, thus costs and benefits associated with children and young people cannot be estimated from this trial
Nahata,L., Insulin therapy in pediatric patients with type I diabetes: continuous subcutaneous insulin infusion versus multiple daily injections. [12 refs], Clinical Pediatrics, 45, 503-508, 2006	Literature review, no cost data
Price,K.J., Wales,J., Eiser,C., Knowles,J., Heller,S., Freeman,J., Brennan,A., McPherson,A., Wellington,J., Does an intensive self-management structured education course improve outcomes for children and young people with type 1 diabetes? The Kids In Control OF Food (KICK-OFF) clusterrandomised controlled trial protocol, BMJ Open, 3, -, 2013	Not reporting results
Slover,I.I.R.H., Continuous glucose monitoring in children and adolescents, Current Diabetes Reports, 12, 510-516, 2012	Literature review, cost effectiveness information from Huang 2010
St,Charles M., Lynch,P., Graham,C., Minshall,M.E., A cost-effectiveness analysis of continuous subcutaneous insulin injection versus multiple daily injections in type 1 diabetes patients: a third-party US payer perspective, Value in Health, 12, 674-686, 2009	CSII was not included in the 2015 update scope
Vanelli,M., Chiari,G., Capuano,C., Iovane,B., Bernardini,A., Giacalone,T., The direct measurement of 3-beta-hydroxy butyrate enhances the management of diabetic ketoacidosis in children and reduces time and costs of treatment, Diabetes, Nutrition and Metabolism - Clinical and Experimental, 16, 312-316, 2003	No economic evaluation, only limited information on clinical cost (test, ICU)

Appendix I: Evidence tables

The evidence tables from the 2004 guideline are presented in a separate document.

The evidence tables from the 2015 update are presented in a separate document, except for those related to the review question about diagnosis which are presented below.

I.1 Diagnosis

Review question

What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?

The systematic review for this question was conducted by the guidance-producing centre for the guideline ‘Type 1 diabetes in adults’.

I.1.1 Population: young people only (all sample sizes)

Table 4: Andersson 2013 (NCGC reference 315)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
C. Andersson, F. Vaziri-Sani, Aj Delli, B. Lindblad, A. Carlsson, G. Forsander, J. Ludvigsson, C. Marcus, U. Samuelsson, Sa Ivarsson, A. Lenmark, H. Elding Larsson, and BDD Study Group. Triple specificity of ZnT8 autoantibodies in relation to HLA and other islet autoantibodies in childhood and adolescent type 1 diabetes. <i>Pediatr.Diabetes</i> 14 (2):97-105, 2013. REF ID: Andersson 2013	Observational: cross-sectional Sweden	N=427 young people aged 16-17.9 years Total N=3165 T1D young people and children Inclusion criteria: T1D (ADA criteria) Swedish SWEDIAL KIDS register Exclusion criteria: None given	Young people subgroup (age 16-17.9 years) DIABETES TYPE: T1D	T1D: IAA GADA IA-2A Cut-offs for positivity GADA: >50 U/mL IA-2A: >10 U/mL IAA: >1RU (based on internal + and - standard samples)	Baseline	T1D young people (>15 years: 15-17.9 years)	Funding: Swedish Research Council and other non-pharmaceutical funded sources. Risk of bias: n/a

Table 5: Barker 2014 (NCGC reference 300)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
A. Barker, A. Lauria, N. Schloot, N. Hosszufalusi, J. Ludvigsson, C. Mathieu, D. Mauricio, M. Nordwall, B. Van Der Schueren, T. Mandrup-Poulsen, W. A. Scherbaum, I. Weets, F. K. Gorus, N. Wareham, R. D. Leslie, and P. Pozzilli. Age-dependent decline of beta-cell function in type 1 diabetes after diagnosis: a multi-centre longitudinal study. <i>Diabetes Obes. Metab.</i> 16 (3):262-267, 2014. REF ID: Barker 2014	Observational: prospective case-series 7 European registries	N=995 young people subgroup Total N=3929 T1D adults, young people, and children Inclusion criteria: T1D (ADA and WHO criteria) Exclusion criteria: None given	Young people subgroup (age at onset >10 and ≤18 years) Diabetes type: T1D	T1D: Fasting C-pep Stimulated C-pep (results not given in study due to very small number of stim C-pep mmTs made) Cut-offs for positivity C-pep: detection limit 0.01 nM	Baseline, 1 and 5 years	T1D young people	Funding: Centro Internazionale Studi Diabete. Risk of bias: n/a lots of missing data at follow-up

Table 6: Tung 2008 (NCGC reference 66)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
Y C Tung, JS Lee, WY Tsai, and PH Hsiao. Evaluation of beta-cell function in diabetic Taiwanese children using a 6-min glucagon test.	Observational: cross-sectional study Single centre, Taiwan	Total N=118 T1D (N=20 T2D young people and N=98 T1D children and young people) Inclusion criteria: Newly diagnosed diabetes <18 years of age Received neither oral hypoglycaemic agents nor insulin therapy before the study	Young people with diabetes type 2D T2D N=20 Age, years, median (range) M/F %	T2D: fC-PEPTIDE Cut-offs for positivity fC-PEPTIDE+: 0.1 nmol/L	n/a	T2D young people (N=20) fC-PEPTIDE+, nmol/L (range) 1.0 (0.5 – 5.1)	Funding: Not reported Risk of bias: n/a

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
Eur.J.Pediatr . 167 (7):801-805, 2008. REFID: Tung 2008		IAA, GADA and IA-2 were measured to confirm the Diagnosis Exclusion criteria: None reported					

Table 7: Shivaprasad 2014 (NCGC reference 325)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
C. Shivaprasad, Rajneesh Mittal, Mala Dharmalingam, and Prasanna K. Kumar. Zinc transporter-8 autoantibodies can replace IA-2 autoantibodies as a serological marker for juvenile onset type 1 diabetes in India. Indian J Endocrinol Metab 18 (3):345-349, 2014. REF ID: Shivaprasad 2014	Observational: cross-sectional India	N=88 young people Inclusion criteria: Diabetes (ADA criteria) T1D Diagnosis: ketosis at presentation, lean phenotype, requirement for insulin, and/or low C-peptide Duration from Diagnosis <48 months Exclusion criteria: None given	Young people Diabetes type: T1D (N=21 newly Diagnosis)	T1D: ZnT8 GAD65 IA-2 Cut-offs for positivity ZnT8: ≥15 U/ml GAD65: >20 U/ml IA-2: >75 U/ml	Baseline	T1D young people	Funding: UGC Sri Lanka. Risk of bias: n/a consecutive recruitment
			Age, mean (SD)			T1D all N=88 11.0 (4.2) years	
			HbA1c, % man (SD)			ZnT8 19.3%	
			Duration of diabetes, mean (SD)			GAD+/ZnT8+ 31.8%	
						GAD+/IA-2+ 15.9%	
						GAD+/IA-2+ 9.1%	
						GAD+/IA-2+/ZnT8+ 5.7%	
						IA-2+/ZnT8+ 2.3%	

Table 8: Vermeulan 2011 (NCGC reference 250)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
I. Vermeulen, I. Weets, M. Asanghanwa, J. Ruige, Gaal L. Van, C. Mathieu, B. Keymeulen, V. Lampasona, J. M. Wenzlau, J. C. Hutton, D. G.	Observational: case-control study Single centre, Taiwan	Total N=655 T1D (extra N=761 controls) Data here are for young people only: aged 10-39 (most were >11 years) Inclusion criteria: Newly diagnosed diabetes <18 years of age	Young people diabetes type: T1D controls (health)	T1D: GADA IA-2 ZnT8 Combinations Cut-offs for positivity fC-PEPTIDE+: 0.1 nmol/L	n/a	T1D young people (N=20)	Funding: Not reported Risk of bias: n/a
						T1D N=655	

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
Pipeleers, and F. K. Gorus. Contribution of antibodies against IA-2beta and zinc transporter 8 to classification of diabetes diagnosed under 40 years of age. Diabetes Care 34 (8):1760-1765, 2011. Vermeula 2011		Received neither oral hypoglycaemic agents nor insulin therapy before the study IAA, GADA and IA-2 were measured to confirm the Diagnosis Exclusion criteria: None reported	Age, years, median (range) M/F %	13.3 (11.1 – 15.7) 40/60			

Table 9: Zanone 2003 (NCGC reference 79)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
M. M. Zanone, E. Catalfamo, S. L. Pietropaolo, I. Rabbone, C. Sacchetti, F. Cerutti, M. Trucco, and P. Cavallo-Perin. Glutamic acid decarboxylase and ICA512/IA-2 autoantibodies as disease markers and relationship to residual beta-cell function and glycemic control in young type 1 diabetic patients. Metabolism. 52 (1):25-29, 2003. REF ID: Zanone 2003	Observational: cross-sectional study Single centre, Italy	Total N=154 T1D (N=91 young people and N=63 children) Inclusion criteria: IDDM Adolescents (young people) Exclusion criteria: None reported	Young people Diabetes type: T1D T1D N=91 Age, years, mean (range; SD) Duration of diabetes, years, mean (SD) M/F %	T1D: C-PEPTIDE GADA65 ICA IA-2 Cut-offs for positivity fC-PEPTIDE+: not given ICA512/IA-2+: Index* of 0.032 GAD65+: Index* of 0.069 ICA+: >5 JDF units *INDEX = sample cpm – negative control cpm /positive control cpm - negative control cpm	n/a	T1D young people (N=91) fC-PEPTIDE+, N=23/91 (25%) fC-PEPTIDE+, ng/mL (SD) ICA+ 31 (34%) GAD65+ 40 (44%) IA-2 (ICA 512)+ 41 (45%) GAD+/IA-2+ 19 (21%) GAD+ and/or IA-2+ 62 (68%) ICA+, GAD+ and IA-2+ 8 (9%) ICA- / GAD+ and/or IA-2+ 36 (40%) ICA+ / GAD- and/or IA-2- 6 (6%)	Funding: Not reported Risk of bias: n/a

I.1.2 Population: young people and adults (mixed population studies); N ≥50

Table 10: Besser 2011 (NCGC reference 300)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments										
R. Besser, J. Ludvigsson, A. Jones, T. McDonald, B. Shields, B. Knight, and A. Hattersley. Urine C-peptide creatinine ratio is a noninvasive alternative to the mixed-meal tolerance test in children and adults with type 1 diabetes. Diabetes Care 34 (3):607-609, 2011. REF ID: Besser 2011	Observational: cohort study Adults from diabetes clinic, UK; young people from paediatric clinic, Sweden	Total N=72 T1D (mixture of young people and adults)	Young people (n=21) and adults diabetes type: T1D (n=72)	Patients underwent a standard mixed-meal tolerance test (MMTT) T1D: C-PEPTIDE (serum, sCP) Urine C-peptide creatinine ratio (UCPCR) sCP: collected at 0 and 90 min. Additional samples at 30, 60, and 120min in pediatric patients (n=18), allowing area under the curve (AUC) to be calculated. Urine was collected as a fasting second morning void immediately before the start of the MMTT (0 min) and after 120 min. Significant endogenous insulin secretion was defined as 90-min sCP ≥0.2 nmol/L, in accordance with the DCCT Urine: collected in boric acid 120 mins after evening meal following a premeal void. Adult patients took further home urine samples 120 min after a standard 60-g CHO breakfast and following the patients' own lunch. Urine samples brought to the research centre within 24h.	N/A – immediate testing (up to 120 mins)	T1D (N=75)	Funding: Diabteets UK, Peninsula NIHR Clinical Research Facility, EC program Collaborative European Effort to Develop Diabetes Diagnostics; arndiabetesfonden (The Swedish Child Diabetes Foundation) and the Swedish Research Council. Risk of bias: n/a										
		Inclusion criteria: T1D Young people (<19 years) and adults (≥18 years) Age of Diagnosis: <30 years on insulin since diagnosis Exclusion criteria: known renal impairment (eGFR<60ml/min/1.73m ²) severe hypoglyc. within last 3 months documented hypoglycaemia unawareness with a blood glucose <3mmol/L, and HbA1c >10%.	<table border="1"> <thead> <tr> <th></th> <th>Young (N=21)</th> <th>Adults (N=51)</th> </tr> </thead> <tbody> <tr> <td>Age, years, median (IQR)</td> <td>14 (10.9-16.4)</td> <td>18 (13-24)</td> </tr> <tr> <td>M/F, %</td> <td>33/67</td> <td>51/49</td> </tr> <tr> <td>Diabetes duration, years, median (IQR)</td> <td>2.6 (0.6-5.0)</td> <td>21.4 (2.8-41.0)</td> </tr> <tr> <td>HbA1c, median (IQR), %</td> <td>7.2 (6.6-7.9)</td> <td>7.8 (6.9-9.0)</td> </tr> </tbody> </table> <p>To enrich for patients who had endogenous insulin secretion, 43% patients were either within 5 years of Diagnosis or known to still secrete C-peptide when previously tested.</p>					Young (N=21)	Adults (N=51)	Age, years, median (IQR)	14 (10.9-16.4)	18 (13-24)	M/F, %	33/67	51/49	Diabetes duration, years, median (IQR)	2.6 (0.6-5.0)
	Young (N=21)	Adults (N=51)															
Age, years, median (IQR)	14 (10.9-16.4)	18 (13-24)															
M/F, %	33/67	51/49															
Diabetes duration, years, median (IQR)	2.6 (0.6-5.0)	21.4 (2.8-41.0)															
HbA1c, median (IQR), %	7.2 (6.6-7.9)	7.8 (6.9-9.0)															

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
						sensitive and specific method for detecting insulin secretion. UCPCR may be a practical alternative to serum C-peptide testing, avoiding the need for inpatient investigation.	

Table 11: Borg 2003 (NCGC reference 42)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
H. Borg, H. J. Arnqvist, E. Bjork, J. Bolinder, J. W. Eriksson, L. Nystrom, J. O. Jeppsson, and G. Sundkvist. Evaluation of the new ADA and WHO criteria for classification of diabetes mellitus in young adult people (15-34 years) in the Diabetes Incidence Study in Sweden (DISS). Diabetologia 46 (2):173-181, 2003. REF ID: Borg 2003	Observational: Cohort Registry, Sweden	Total N= 422 T1D & T2D – N=285 T1D, N=81 T2D (mixture of young people and adults) Inclusion criteria: Patients aged 15-34 at diagnosis Exclusion criteria: None stated	Young people and adults Diabetes type: T1D (n=285) T2D (n=81) Unclassified (n=85)	T1D & T2D: ICA GADA GADA+ index IA-2A IA-2A index Any antibody + 3 Ab 2 Ab ICA & GADA ICA & IA-2A 1 Ab ICA GADA IA-2A C-PEPTIDE Cut-offs for positivity C-PEPTIDE+: 0.10 nmol/L ICA512/IA-2+: Index* of IA-2A: Index* of 1.0 GADA+: Index* of 4.6 ICA+: >4 JDF units *INDEX = sample cpm	1 year	T1D (N=285) ICA N (%) = 143 (54)	Funding: Juvenile diabetes foundation-Wallenberg Diabetes research program, Lundstrom foundation, Novo-Nordisk foundation, Research funds of Malmo universityhospital, faculty of medicine at Lund university, Albert Pahlson Foundation, Swedish Diabetes association Risk of bias: n/a
			GADA GADA+ index IA-2A			206 (77) 53 (78) 123 (46)	
			IA-2A index Any antibody +			91 (90) 220 (83)	
			3 Ab 2 Ab ICA & GADA ICA & IA-2A			89 (40) 74 (34) 47 (21) 6 (3)	
			GADA & IA-2A 1 Ab ICA GADA IA-2A			21 (10) 57 (26) 1 (0.5) 49 (22) 7 (3)	
			T2D (N=81) ICA GADA GADA+ index			12 (15) 16 (21) 72 (85)	

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
				– negative control cpm /positive control cpm -negative control cpm		IA-2A 12 (15)	
						IA-2A index 94 (101)	
						Any antibody + 18 (23)	
						3 Ab 7 (39)	
						2 Ab 8 (44)	
						ICA & GADA 3 (17)	
						ICA & IA-2A 2 (11)	
						GADA & IA-2A 3 (17)	
						1 Ab 3 (17)	
						ICA 0	
						GADA 3 (17)	
						IA-2A 0	
						P-C-PEPTIDE: Carried out in patients that were tested for C peptide within 1 week after diagnosis At diagnosis: Undetectable (<0.10 nmol/L): Ab+: 30/123 (24.4%) Ab-: 1/36 (2.8) Low (<0.25 nmol/L) Ab+: 72/123 (58.5) Ab-: 2/36 (5.6) Follow up: Undetectable (<0.10 nmol/L): Ab+: 13/123 (10.6) Ab-: 3/36 (8.3) Along all Ab- patients, 13/93 had low fasting P-C Peptide (0.25 nmol/L) and 12/13 had T1D	

Table 12: Brunova 2002 (NCGC reference 28)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
J. Brunova, J. Bruna, M. Koning, M. Meyer, G. Joubert, and W. Mollentze. GAD65Ab and primary hypothyroidism in type 1 and 2 diabetic subjects.	Observational: cross-sectional study Single centre, South Africa	Total N=192 (N=55 T1D and N=137 T2D) Inclusion criteria: Clinical Diagnosis of T1D and T2D Exclusion criteria: None reported	Adults and young people Diabetes type: T2D T1D T1D N=55; T2D N=137 Age, years, (range) 13 – 85 years M/F % 50/50	T1D: GAD65 T2D: fC-PEPTIDE GAD65 Cut-offs for positivity fC-PEPTIDE+: not given GAD65+: not given	n/a	T1D (N=55) GAD65+ 17/55 (30.9%) T2D (N=137) GAD65+ 9/137 (6.6%) fC-PEPTIDE in GAD-patients, pmol/L (SD) 637.6 (503) fC-PEPTIDE in GAD-patients, pmol/L (SD) 1168.1 (732) The presence of GAD65 in T2D was	Funding: Not reported Risk of bias: n/a

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
J.Endocrinol.M etab.Diabetes S.Afr. 7 (1):6-8, 2002. REFID: Brunova 2002						associated with lower levels of fC-PEPTIDE	

Table 13: Laadhar 2007 (reference 30)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments	
L. Laadhar, M. Zitouni, M. Kallel-Sellami, R. Bouguerra, H. Chaabouni, and S. Makni. Spectrum of autoantibodies in Tunisian adult type 1 diabetes mellitus. Ann.N.Y.Acad. Sci. 1107:356-362, 2007. REFID: Laadhar 2007	Observational: cross-sectional study Single centre, Tunisia	Total N=261 T1D Inclusion criteria: Clinical diagnosis of T1D Exclusion criteria: None reported	Adults and young people Diabetes type: T1D	T1D: fC-PEPTIDE	n/a	T1D (N=261) ICA+ 88 (33.7%) ICA+ in patients <1yr Diabetes 47.7%	Funding: Not reported Risk of bias: n/a	
			T1D N=261	Cut-offs for positivity ICA+: not given				
			Age, years, mean (SD; range)					29.1 (1.9; 16-60)
			Age at Diagnosis, years, mean (SD)					20.3 (10.3)
M/F %	48/52							

Table 14: Lu 2014 (NCGC reference 321)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes (baseline)	Comments
H Lu, F Hu, Y Zeng, L Zou, S Luo, Y Sun, H Liu, and L Sun. Ketosis onset type 2 diabetes	Observational: cross-sectionals tudy	N=140 Inclusion criteria: Newly diagnosed T2D Without islet-associated	Adults and young people Diabetes type: T2D	T2D: Fasting C-PEPTIDE	n/a	T2D adults and young people	Funding: Not reported Risk of bias: n/a
						f-C-PEP, pmol/L (SD)	

<p>had better islet beta-cell function and more serious insulin resistance. J Diabetes Res 2014:510643, 2014.</p> <p>REF ID: Lu 2014</p>	<p>China</p>	<p>autoantibodies</p> <p>Age 16-68 years</p> <p>Diagnosis: WHO criteria</p> <p>If had Plasma glucose >250 mg/ml and positive urine ketone body = diabetic ketosis</p> <p>Diagnosis.</p> <p>Exclusion criteria:</p> <p>Evidence of other disease</p> <p>Taking agents known to affect CHO metabolism</p> <p>Obvious precipitating causes for the development of ketosis</p>				<p>Cut-offs for positivity</p> <p>AUC</p>					
				Ketosis onset T2D N=62	Nonketotic onset T2D N=78						
			Age, years mean	44.8	47.0						
			M/F %	66	72						
			BMI, mean	25.0	24.4						
			HbA1c	11.0%	11.8%						
			Drop-outs / missing data: none								
<p>T1D patients vs. LADA: T1D were younger, lower age of onset. NS difference in number of patients with high GAD titer.</p>											

Table 15: McDonald 2011 (NCGC reference 85)

Reference	Study type	Number of patients	Patient characteristics			Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes		Comments
<p>T.McDonald, K. Colclough, R. Brown, B. Shields, M. Shepherd, P. Bingley, A. Williams, A. Hattersley, and Sian Ellard. Islet autoantibodies can discriminate maturity-onset diabetes of the young (MODY) from Type 1 diabetes. Diabet.Med. 28 (9):1028-1033, 2011.</p> <p>REF ID: McDonald 2011</p>	<p>Observational: cross-sectional study</p> <p>UK study</p>	<p>Total N=616</p> <p>N=98 T1D – adults and young people</p> <p>N=508 MODY – but adults only</p> <p>Inclusion criteria:</p> <p>Clinical history of diabetes</p> <p>HbA1c <6.0%</p> <p>MODY Diagnosis by genetic testing</p> <p>T1D Diagnosis in last 6 mths</p> <p>Exclusion criteria: None given</p>	<p>Adults and young people</p> <p>Diabetes type:</p> <p>T1D</p> <p>MODY</p>			<p>T1D: GAD IA-2</p> <p>MODY: GAD IA-2</p> <p>Cut-offs for positivity</p> <p>GAD+: 64 WHO units/ml (99th percentile)</p> <p>IA-2+: 15 WHO units/ml (99th percentile; lowest calibrator)</p>	<p>n/a</p>	<p>T1D</p>		<p>Funding: None reported</p> <p>Risk of bias: n/a</p>
				T1D N=98	MODY N=508					
			Age, years, median (IQR)	15 (12-25)	36 (18-50)					
			Duration of diabetes, years, median (IQR)	< 6 months	9 (4-25)					
						<p>GAD+ 24/98 (24.5%)</p> <p>IA-2+ 19/98 (94.5%)</p>				
						<p>GAD+ and/or IA-2)+ 80/98 (82%)</p> <p>GAD+ and IA-2+ 37/98 (37.8%)</p> <p>MODY</p>				
						<p>GAD+ 5 (1%)</p> <p>IA-2+ 0 (0%)</p> <p>GAD+ and/or IA-2+ 5/508 (1%)</p>				

Table 16: Oram 2014 (NCGC reference 316)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments														
R. A. Oram, A. G. Jones, R. E. J. Besser, B. A. Knight, B. M. Shields, R. J. Brown, A. T. Hattersley, and T. J. McDonald. The majority of patients with long-duration type 1 diabetes are insulin microsecretors and have functioning beta cells. <i>Diabetologia</i> 57 (1):187-191, 2014. REF ID: Oram 2014	Observational: cross-sectional UK	N=74 adults and young people Inclusion criteria: T1D for >5 years Diagnosis at either <30 years age (n=68) or >30 years age with islet autoAbs present (n=6) All patients on insulin since Diagnosis. Exclusion criteria: None given	Adults and young people diabetes type: T1D	T1D: UCPCR (urinary c-peptide:creatinine ratio) Fasting C-pep Stim C-pep Cut-offs for positivity C-PEPTIDE: 3.3 pmol/L	Baseline	T1D adults and young people	Funding: Diabetes UK, and NIHR. Risk of bias: n/a														
			<table border="1"> <tr> <td>T1D all</td> <td>N=74</td> </tr> <tr> <td>Age at Diagnosis, median (IQR)</td> <td>16 (9-23) years</td> </tr> <tr> <td>Male</td> <td>51%</td> </tr> <tr> <td>Duration of diabetes, median (IQR)</td> <td>30 (19-41) years</td> </tr> <tr> <td>BMI, median (IQR)</td> <td>25 (23 – 28) kg/m²</td> </tr> <tr> <td>HbA1c, median (IQR)</td> <td>7.9 (7.2 – 9.0) kg/m²</td> </tr> </table>			T1D all		N=74	Age at Diagnosis, median (IQR)	16 (9-23) years	Male	51%	Duration of diabetes, median (IQR)	30 (19-41) years	BMI, median (IQR)	25 (23 – 28) kg/m ²	HbA1c, median (IQR)	7.9 (7.2 – 9.0) kg/m ²	<table border="1"> <tr> <td>Fasting C-Peptide</td> <td>73%</td> </tr> <tr> <td>Non-fasting C-Peptide</td> <td>66%</td> </tr> <tr> <td>Fasting UCPCR</td> <td>68%</td> </tr> <tr> <td>Non-fasting UCPCR</td> <td>68%</td> </tr> </table> <p>C-peptide titres are compared using different assays; results not been extracted for this review as do not know which is the best (in terms of Diagnosis accuracy) assay method to us</p>	Fasting C-Peptide	73%
T1D all	N=74																				
Age at Diagnosis, median (IQR)	16 (9-23) years																				
Male	51%																				
Duration of diabetes, median (IQR)	30 (19-41) years																				
BMI, median (IQR)	25 (23 – 28) kg/m ²																				
HbA1c, median (IQR)	7.9 (7.2 – 9.0) kg/m ²																				
Fasting C-Peptide	73%																				
Non-fasting C-Peptide	66%																				
Fasting UCPCR	68%																				
Non-fasting UCPCR	68%																				

Table 17: Ota 2005 (NCGC reference 126)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments																					
T Ota, T Takamura, Y Nagai, Y Bando, and R Usuda. Significance of IA-2 antibody in Japanese type 1 diabetes: its association with GAD antibody. <i>Diabetes Res.Clin.Pract.</i>	Observational: cross-sectional study	Total N=101 T1D Inclusion criteria: T1D classified by American diabetes association Exclusion criteria: None reported	ADULTS AND YOUNG PEOPLE DIABETES TYPE: T1D	T1D: C-PEPTIDE GADA65 IA-2A Cut-offs for positivity ICA512/IA-2: 0.4 U/mL GAD65+: 1.3 U/mL	n/a	T1D (N=101)	Funding: Not reported																					
			<table border="1"> <tr> <td>T1D N=101</td> <td></td> </tr> <tr> <td>Age, years, mean (range; SD)</td> <td>41.3 (14.0-89.0; 15.3)</td> </tr> <tr> <td>Duration of diabetes, years, mean (SD)</td> <td>10.4 (9.6)</td> </tr> <tr> <td>M/F %</td> <td>47/54</td> </tr> </table>			T1D N=101			Age, years, mean (range; SD)	41.3 (14.0-89.0; 15.3)	Duration of diabetes, years, mean (SD)	10.4 (9.6)	M/F %	47/54	<table border="1"> <tr> <td>GAD65+</td> <td>N=60/101 (59%)</td> </tr> <tr> <td>IA-2+</td> <td>37/101 (37)</td> </tr> <tr> <td>IA-2+/ GAD65-</td> <td>10 (10)</td> </tr> <tr> <td>GAD65+/ IA-2+</td> <td>27 (27)</td> </tr> <tr> <td>GAD65+/IA-2-</td> <td>33 (32)</td> </tr> </table> <p>Acute onset T1D (N=64)</p> <table border="1"> <tr> <td>IA-2 Ab+: GAD Ab conc (U/mL)</td> <td>N=19</td> </tr> <tr> <td>Mean (SD)</td> <td>67.7 (97.2)</td> </tr> </table> <table border="1"> <tr> <td>IA-2 Ab-: GAD Ab conc (U/mL)</td> <td>N=45</td> </tr> <tr> <td></td> <td>31.1 (132.1)</td> </tr> </table>	GAD65+	N=60/101 (59%)	IA-2+	37/101 (37)	IA-2+/ GAD65-	10 (10)	GAD65+/ IA-2+	27 (27)	GAD65+/IA-2-	33 (32)	IA-2 Ab+: GAD Ab conc (U/mL)	N=19	Mean (SD)
T1D N=101																												
Age, years, mean (range; SD)	41.3 (14.0-89.0; 15.3)																											
Duration of diabetes, years, mean (SD)	10.4 (9.6)																											
M/F %	47/54																											
GAD65+	N=60/101 (59%)																											
IA-2+	37/101 (37)																											
IA-2+/ GAD65-	10 (10)																											
GAD65+/ IA-2+	27 (27)																											
GAD65+/IA-2-	33 (32)																											
IA-2 Ab+: GAD Ab conc (U/mL)	N=19																											
Mean (SD)	67.7 (97.2)																											
IA-2 Ab-: GAD Ab conc (U/mL)	N=45																											
	31.1 (132.1)																											

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
67 (1):63-69, 2005. REF ID: Ota 2005						GAD+: IA-2 Ab conc (U/mL) N=28 1.8 (3.0) GAD-: IA-2 Ab conc (U/mL) N=36 1.0 (2.4)	

Table 18: Rajalakshmi (NCGC reference 322)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments			
R Rajalakshmi, A Amutha, Harish Ranjani, Mohammed K. Ali, Ranjit Unnikrishnan, Ranjit Mohan Anjana, K. M. V. Narayan, and Viswanathan Mohan. Prevalence and risk factors for diabetic retinopathy in Asian Indians with young onset type 1 and type 2 diabetes. J.Diabetes Complications 28 (3):291-297, 2014. REF ID: Rajalshmi 2014	Observational:cross-sectional study India	N=300 T1D and T2D (N=150 of each) Inclusion criteria: Diagnosis between ages 10 and 25 years Duration of diabetes >2 years Diagnosis: FPG ≥126 mg/dl, and/or 2hr post-load glc level ≥200 mg/dl, or self-reported diabetes treated by a physician or on hypoglyc. Medications or insulin. T1D Diagnosis: accompanied by abrupt onset of symptoms like polyuria, polydipsia, or unexplained wt loss, DKA, absent insulin reserve, requirement of insulin from time of Diagnosis for control of hyperglycaemia. T2D Diagnosis: absence of ketosis, good B-cell functional reserve, absence of pancreatic calculi, and good response to oral hypoglyc. Agents for >2 years. Exclusion criteria: None reported.	Adults and young people Diabetes type: T1D, T2D	T1D and T2D: Fast C-peptide Stimulated C-peptide Cut-offs for positivity Not reported	n/a	T1D adults and young people	Funding: Global diabetes research centre. Risk of bias: n/a no missing data			
			Adults and young people:			Fasting C-peptide, pmol/ml		0.29		
			T1D (n=150)			T2D (n=150)		Stimulated C-peptide, pmol/ml	0.32	
			Age			28		33	T2D adults and young people	
			Male			54%		62%	Fasting C-peptide, pmol/ml	0.79
			Diabetes duration, years			12		12	Stimulated C-peptide, pmol/ml	1.60
			Drop-outs / missing data: none							

Table 19: Samuelsson 2013 (NCGC reference 317)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
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Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments	
U. Samuelsson, B. Lindblad, A. Carlsson, G. Forsander, S. Ivarsson, I. Kockum, A. Lernmark, C. Marcus, J. Ludvigsson, and Better Diabetes Diagnosis study group. Residual beta cell function at diagnosis of type 1 diabetes in children and adolescents varies with gender and season. Diabetes.Metab.Res .Rev. 29 (1):85-89, 2013. REF ID: Samuelsson 2013	Observational: cross-sectional Sweden:4 3 centres	N=979 young people aged 11-18 years Total N=3824 T1D young people and children 0-18 years Inclusion criteria: T1D (ADA criteria) Swedish Better Diabetes Diagnosis, BDD register Exclusion criteria: None given	Young people subgroup (age 11-18 years) Diabetes type: T1D	T1D: Non-fasting C-Peptide	Baseline	T1D young people (11-18 years) Non-fasting C-Peptide, nmol/L (SD) 0.34 (0.28)	Funding: Swedish Child Diabetes Foundation. Risk of bias: n/a	
				T1D all N=3165				Cut-offs for positivity Non-fasting C-PEPTIDE: 0.03 nmol/L
			Age range	0 – 18 years; mean of separated boys and girls = 9.8years				
			Male	N=1913				

Table 20: Scholin 2004a (NCGC reference 144)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments	
Anna Scholin, Agneta Siegbahn, Lars Lind, Christian Berne, Goran Sundkvist, Elisabeth Bjork, F. Anders Karlsson, and Diabetes Incidence Study in Sweden group. CRP and IL-6 concentrations are associated with poor glycemic control despite preserved beta-cell function during the first year after diagnosis of type 1	Observational study: Diabetic incidence in Sweden study.	Total N= 100 T1D . N=3ter excluded as pregnant. Inclusion criteria: Not pregnant. Exclusion criteria: None reported	Adult (15-34 years) Diabetes type: T1D	T1D: C-peptide ICA+ GADA+ IA-2A+	12 months	Assays divided into islet antibody positive (ab+) and negative (ab-) Ab+ (N=78) C peptide (nmol/l) 0.25 (0.04-1.4) ICA+ 58/78 (74%) GADA+ 69/78 (88%) IA-2A+ 55/78 (70%) Ab- (N=19 : 19.7%) C peptide (nmol/l) 0.34 (0.08-1.41) Total population (I have added Ab+ and Ab-) ICA+ 58/97 (59.8%) GADA+ 69/97 (71.1%) IA-2A+ 55/97 (56.7%) C-peptide – 0.25 + 0.34 /2 =	Funding: Supported by Grant from the Swedish Research Council, the Swedish Heart Lung Foundation, the Swedish Diabetes Association, the family Ernfors Fund, and the Juvenile Diabetes Foundation	
			Age of T1D patients (n=97) at diagnosis	Cut-offs for positivity C-peptide: reference interval for fasting plasma concentration was 0.25 to 0.75 nmol/L GADA index: >4.6 u/ml IA-2A index: >1.0 ICA: Not reported				
			All (n = 97)					

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
diabetes. Diabetes.Metab.Res.Rev. 20 (3):205-210, 2004. REF ID: Scholin 2004A			Age (years) 28.1 (15.3-34.8)			mean of Ab+ and Ab- (nmol/l) 0.295	International and Knut and Alice Wallenberg Foundation.

Table 21: Scholin 2004b (NCGC reference 112)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
A. Scholin, C. Torn, L. Nystrom, C. Berne, H. Arnqvist, G. Blohme, J. Bolinder, J. W. Eriksson, I. Kockum, M. Landin-Olsson, J. Ostman, F. A. Karlsson, G. Sundkvist, and E. Bjork. Normal weight promotes remission and low number of islet antibodies prolong the duration of remission in Type 1 diabetes. Diabet.Med. 21 (5):447-455, 2004. REF ID: Scholin 2004B	Observational: prospective cohort	Total N=362 T1D Inclusion criteria: People with T1D Aged 15-34 years Clinically classified as T1D according to WHO criteria Exclusion criteria: None reported	Adults and young people Diabetes type: T1D T1D N=362 Age, years, mean (range; SD) 24.7 (5.6) Duration of diabetes, years, mean (SD) M/F % 242/120	T1D: C-PEPTIDE GADA ICA IA-2 IAA Cut-offs for positivity C-PEPTIDE+: 0.25 nmol/L ICA512/IA-2+: Index* of 0.05 GAD65+: Index* of 0.07 ICA+: >5 JDF units IAA: 0.7% *INDEX = sample cpm – negative control cpm /positive control cpm - negative control cpm	n/a	T1D - All cases (N=362) P-C-PEPTIDE+ (nmol/L) 0.27 (0.10, 2.13) Median (range) ICA+ 213/346 (62%) IA-2A+ 162/345 (47%) GADA+ 229/346 (66%) IAA+ 58/248 (23%) T1D Ab+ (n=307) P-C-PEPTIDE+ (nmol/L) 0.26 (0.10, 2.13) Median (range) ICA+ 213/295 (72%) IA-2A+ 162/294 (55%) GADA+ 229/295 (78%) IAA+ 58/215 (27%) T1D Ab- (n=53) P-C-PEPTIDE+ (nmol/L) 0.38 (0.10, 1.63) Median (range)	Funding: Juvenile diabetes foundation-Wallenberg Diabetes research program, Swedish Diabetes association, swedish society of medicine, Agnes & Mac Rudbergs foundation Risk of bias: n/a

Table 22: Scholin 2004c (NCGC reference 69)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
A. Scholin, L. Bjorklund, H. Borg, H. Arnqvist, E. Bjork,	Observational:	Total N=312 (patients with blood samples at	Adults and young people Diabetes type: T1D	T1D: C-PEPTIDE GADA	8 years	T1D Baseline (N=312) ICA+ N=199/312 (64%) GADA 235/311 (76)	Funding: Juvenile diabetes

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
G. Blohme, J. Bolinder, JW. Eriksson, S. Gudbjornsdottir, L. Nystrom et al., and Diabetes Inc. Islet antibodies and remaining beta-cell function 8 years after diagnosis of diabetes in young adults: a prospective follow-up of the nationwide Diabetes Incidence Study in Sweden. J.Intern.Med. 255 (3):384-391, 2004. REF ID: SCHOLIN 2004C		diagnosis and follow up) - N=254 T1D, N=30 T2D Inclusion criteria: Aged 15-34 years Diagnosed* with diabetes between 1987-1988 Exclusion criteria: None reported *diagnosis based on clinical judgement as reported by diagnosing clinician to DISS registry	T2D T1D Age, years, mean (range; SD) 24.8 (9.5) M/F % 182 (58%)/130 (42%) T1D 254 (81) T2D 30 (10) Unclassifiable 27 (9) Secondary 1 (0)	ICA IA-2 ICA & IA-2A ICA & GADA GADA & IA-2A Cut-offs for positivity P-C-PEPTIDE+: <0.1 nmol/L ICA512/IA-2+: Index* of >1 GAD65+: Index* of >4.6 *INDEX = sample cpm – negative control cpm /positive control cpm - negative control cpm		IA-2A+ 143/311 (46) T1D: follow up (n=312) ICA+ 73/309 (24%) GADA 200/309 (65%) IA-2A+ 106/310 (34%) C-peptide at baseline ≥0.1 nmol/L: T1D: 25/42 (60%) T2D: 8/42 (21%) <0.1 nmol/L: T1D: 204/227 (90%) T2D: 10/227 (4%) C peptide at follow up ≥0.1 nmol/L: T1D: 31/42 (76) T2D: 8/42 (20) <0.1 nmol/L: T1D: 208/227 (95) T2D: 7/227 (3)	foundation and Wallenberg diabetes research program, Lundstrom foundation, Novo-nordisk foundation, Albert Palson foundation, Swedish diabetes association, childrens diabetes fund, Swedish medical research council Risk of bias: n/a

Table 23: Scholin 2011 (NCGC reference 93)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
A. Scholin, L. Nystrom, H. Arnqvist, J. Bolinder, E. Bjork, C. Berne, F. A. Karlsson, and Diabetes Incidence Study Group. Proinsulin/C-peptide ratio, glucagon and remission in new-onset Type 1 diabetes mellitus in young adults. Diabet.Med.	Observational: cross-sectional study and prospective Swedish study	Total recruited: N=203 N=78 T1D (had complete data at all the time-points and were confirmed T1D) Inclusion criteria: T1D Age 15-34 years In the nationwide Diabetes Study in Sweden (DISS) T1D defined as islet-cell Ab+ and/or need for insulin Tx at Diagnosis) Blood samples taken	Adults and young people Diabetes type: T1D T1D N=78 Age, years, mean (SD; range) 26.2 (6.0) M/F % 60/40 Islet Ab+, % 86%	T1D: fC-PEPTIDE Cut-offs for positivity fC-PEPTIDE+: not given	3 years follow-up post Diagnosis.	T1D (N=78) FC-peptide over time: mths after Diagnosis nmol/L MEDIAN (min-max) Baseline 0.24 (0.04-1.4) 3 0.26 (0.04-1.8) 6 0.31 (0.04-1.3) 9 0.27 (0-1.9) 12 0.27 (0-1.6) 15 0.19 (0-1.7) 18 0.17 (0-1.1) 24 0.16 (0-1.5) 30 0.12 (0.04-1.3) 36 0.19 (0.02-1.8)	Funding: Not reported Risk of bias: n/a

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
28 (2):156-161, 2011. REFID: Scholin 2011		Exclusion criteria: Pregnant T2D					

Table 24: Tridgell 2011 (NCGC reference 46)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
DM. Tridgell, C Spiekerman, Richard S. Wang, and Carla J. Greenbaum. Interaction of onset and duration of diabetes on the percent of gad and ia-2 antibody-positive subjects in the type 1 diabetes genetics consortium database. Diabetes Care 34 (4):988-993, 2011. REF ID: Tridgell 2011	Observational: cross-sectional study	Total N= 5,020 T1D	Adults and young people	T1D: GADA IA-2A GADA and/or IA-2A	n/a	T1D: onset aged 2-7 (N=1,739) -univariate analyses	Funding: T1D Genetics consortium, National institute of diabetes and digestive and kidney diseases, juvenile diabetes research foundation
		Inclusion criteria: Diagnosed with T1D before aged 35 years Treated with insulin within 6 months of diagnosis without subsequent discontinuation of insulin treatment Families with at least 2 non-monozygotic siblings with T1D and families where there was a single affected child from a population with a low prevalence of T1D	Diabetes type: T1D	Cut-offs for positivity		GADA+ 35.7%	
		Exclusion criteria: None reported		GAD65+: NR		IA-2+ 43.1%	
				ICA+: NR		T1D: onset aged 8-13 years (N=1,767) -univariate analyses	
						GADA+ 47.6%	
						IA-2+ 53.1%	
						T1D: onset aged ≥14 years (N=1,514) -univariate analyses	
						GADA+ 58.9%	
						IA-2+ 40.6%	
						T1D: duration 0-5 yr- univariate analyses	
			GADA+ 58.6%				
			IA-2+ 60.4%				
			T1D: duration 6-13 yr- univariate analyses (referent group 0-5 years duration)				
			GADA+ 44.8%				
			IA-2+ 47.2%				
			T1D: duration ≥14 yr- univariate analyses (referent group 0-5 years duration)				
			GADA+ 35.6%				
			IA-2+ 28.3%				
			T1D: duration 0-5 yr- multivariate analyses				
			GADA+ 70.5%				
							Risk of bias: n/a

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments
						IA-2A+ 53.4%	
						GADA+ and/orIA-2A+ 82.2%	
						T1D: duration 6-13 yr-multivariate analyses	
						GADA+ 65.3%	
						IA-2A+ 42.7%	
						GADA+ and/orIA-2A+ 73.8%	
						T1D: duration ≥14 yr-multivariate analyses	
						GADA+ 42.5%	
						IA-2A+ 26.2%	
						GADA+ and/orIA-2A+ 53.4%	

Table 25: Vermeulen 2011 (NCGC reference 250)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments	
I. Vermeulen, I. Weets, M. Asanghanwa, J. Ruige, Gaal L. Van, C. Mathieu, B. Keymeulen, V. Lampasona, J. M. Wenzlau, J. C. Hutton, D. G. Pipeleers, and F. K. Goris. Contribution of antibodies against IA-2beta and zinc transporter 8 to classification of diabetes diagnosed under 40 years of age. Diabetes Care 34 (8):1760-1765, 2011. REF ID:	Observational: Case-control study Registry, Belgium	Total N= 665 T1D (n=170 aged 0-9 years; n=223 aged 10-19 years; n=149 aged 20-29 years; n=113 aged 30-39 years) Inclusion criteria: Diagnosis with diabetes before age 40 Physician Diagnosis of T1D on clinical grounds and treated with insulin with 7 days after Diagnosis Blood sampled within 7 days after Tx started CONTROLS: sex-matched non-diabetic controls aged 0-39 years. None had relatives with T1D.	Young people and adults (data separated for some age-groups and markers) DIABETES TYPE: T1D	T1D IA-2A IA-2βA ZnT8 IAA GADA Combinations	1 year	T1D Adults aged 20-29 (N=149)	Funding: Juvenile diabetes Research F, EU and Belgian fund for Scientific Research Risk of bias: n/a	
								MARKER N (%)
								IA-2βA 47 (32)
								ZnT8 76 (51)
								T1D ADULTS aged 30-39 (N=113)
								MARKER N (%)
								IA-2βA 21 (19)
								ZnT8 44 (39)
								T1D Young people aged 10-19 (N=223)
								MARKER N (%)
			IA-2βA 105 (47)					
			ZnT8 152 (68)					
			≥1 Ab+ (GADA, IA-2A or IAA) 207 (93)					
			≥1 Ab+ (GADA, IA-2A or ZnT8) 209 (94)					

Vermeulen 2011		Exclusion criteria: None stated				GADA+: ≥2.6% tracer binding	ZnT8+: Age 0-14 years = ≥1.28% tracer binding Age 15-39 years = ≥1.02% tracer binding	≥2 Ab+ (GADA, IA-2A and/or IAA)	154 (69)	
								≥2 Ab+ (GADA, IA-2A and/or ZnT8)	162 (73)	
								T1D ADULTS aged 20-39 (N=262)		
								≥1 Ab+ (GADA, IA-2A or IAA)	207 (79)	
								≥1 Ab+ (GADA, IA-2A or ZnT8)	206 (79)	
								≥2 Ab+ (GADA, IA-2A and/or IAA)	129 (49)	
								≥2 Ab+ (GADA, IA-2A and/or ZnT8)	139 (53)	
								Young people and adults: >age 15:		
								≥1 Ab+ (IAA, GADA and IA-2A)	82%	
								≥2 Ab+ (IAA, GADA or IA-2A)	51%	
								≥2 Ab+ (IA-2βA plus one of IAA, GADA or IA-2A)	56%	
								≥2 Ab+ (ZnT8 plus one of IAA, GADA or IA-2A)	63%	
								≥2 Ab+ (ZnT8 and IA-2βA plus one of IAA, GADA or IA-2A)	65%	
								The prevalence of IA-2βA and ZnT8 decreased with age at Diagnosis (esp after age 20 years).		

Table 26: Wenzlau 2010 (NCGC reference 55)

Reference	Study type	Number of patients	Patient characteristics	Diagnostic markers assessed	Length of follow-up	Outcome measure and effect sizes	Comments	
J. M. Wenzlau, M. Walter, T. J. Gardner, L. M. Frisch, L. Yu, G. S. Eisenbarth, A. G. Ziegler, H. W. Davidson, and J. C. Hutton. Kinetics of the post-onset decline in zinc	Observational: cross-sectional study	Total N=506 Inclusion criteria: New onset patients within 6 weeks of diagnosis T1D new onset	Adults and young people Diabetes type: T1D	T1D: C-PEPTIDE ZnT8 GADA IA-2 Cut-offs for positivity	Group 1: 2.5 years Group 2: 7 years Group 3: 3-10.9 years	Group 1: New onset diabetes (n=21) baseline	Funding: Childhood diabetes foundation, Denver; university of Colorado health sciences centre diabetes endocrinology research centre	
						ZnT8A+		85.7%
						GADA+		95.2%
						IA-2A+		90.5%
C Peptide+	100%							
Group 1: New onset diabetes (n=21) 2.5 years follow up	ZnT8A+	76.2%						
	Age,	1	2	3				
		(n=21)	(n=61)	(n=424)				
		20.3	9.8	11.4				

Diagnosis and management of type 1 diabetes in children and young people

Appendix I: Evidence tables

transporter 8 autoantibodies in type 1 diabetic human subjects. J.Clin.Endocrinol .Metab. 95 (10):4712-4719, 2010.	patients (4 years duration) Patients with longstanding diabetes (>20 years)	years, median (SD; range)	(6.2; 12.2-34.6)	(5.2; 1.6-36.7)	(7.6; 0.5-52.7)	C-PEPTIDE+.:3 pmol/mL ZnT8: index* of 0.015-0.020 ICA512/IA-2+: Index* of 0.032 GAD65+: Index* of 0.069	GADA+	85.7%	(NIH), juvenile diabetes research foundation autoimmunity prevention centre grant
REF ID: Wenzlau 2010	Exclusion criteria: None reported					*INDEX = sample cpm – negative control cpm /positive control cpm - negative control cpm	C Peptide+	5.7%	8
							Group 1: new onset diabetes at 12 years follow up (prevalence)		
							GAD+	11.5%	
							CWCR	3.3%	
							IA2+	4.9%	
							GAD/CWCR	4.9%	
							GAD/ IA2	6.6%	
							IA2 / CWCR	21.3%	
							GAD/CWCR/IA2	41%	
							Group 2: New onset T1D diabetes (n=61) Baseline		
							ZnT8A+	80.3%	
							GADA+	63.0%	
							IA-2A+	73.8%	
							C Peptide+	NR	
							Group 2: New onset T1D diabetes (n=61) 12 years follow up		
							ZnT8A+	42.6%	
							GADA+	32.4%	
							IA-2A+	47.5%	
							C Peptide+ (detected >0.02 pmol/mL)	27.6%	
							Group 2: patients with 4 years duration of T1D at 12 years follow up (prevalence)		
							GAD+	10.7%	
							CWCR	8.9%	
							IA2+	16.1%	
							GAD/CWCR	3.6%	
							GAD/ IA2	10.7%	
							IA2 / CWCR	19.6%	
							GAD/CWCR/IA2	20%	

										Group 3: Patients with longstanding diabetes(>20 years) (n=282)
										12 year follow up (prevalence)
										GAD+
										11.0%
										CWCR
										1.4%
										IA2+
										7.8%
										GAD/CWCR
										0.7%
										GAD/ IA2
										7.1%
										IA2 / CWCR
										2.1%
										GAD/CWCR/IA2
										2.5%

Appendix J: Forest plots

J.1 Original (2004) forest plots

J.1.1 Type 1 diabetes – insulin preparations

Figure I.1: HbA1c – all included studies providing HbA1c levels; HbA1c is significantly lower with rapid-acting analogues than regular insulin; eleven parallel group studies with a total of 4246 patients showed a significant decrease in HbA1c levels (WMD -0.14%, 95% CI -0.19 to -0.08%); twelve crossover studies with a total of 2441 patients showed no difference in HbA1c (WMD 0.00, 95% CI -0.09 to 0.08)

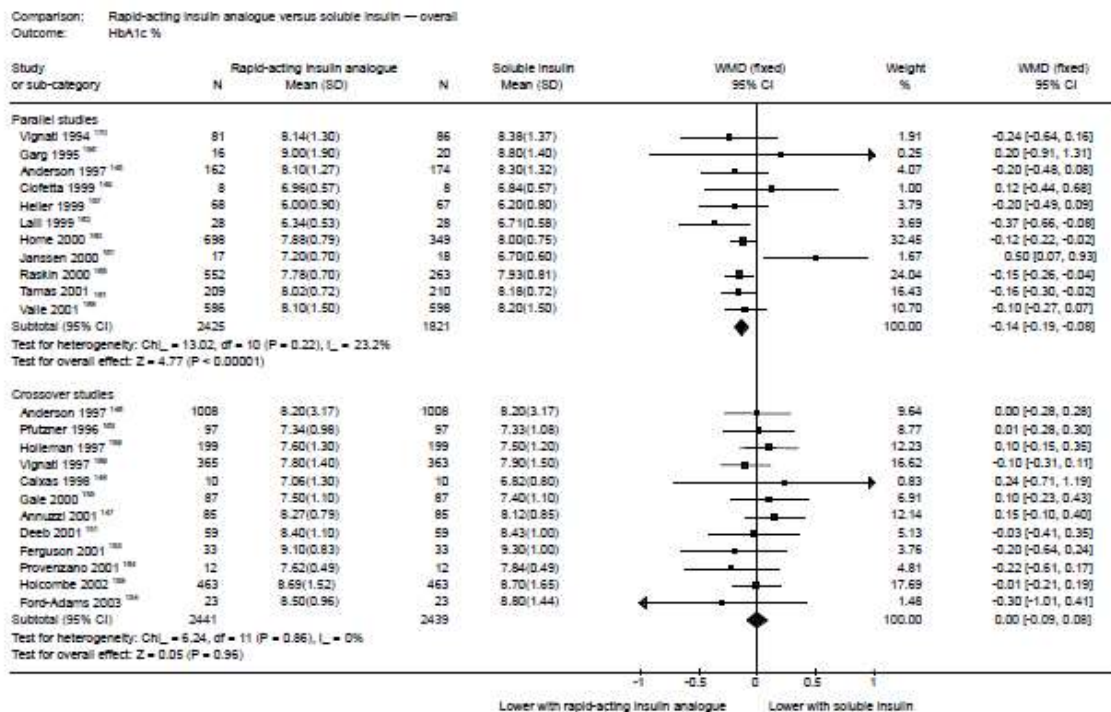


Figure I.2: HbA1c – studies separated into children/young people and adults; three studies with a total of 545 children and young people investigated HbA1c levels; the studies did not show a significant difference between rapid-acting analogues and regular insulin (WMD -0.03%, 95% CI -0.21 to 0.14%); nine studies with a total of 1896 adult patients did not show a significant difference between rapid-acting analogues and regular insulin (WMD 0.01%, 95% CI -0.09 to 0.11%)

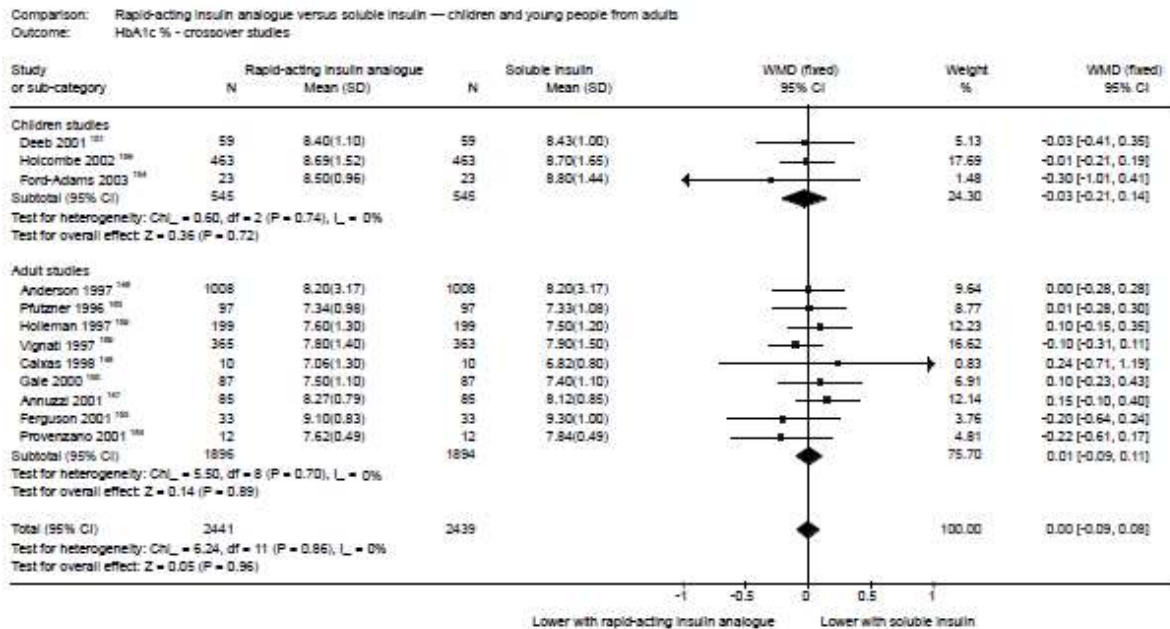


Figure I.3: HbA1c – studies separated into type of analogue (insulin aspart and insulin lispro); HbA1c was significantly lower with both types of rapid-acting analogue when compared with regular insulin (insulin aspart with a total of 2281 patients: WMD -0.14% 95% CI -0.20 to - 0.07%; insulin lispro with a total of 1965 patients: WMD -0.13%, 95% CI -0.24 to -0.02%); there was no significant difference in HbA1c reduction between studies using insulin aspart or insulin lispro

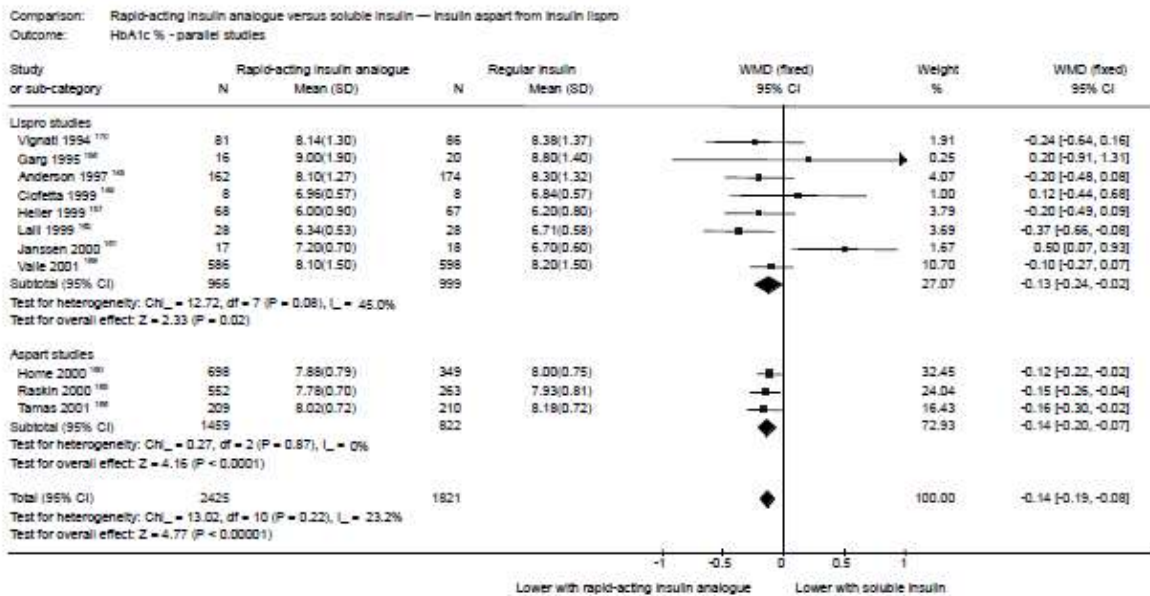


Figure I.4: Hypoglycaemic episodes/30 days; there was no significant difference between rapid-acting analogues and regular insulin regarding hypoglycaemic episodes

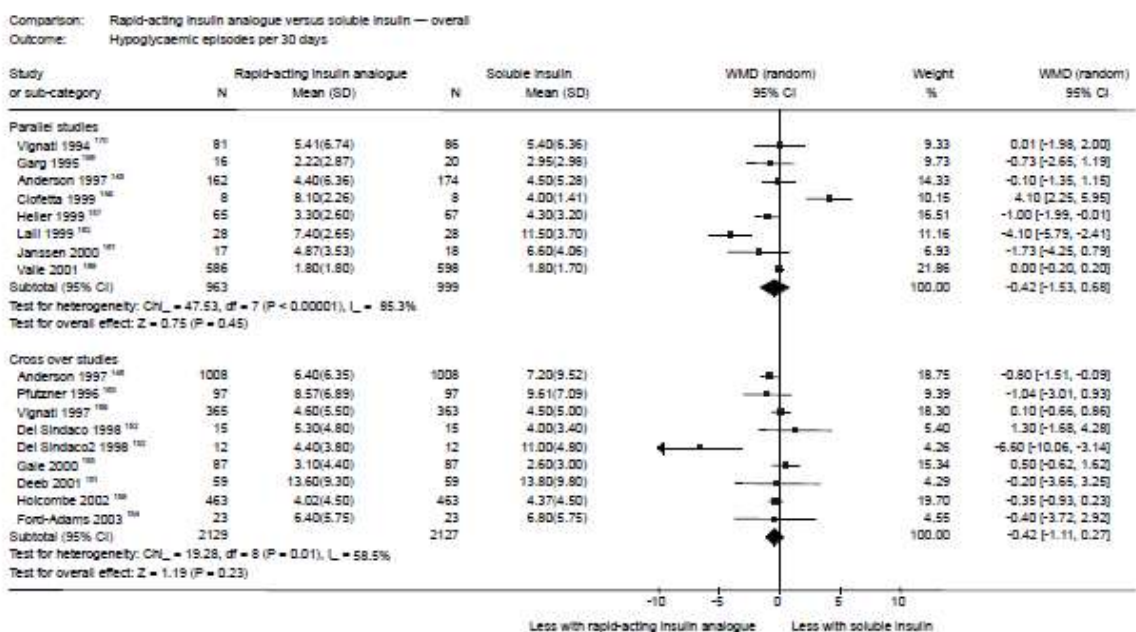


Figure I.5: Hypoglycaemic episodes/30 days with adults' and children's/young people's studies separated; there was no significant difference between rapid-acting analogues and regular insulin regarding hypoglycaemic episodes in either adults or children/young people; furthermore, there was no apparent difference between children/young people and adults in terms of the number of hypoglycaemic episodes/30 days

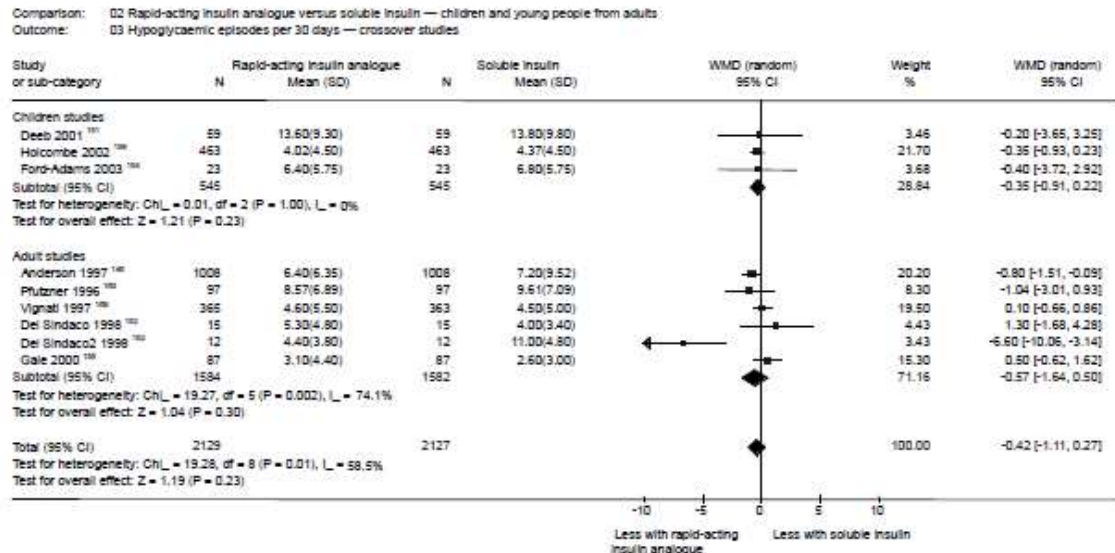


Figure I.6: Patient preference – patients preferred rapid-acting analogues to regular insulin; the overall estimate contained significant heterogeneity, which could be due to statistical and/or clinical reasons; these data should, therefore, be interpreted with caution

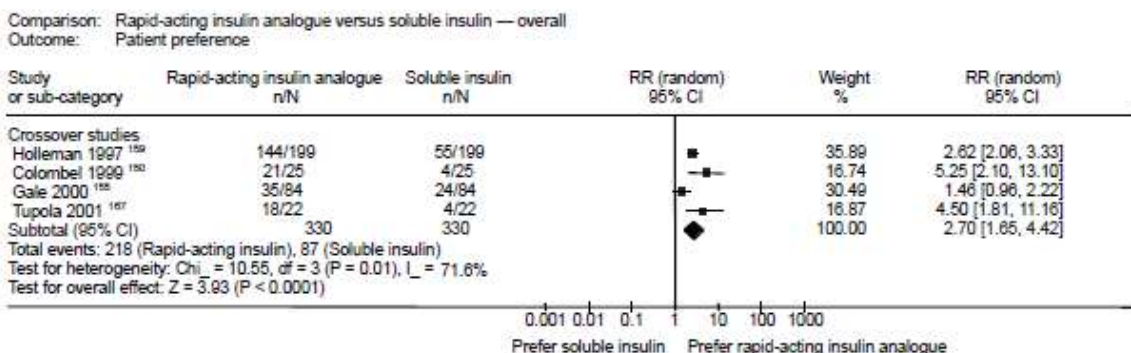
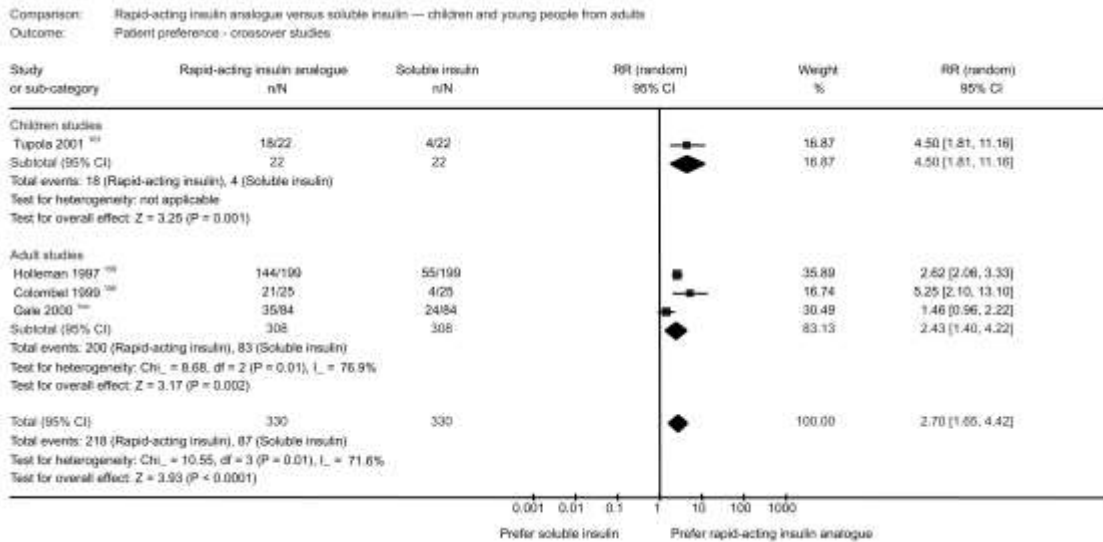
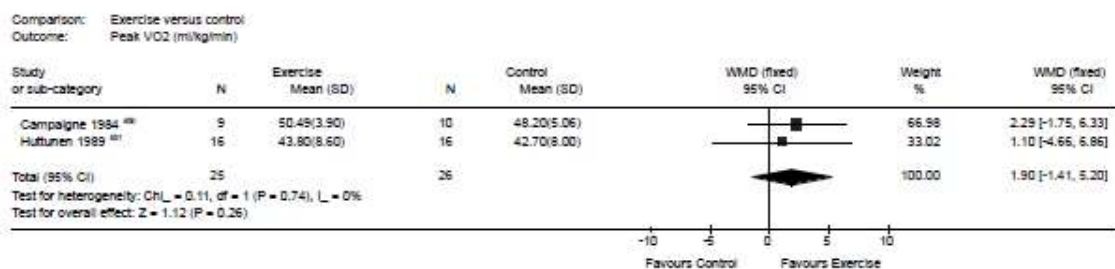


Figure I.7: Patient preference – separated according to children’s/young people’s and adults’ studies; both children/young people and adults preferred rapid-acting insulin analogue to regular insulin; the overall result was heterogeneous, and only one study contributed data for studies in children and young people; heterogeneity could be due to statistical and/or clinical reasons; these data should, therefore, be interpreted with caution



J.1.2 Type 1 diabetes – exercise

Figure I.8: Ideal frequency of exercise – exercising one to three times/week compared with control (no exercise)



J.2 2015 update forest plots

J.2.1 Diagnosis

Review question: What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?

The systematic review for this question was conducted by the guidance-producing centre for the guideline ‘Type 1 diabetes in adults’.

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.2 Type 1 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.3 Type 1 diabetes – behavioural interventions

Review question: What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.4 Type 1 diabetes – multiple daily injections

Review question: What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.5 Type 1 diabetes – HbA1c targets

Review question: What is the optimal haemoglobin A1c (HbA1c) target for children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.6 Type 1 diabetes – blood glucose targets

Review question: What are the optimal blood glucose targets for children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.7 Type 1 diabetes – blood glucose monitoring

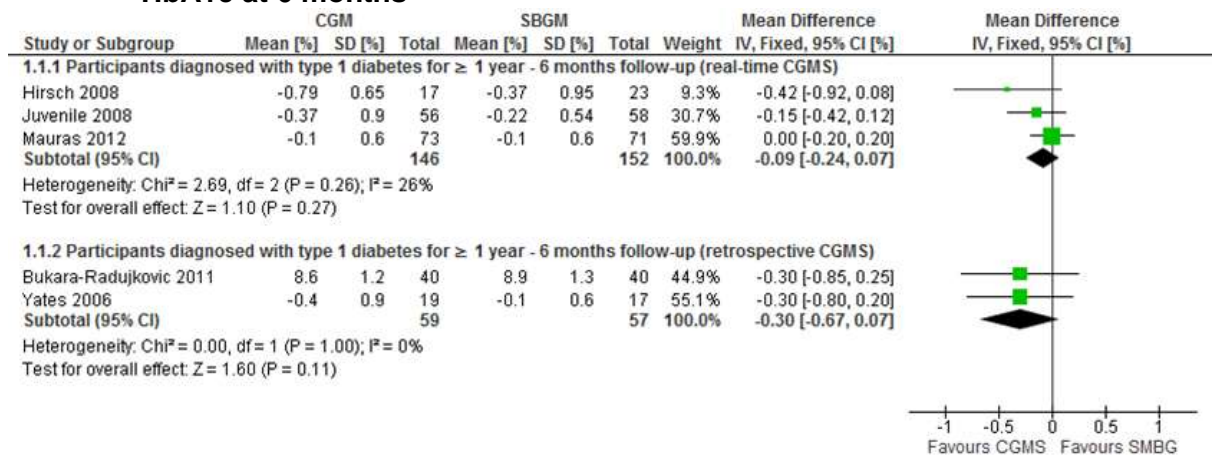
Review questions:

How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

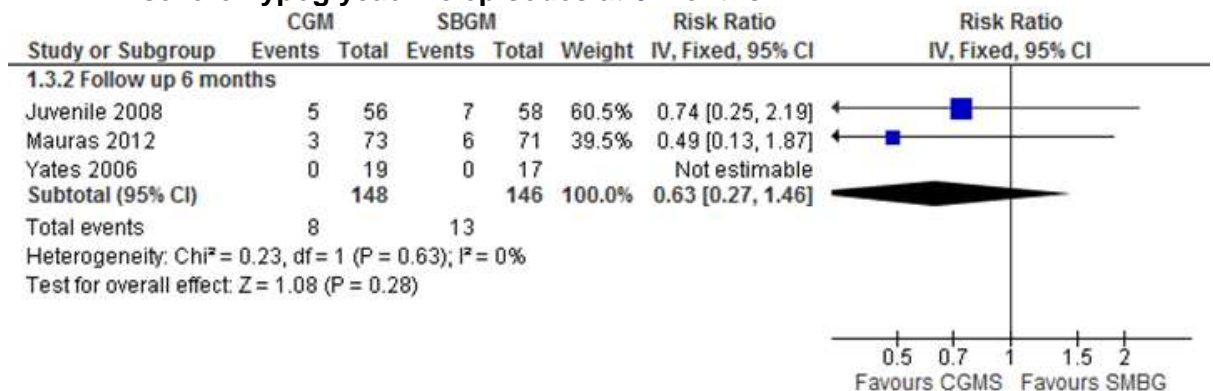
What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?

Figure 1: Continuous glucose monitoring versus capillary blood glucose monitoring – HbA1c at 6 months



Note: Hirsch 2008 Juvenile 2008 and Yates 2006 were reported in Langendam 2012 systematic review

Figure 2: Continuous glucose monitoring versus capillary blood glucose monitoring – severe hypoglycaemic episodes at 6 months



Note: Juvenile 2008 and Yates 2006 were reported in Langendam 2012 systematic review

What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.8 Type 1 diabetes – blood ketone monitoring

Review question: What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.9 Type 1 diabetes – dietary advice

Review questions:

What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?

Figure 3: HbA1c at 12 months (2 studies)

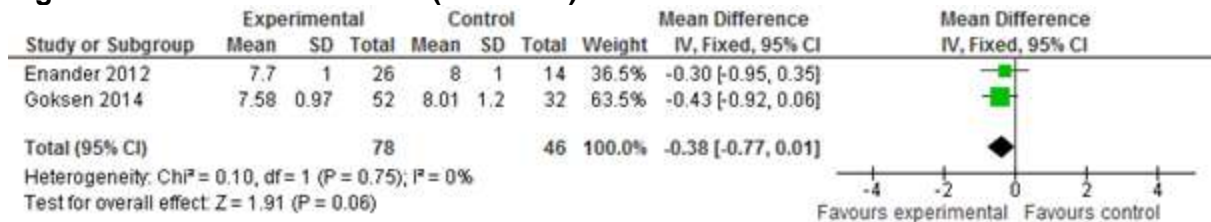
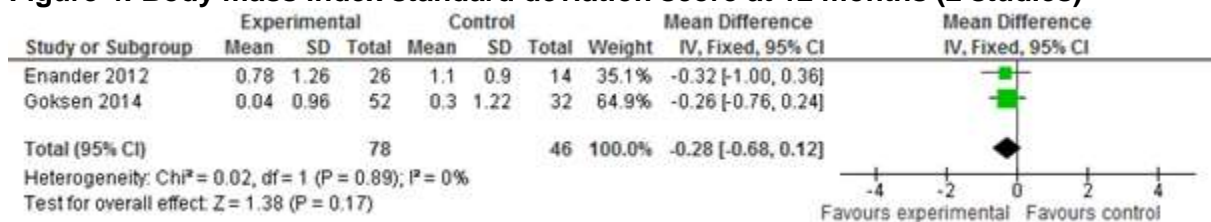


Figure 4: Body mass index standard deviation score at 12 months (2 studies)



What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.10 Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

Review question: What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions:

What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:

- general observations (for example, heart and respiratory rate and blood pressure)
- body weight
- hydration status
- fluid balance
- neurological observations
- electrocardiographic (ECG) monitoring?

No meta-analyses were conducted for this review question and so there are no forest plots.

Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:

- blood glucose

- blood or urine ketones
- serum urea or electrolytes
- acid/base status?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.12 Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

Review questions:

What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

At what rate should children and young people with diabetic ketoacidosis be rehydrated?

No meta-analyses were conducted for this review question and so there are no forest plots.

What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.13 Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents

Review question: What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

Review questions:

When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.15 Type 1 and type 2 diabetes – diabetic ketoacidosis –anticoagulant prophylaxis

Review question: What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.16 Type 1 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.16.1 Type 1 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.17 Type 2 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.18 Type 2 diabetes – behavioural interventions

Review questions:

What is the effectiveness of behavioural interventions to promote engagement with clinical services in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.19 Type 2 diabetes – dietary advice

Review question: What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.20 Type 2 diabetes – weight loss

Review question: Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.21 Type 2 diabetes – metformin

Review question: What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.22 Type 2 diabetes – HbA1c targets

Review question: what is the optimal HbA1c target for children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.23 Type 2 diabetes – hypertension

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.24 Type 2 diabetes – dyslipidaemia

Review question: What is the optimal monitoring strategy for identifying dyslipidaemia in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.25 Type 2 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.26 Type 2 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

Appendix K: GRADE tables

K.1 Diagnosis

Review question: What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?

The systematic review for this question was conducted by the guidance-producing centre for the guideline 'Type 1 diabetes in adults'. There are no evidence profiles (GRADE tables) for this question because nearly all of the studies included in the evidence review were cross-sectional observational studies and thus were not able to be combined in a meta-analysis or GRADE evidence profile. All non-comparative observational studies included for this question were graded as low quality due to the inherent high risk of bias associated with these study designs. The specific methodological limitations of the included studies are summarised in the table below.

Table 27: Methodological limitations of non-comparative observational studies included for the review question about diagnosis

Study	Propsective or cross-sectional study design	Representative population sample	Outcomes measured adequately	Appropriate statistical analysis conducted (adjusted for confounders where applicable)	Quality
ZANONE 2003	Yes	Yes	Yes	NA	Low
TUNG 2008	Yes	Yes	Yes	NA	Low
VERMEULEN 2011	Yes	Yes	Yes	NA	Low
BARKER 2014	Yes	Yes	Yes	NA	Low
ANDERSSON 2013	Yes	Yes	Yes	NA	Low
SAMUELSSON 2013	Yes	Yes	Yes	NA	Low
SHIVAPRASAD 2014	Yes	Yes	Yes	NA	Low
SCHOLIN 2004a	Yes	Yes	Yes	NA	Low
BORG 2003	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
BESSER 2011	Yes	Partially (mixed young	Yes	NA	Low

Study	Propsective or cross-sectional study design	Representative population sample	Outcomes measured adequately	Appropriate statistical analysis conducted (adjusted for confounders where applicable)	Quality
		people and adult population)			
LAADHAR 2007	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
BRUNOVA 2002	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
OTA 2005	Yes	Partially (mostly the population of interest based on the mean age of participants)	Yes	NA	Low
SCHOLIN 2011	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
SCHOLIN 2004b	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
TRIDGELL 2011	Yes	Partially (mostly the population of interest based on the mean age of participants)	Yes	NA	Low
SCHOLIN 2004c	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
WENZLAU 2010	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
MCDONALD 2011	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
ORAM 2014	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
LU 2014	Yes	Partially (mixed young people and adult population)	Yes	NA	Low
RAJALAKSHMI 2014	Yes	Partially (mixed young	Yes	NA	Low

Study	Propsective or cross-sectional study design	Representative population sample	Outcomes measured adequately	Appropriate statistical analysis conducted (adjusted for confounders where applicable)	Quality
		people and adult population)			

NA not applicable

K.2 Type 1 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

Table 28: Evidence profile for effectiveness of structured education programmes in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Structured education	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Mean HbA_{1c} at 6 months (education only versus standard care)											
1 (Howe 2005)	21	28	NA	MD 0.2 lower (1.21 lower to 0.81 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None
Mean HbA_{1c} at 6 months (education plus telephone case management versus standard care)											
1 (Howe 2005)	26	28	NA	MD 0.4 lower (1.28 lower to 0.48 higher)	Low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Serious imprecision ⁵	None
Mean HbA_{1c} at 6 months (TeenCope versus Managing Diabetes)											
1 (Grey 2013)	167	153	NA	MD 0.02 higher (0.31 lower to 0.35 higher)	Moderate	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Structured education	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Mean HbA_{1c} at 12 months (TeenCope versus Managing Diabetes)											
1 (Grey 2013)	167	153	NA	MD 0.18 lower (0.49 lower to 0.13 higher)	Moderate	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None
Mean HbA_{1c} at 12 months (family-centred group education versus conventional clinical care)											
1 (Murphy 2012)	158	147	NA	MD 0.2 lower (0.55 lower to 0.15 higher)	Low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Serious imprecision ⁵	None
HbA_{1c} change over 12 months (family-centred group education versus waiting list)											
1 (Murphy 2007)	33	34	NA	MD 0.01 lower (0.17 lower to 0.15 higher)	Moderate	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None
Mean HbA_{1c} at 12 months (care ambassador plus versus standard care)											
1 (Katz 2014)	52	51	NA	MD 0.1 lower (0.45 lower to 0.25 higher)	Moderate	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None
Mean HbA_{1c} at 12 months (care ambassador ultra versus standard care)											
1 (Katz 2014)	50	51	NA	MD 0.1 higher (0.26 lower to 0.46 higher)	Moderate	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None
Mean HbA_{1c} at 12 months (CASCADE versus control)											
1 (Christie 2014)	143	155	NA	MD 0.1 (0.28 lower to 0.50 higher)	Low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Serious imprecision ⁶	None
Mean HbA_{1c} at 12 months (supportive self-care versus conventional treatment)											
1 (Delamater 1990)	9	12	NA	MD 0.4 lower (not reported) ⁷	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁷	None
Mean HbA_{1c} at 24 months (care ambassador plus versus standard care)											
1 (Katz 2014)	52	51	NA	MD 0.2 lower (0.59 lower to 0.19 higher)	Low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Serious imprecision ⁵	None
Mean HbA_{1c} at 24 months (care ambassador ultra versus standard care)											
1 (Katz 2014)	50	51	NA	MD 0 (0.39 lower to 0.39 higher)	Moderate	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Structured education	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Average mean HbA_{1c} at 24 months (care ambassador plus versus standard care)											
1 (Katz 2014)	52	51	NA	MD 0.1 lower (0.41 lower to 0.21 higher)	Moderate	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None
Average mean HbA_{1c} at 24 months (care ambassador ultra versus standard care)											
1 (Katz 2014)	50	51	NA	MD 0 (0.36 lower to 0.36 higher)	Moderate	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None
Mean HbA_{1c} at 24 months (CASCADE versus control)											
1 (Christie 2014)	135	149	NA	MD 0.03 (0.36 lower to 0.41 higher)	Moderate	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None
Mean HbA_{1c} at 24 months (supportive self-care versus conventional treatment)											
1 (Delamater 1990)	9	12	NA	MD 0.9 lower (not reported) ⁷	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁷	None
Mean number of severe hypoglycaemic episodes (per participant) - over 12 months (Family-centred group education vs. Conventional clinical care)											
1 (Murphy 2012)	158	147	NA	MD 0.05 lower (0.21 lower to 0.11 higher)	Moderate	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None
Severe hypoglycaemic episodes (1 or more episodes versus no episodes, parent- or adult-reported) over 12 months (CASCADE versus control)											
1 (Christie 2014)	143	155	OR 0.76 ^a (0.32 lower to 2.59 higher)	NA	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None
Mean number of severe hypoglycaemic episodes (per participant) over 24 months (care ambassador plus psycho-education versus care ambassador only)											
1 (Svoren 2003)	97	94	NA	MD 0.17 higher (0.18 lower to 0.52 higher)	Low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Serious imprecision ⁵	None
Severe hypoglycaemic episodes (1 or more episodes versus no episodes, parent- or adult-reported) over 24 months (CASCADE versus control)											
1 (Christie 2014)	137	140	OR 0.92 ^a (0.32 lower to 2.59 higher)	NA	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None
Mean number of episodes of diabetic ketoacidosis (per participant) over 12 months (family-centred group education versus conventional clinical care)											
1 (Murphy 2012)	158	147	NA	MD 0.01 higher	Moderate	RCT	Serious ¹	No serious inconsistency	No serious indirectness	No serious imprecision ⁶	None

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Structured education	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
				(0.09 lower to 0.11 higher)				ncy ²	s ³		
Adherence to diabetes treatment (percentage of positive adherence) at 6 months (education versus standard care)											
1 (Howe 2005)	21	28	NA	MD 4.9 higher (10.39 lower to 20.19 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None
Children and young people's quality of life, impact, at 6 months, higher score indicates better quality of life (family-centred group education versus conventional clinical care)											
1 (Murphy 2012)	158	147	NA	MD 0.7 higher (3.28 lower to 4.68 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁶	None
Children and young people's quality of life, worry, at 6 months, higher score indicates better quality of life (family-centred group education versus conventional clinical care)											
1 (Murphy 2012)	158	147	NA	MD 3 lower (5.51 lower to 0.49 higher)	Low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Serious imprecision ⁴	None
Children and young people's quality of life, parental involvement, at 6 months, higher score indicates better quality of life (family-centred group education versus conventional clinical care)											
1 (Murphy 2012)	158	147	NA	MD 0.3 lower (1.04 lower to 0.44 higher)	Low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Serious imprecision ⁴	
Children and young people's quality of life at 6 months (TeenCope versus Managing Diabetes)											
1 (Grey 2013)	167	153	NA	MD 4.63 higher (2.18 lower to 7.08 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None
Children and young people's quality of life at 12 months (TeenCope versus Managing Diabetes)											
1 (Grey 2013)	167	153	NA	MD 3.62 higher (0.98 lower to 6.26 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None
Children and young people's quality of life at 12 months, parent-reported (care ambassador plus versus standard care)											
1 (Katz 2014)	52	51	NA	MD 2.7 higher (1.93 lower to 7.33 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Structured education	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Children and young people's quality of life at 12 months, child- or young person-reported (care ambassador plus versus standard care)											
1 (Katz 2014)	52	51	NA	MD 0.1 lower (3.07 lower to 2.87 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None
Children and young people's quality of life at 12 months, parent-reported (care ambassador ultra versus standard care)											
1 (Katz et al. 2014)	50	51	NA	MD 4.6 higher (0.06 lower to 9.26 higher)	Low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Serious imprecision ⁵	None
Children and young people's quality of life at 12 months, child- or young person-reported (care ambassador ultra versus standard care)											
1 (Katz 2014)	50	51	NA	MD 0.8 lower (3.78 lower to 2.18 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None
Children and young person's quality of life, general module, at 12 months follow-up, young person-reported (CASCADE versus control)											
1 (Christie 2014)	148	159	NA	MD 1.09 lower (3.15 lower to 0.03 higher)	Low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Serious imprecision ⁶	None
Children and young people's quality of life, diabetes module, at 12 months, young person-reported (CASCADE versus control)											
1 (Christie 2014)	148	159	NA	MD 0.62 higher (2.35 lower to 3.04 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None
Children and young people's quality of life at 24 months, parent-reported (care ambassador plus versus standard care)											
1 (Katz 2014)	52	51	NA	MD 3.3 lower (7.74 lower to 1.14 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None
Children and young people's quality of life at 24 months, child- or young person-reported (care ambassador plus versus standard care)											
1 (Katz 2014)	52	51	NA	MD 2.1 lower (5.46 lower to 1.26 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None
Children and young people's quality of life at 24 months, parent-reported (care ambassador ultra versus standard care)											
1 (Katz 2014)	50	51	NA	MD 0.2 higher (4.22 lower to 4.62 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Structured education	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Children and young person's quality of life at 24 months, child- or young person-reported (care ambassador ultra versus standard care)											
1 (Katz 2014)	50	51	NA	MD 2.1 lower (5.44 lower to 1.24 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None
Children and young people's quality of life, general module, at 24 months, young person-reported (CASCADE versus control)											
1 (Christie 2014)	144	151	NA	MD 0.33 lower (2.53 lower to 1.97 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None
Children and young person's quality of life, diabetes module, at 24 months, young person-reported (CASCADE versus control)											
1 (Christie 2014)	144	151	NA	MD 0.02 lower (3.19 lower to 2.72 higher)	Very low	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None
Children and young people's satisfaction with treatment or intervention, follow-up time not reported (TeenCope versus Managing Diabetes)											
1 (Grey 2013)	167	153	NA	MD 0.08 lower (0.22 lower to 0.06 higher)	Moderate	RCT	Serious ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None

CASCADE Child and Adult Structured Competencies Approach to Diabetes Education, MD mean difference, NA not applicable, OR odds ratio, RCT randomised controlled trial
 a Adjusted for baseline and accounting for clustering within clinics

1 Some risk of bias due to identification of several limitations and absence of reported information

2 Single-study analysis

3 No serious indirectness

4 Confidence interval crosses three zones related to precision (see 'Methodology for 2015 update')

5 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')

6 Confidence interval is entirely within one zone related to precision (see 'Methodology for 2015 update')

7Unable to assess precision using data reported in the article, 12 months HbA1 self-management mean (SD) 8.1% ± 1.5% versus conventional mean (SD) 9.3 ± 1.7, P<0.01; 24 months HbA1 self-management mean (SD) 8.2±1.5 versus conventional mean (SD) 9.8 ± 2.4, P <0.05

K.3 Type 1 diabetes – behavioural interventions

Review question: What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 1 diabetes?

Table 29: Evidence profile for effectiveness of motivational interviewing versus support visits in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Motivational interviewing	Support visits	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c at 12 months											
1 (Channon 2007)	35	25	NA	MD 0.5 lower (1.43 lower to 0.43 higher)	Moderate	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	Serious ⁴	None
Depression (wellbeing questionnaire) at 12 months (lower scores indicate better outcomes)											
1 (Channon 2007)	35	25	NA	MD 1.77 lower (2.80 lower to 0.74 lower)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁵	None
Health-related quality of life (Diabetes Quality of Life for Youths, impact) at 12 months (lower scores indicate better outcomes)											
1 (Channon 2007)	35	25	NA	MD 10.56 lower (17.81 lower to 3.31 lower)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None

MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk, SMD standardised mean difference

1 No apparent risk of bias in the included study

2 Single-study analysis

3 Population, intervention and outcome as specified in the review protocol

4 Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')

5 No minimally important difference for wellbeing quality of life specified by GDG

6 No minimally important difference for diabetes quality of life for youths specified by GDG

Table 30: Evidence profile for effectiveness of motivational interviewing skills training versus standard care in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Motivational interviewing delivered by trained HCPs	No motivation interviewing (waiting list)	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c at 15 months											
1 (Robling 2012)	342	318	NA	MD 0.2 higher (0.06 lower to 0.46 higher)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁴	None
Adherence to diabetes management (measured with Diabetes Mismanagement Questionnaire) at 15 months (lower scores indicate better outcomes)											
1 (Robling 2012)	186	163	NA	MD 4.6 lower (8.04 lower to 1.16 lower)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁵	None
Health-related quality of life (measured with Diabetes Quality of Life Questionnaire, impact subscale) at 15 months (higher scores indicate better outcomes)											
1 (Robling 2012)	167	166	NA	MD 5.8 lower (9.85 lower to 1.75 lower)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁵	None

MD mean difference, NA not applicable, RCT randomised controlled trial

1 No apparent risk of bias in the included study

2 Single-study analysis

3 Population, intervention and outcome as specified in the review protocol

4 Confidence intervals entirely within one zone related to precision (see 'Methodology for 2015 update')

5 No minimally important difference for Diabetes Quality of Life Questionnaire specified by the GDG

Table 31: Evidence profile for effectiveness of motivational interviewing versus structured education in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Motivational interviewing	Structured education	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c at 6 months											
1 (Wang 2010)	21	23	NA	MD 1.1 higher (0.27 higher to 1.93 higher)	Low	RCT	No serious risk of bias ¹	No serious inconsistency ²	Serious ³	Serious ⁴	None
Depression (CES-D) at 6 months (lower scores indicate better outcomes)											
1 (Wang 2010)	21	23	NA	MD 0.07 higher (1.53 lower to 1.67 higher)	Moderate	RCT	No serious risk of bias ¹	No serious inconsistency ²	Serious ³	No serious imprecision ⁵	None
Health-related quality of life (EDIC-QoLY, lifestyle subscale) at 6 months (lower scores indicate better outcomes)											
1 (Wang 2010)	21	23	NA	MD 0.01 lower (1.61 lower to 1.59 higher)	Moderate	RCT	No serious risk of bias ¹	No serious inconsistency ²	Serious ³	No serious imprecision ⁵	None

MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk, SMD standardised mean difference

1 No apparent risk of bias in the included study

2 Single-study analysis

3 Population and outcome as specified in the review protocol, but intervention was not delivered by psychologists and staff did not have an appropriate level of training

4 Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')

5 No minimally important difference for EDIC-QoLY specified by GDG

Table 32: Evidence profile for effectiveness of cognitive behavioural therapy focused on quality of life versus standard care in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Cognitive behavioural therapy focused on quality of life	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)							

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations	
	Cognitive behavioural therapy focused on quality of life	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)								
HbA1c at 12 months												
1 (de Wit 2008)	41	40	NA	MD 0.1 higher (0.53 lower to 0.73 higher)	Moderate	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	Very serious ⁴	None	
Depression (CES-D) at 12 months (lower scores indicate better outcomes)												
1 (de Wit 2008)	41	40	NA	MD 1.04 higher (1.26 lower to 3.34 higher)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁵	None	
Health-related quality of life (CHQ-CF87, global health subscale) at 12 months (higher scores indicate better outcomes)												
1 (de Wit 2008)	41	40	NA	MD 10.08 higher (2.16 higher to 18 higher)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁵	None	

CBT cognitive behavioural therapy, MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk, SMD standardised mean difference

1 Concerns about selection of participants and performance bias, but these are unlikely to affect outcome

2 Single-study analysis

3 Population, intervention and outcome as specified in the review protocol

4 Confidence intervals cross three zones related to precision (see 'Methodology for 2015 update')

5 No minimally important difference for CHQ-CF87 specified by GDG

Table 33: Evidence profile for effectiveness of cognitive behavioural therapy not specifically focused on quality of life versus standard care in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations	
	Cognitive behavioural therapy	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)								
Adherence to diabetes management (measured with Diabetes Self- Management Profile, child domain) at 12 months												
1 (Nansel 2007)	40	41	NA	MD 0.01 lower (0.07 lower to 0.05 higher)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁴	None	
Health-related quality of life (measured with Diabetes Quality of Life for Youth, impact subscale) at 15 months (higher scores indicate better outcomes)												
1 (Nansel 2007)	40	41	NA	MD 3.67 higher (3.1 higher to 4.24 higher)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁴	None	

MD mean difference, NA not applicable, RCT randomised controlled trial

1 No apparent risk of bias in the included study

2 Single-study analysis

3 Population, intervention and outcome as specified in the review protocol

4 No minimally important difference for Diabetes Quality of Life for Youth specified by GDG

Table 34: Evidence profile for effectiveness of counselling versus standard care in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations	
	Counselling	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)								
HbA1c at 15 months												
1 (Graue 2005)	45	38	NA	MD 0.44 lower (1.04 lower to 0.16 higher)	Moderate	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	Serious imprecision ⁴	None	
Adverse events (severe hypoglycaemic episodes at 15 months)												
1 (Graue 2005)	7/45 (15.6%)	5/38 (13.2%)	RR 1.18 (0.41 to 3.42)	24 more per 1000 (from 78 fewer to 318 more)	Low	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁵	None	
Health-related quality of life (measured with Diabetes Quality of Life Questionnaire, impact subscale) at 15 months (higher scores indicates better outcomes)												
1 (Graue 2005)	45	38	NA	MD 4.3 higher (0.16 higher to 8.44 higher)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁵	None	

MD mean difference, NA not applicable, RCT randomised controlled trial

1 Concern about performance bias, but this is unlikely to affect outcome

2 Single-study analysis

3 Population, intervention and outcome as specified in the review protocol

4 Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')

5 No minimally important difference for Diabetes Quality of Life Questionnaire specified by the GDG

6 Confidence intervals cross three zones related to precision (see 'Methodology for 2015 update')

Table 35: Evidence profile for effectiveness of multi-systemic therapy (including behavioural family systems therapy) versus standard care in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations	
	Multi-systemic therapy	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)								
HbA1c at 6 to 7 months' follow-up												
1 (Ellis 2004)	13	15	NR	MD 1.9 lower (4.24 lower to 0.44 higher)	Low	RCT	Serious risk of bias ¹²	No serious inconsistency ⁶	No serious indirectness ³	Serious imprecision ¹⁰	None	
1	64	63	NR	MD 0.77 lower	Moderate	RCT	No serious	No serious	No serious	Serious	None	

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Multi-systemic therapy	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)							
(Ellis 2005)				(1.35 to 0.19 lower)			risk of bias	inconsistency ⁶	indirectness ³	imprecision ¹⁰	
HbA1c at 6 months' follow-up											
1 (Wysocki 2001)	36	40	NR	MD 0.4 lower (not reported)	Very low	RCT	Very serious risk of bias ⁵	No serious inconsistency ⁶	No serious indirectness ³	Very serious imprecision ⁷	None
1 (Wysocki 2007)	36	32	NR	MD 0.7 lower (1.42 lower to 0.02 higher)	Low	RCT	Serious risk of bias ¹¹	No serious inconsistency ⁶	No serious indirectness ³	Serious imprecision ¹⁰	None
HbA1c at 12 months' follow-up											
1 (Wysocki 2001)	36	40	NR	MD 0.2 lower (not reported)	Very low	RCT	Very serious risk of bias ⁵	No serious inconsistency ⁶	No serious indirectness ³	Very serious imprecision ⁷	None
1 (Wysocki 2007)	36	32	NR	MD 0.8 lower (1.57 to 0.03 lower)	Low	RCT	Serious risk of bias ¹¹	No serious inconsistency ⁶	No serious indirectness ³	Serious imprecision ¹⁰	None
Adherence to diabetes treatment											
1 (Ellis 2004)	16	15	NR	MD 0.17 higher (0.53 lower to 0.87 higher)	Low	RCT	Serious risk of bias ¹²	No serious inconsistency ⁶	No serious indirectness ³	Serious imprecision ¹⁰	None
1 (Ellis 2005)	64	63	NR	MD 0.87 higher (0.46 to 1.28 higher)	Moderate	RCT	No serious risk of bias	No serious inconsistency ⁶	No serious indirectness ³	Serious imprecision ¹⁰	None
Adherence to diabetes (measured with self-care inventory) at 6 months' follow-up (higher scores indicate better adherence)											
1 (Wysocki 2001)	36	40	NR	MD 4.4 higher (not reported)	Very low	RCT	Very serious risk of bias ⁵	No serious inconsistency ⁶	No serious indirectness ³	Very serious imprecision ⁷	None
1 (Wysocki 2007)	36	32	NR	MD 6.6 higher (1.77 to 11.43 higher)	Moderate	RCT	Serious risk of bias ¹¹	No inconsistency ⁶	No serious indirectness ³	No serious imprecision	None
Adherence to diabetes (measured with self-care inventory) at 12 months' follow-up (higher scores indicate better adherence)											
1 (Wysocki 2001)	34	38	NR	MD 8.7 higher (not reported)	Very low	RCT	Very serious risk of bias ⁵	No serious inconsistency ⁶	No serious indirectness ³	Very serious imprecision ⁷	None
1 (Wysocki 2007)	36	32	NR	MD 4 higher (1.08 lower to 9.08 higher)	Moderate	RCT	Serious risk of bias ¹¹	No serious inconsistency ⁶	No serious indirectness ³	No serious imprecision	None

MD mean difference, MID minimally important difference, NA not applicable, RCT randomised controlled trial

1 No apparent risk of bias in the included studies

2 No heterogeneity present (I-squared < 33%)

3 Population, intervention and outcome as specified in the review protocol

4 Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')

5 Concern about selection and performance bias, some participants received psychological support outside the study

6 Single-study analysis

7 Unable to assess precision using data reported in the article, 6 months HbA1c BFST mean (SD) 0.2% versus conventional treatment mean (SD) 0.6, not significant; 6 months self-care inventory BFST mean 1.8 versus conventional treatment mean -2.6, not significant; 12 months self-care inventory BFST mean 3.3 versus conventional treatment mean -5.4, not significant

8 Heterogeneity present (I-squared between 33% and 67%)

9 No minimally important difference for adherence specified by GDG

10 Confidence interval crosses one zone related to precision (MID -0.5 to +0.5; see 'Methodology for 2015 update')

11 Concern about attrition and detection bias

12 Concern about selection and performance bias (unclear reporting, lack of blinding)

Table 36: Evidence profile for effectiveness of family-based teamwork intervention versus standard care in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Family-based teamwork intervention	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c at 12 months											
1 (Laffel 2003)	50	50	NA	MD 0.5 lower (1.02 lower to 0.02 higher)	Moderate	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	Serious imprecision ⁴	None
1 (Anderson 1999)	28	27	NA	MD 0.2 higher (not reported)	Very low	RCT	Serious risk of bias ⁵	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁶	None
Health-related quality of life (PedsQL) at 12 months (higher scores indicate better outcomes)											
1 (Laffel 2003)	50	50	NA	MD 0.4 higher (3.91 lower to 4.71 higher)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁷	None

MD mean difference, NA not applicable, RCT randomised controlled trial

1 Concern over performance bias possibly due to poor reporting, but this is unlikely to affect outcomes

2 Single-study analysis

3 Population, intervention and outcome as specified in the review protocol

4 Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')

5 Some risk of bias due to identification of several limitations and absence of reported information

6 Unable to assess precision using data reported in the article, 12 months HbA1c mean (SD) 8.9% ± 1.05% versus standard care mean (SD) 8.7 ± 0.63, not significant

7 No minimally important difference for PedsQL specified by GDG

Table 37: Evidence profile for effectiveness of family-based behavioural intervention not specifically based on teamwork versus standard care in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations	
	Family-based behavioural intervention	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)								
HbA1c at 6 months												
1 (Wysocki 2001a)	37	40	NR	MD 0.1 lower (not reported)	Very low	RCT	Very serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None	
1 (Wysocki 2007) ^a	36	32	NR	MD 0.3 lower (not reported)	Very low	RCT	Serious risk of bias ⁸	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ¹⁰	None	
HbA1c at 12 months												
1 (Nansel 2009)	58	58	NR	MD 0.2 higher (0.38 lower to 0.78 higher)	Very low	RCT	Serious risk of bias ⁸	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁷	None	
1 (Anderson 1999) ^b	30	27	NA	MD 0.0 (not reported)	Very low	RCT	Serious risk of bias ⁸	No serious inconsistency ⁹	No serious indirectness ³	Very serious imprecision ⁴	None	
1 (Wysocki 2001a)	36	38	NR	MD 0.8 lower (not reported)	Very low	RCT	Very serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None	
1 (Wysocki 2007) ^a	36	32	NR	MD 0.1 lower (not reported)	Very low	RCT	Serious risk of bias ⁸	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ¹⁰	None	
Adherence to diabetes management (measured with Diabetes Self-Management Profile) at 12 months (higher scores indicate better outcomes)												
1 (Nansel 2009)	58	58	NR	MD 0.2 higher (3.45 lower to 3.85 higher)	Very low	RCT	Serious risk of bias ⁸	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁷	None	
1 (Wysocki 2007) ^a	28	29	NR	MD 6.6 higher (1.37 to 11.83 higher)	Moderate	RCT	Serious risk of bias ⁸	No serious inconsistency ²	No serious indirectness ³	No serious imprecision	None	
Adherence to diabetes (measured with Self-care inventory) at 6 months follow-up (higher scores indicate better adherence)												
1 (Wysocki 2001a)	37	40	NR	MD 2.3 higher (not reported)	Very low	RCT	Very serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁴	None	
1 (Wysocki 2007) ^a	36	32	NR	MD 4 higher (1.4 lower to 9.4 higher)	Very low	RCT	Serious risk of bias ⁸	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁷	None	
Adherence to diabetes (measured with Self-care inventory) at 12 months follow-up (higher scores indicate better adherence)												
1 (Wysocki)	36	38	NR	MD 4.2 higher (not reported)	Very low	RCT	Very serious	No serious inconsistency	No serious indirectness	Very serious imprecision ⁴	None	

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Family-based behavioural intervention	Standard care	Relative (95% confidence interval)	Absolute (95% confidence interval)							
2001a)							risk of bias ¹	ncy ²	s ³		
1 (Wysocki 2007) ^a	36	32	NR	MD 2 higher (3.26 lower to 7.26 higher)	Very low	RCT	Serious risk of bias ⁸	No serious inconsistency ²	No serious indirectness ³	Very serious imprecision ⁷	None

MD mean difference NA not applicable, NR not reported, RCT randomised controlled trial

a Education plus support versus conventional treatment (standard care)

b Attention control versus standard care

1 Concern about selection and performance bias, some participants received psychological support outside the study

2 Single-study analysis

3 Population, intervention and outcome as specified in the review protocol

4 Unable to assess precision using data reported in the article, 6 months HbA1 education support mean 0.5% versus conventional therapy mean 0.6%, not significant; 12 months HbA1 education support mean 0.3% versus conventional therapy mean 1.1%, not significant; 6 months SCI education support mean -0.3 versus conventional therapy mean -2.6, not significant; 12 months SCI education support mean -1.2 versus conventional therapy mean -5.4, not significant

5 Concern about performance bias, but this is unlikely to affect outcomes

6 Serious heterogeneity present (I-squared > 67%)

7 Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')

8 Some risk of bias due to identification of several limitations and absence of reported information

9 No minimally important difference for Diabetes Self-Management Profile specified by GDG

10 Unable to assess precision using data reported in the article, 6 months post-intervention HbA1 education support mean 9.3% ± 1.4% versus standard care mean 9.6% ± 1.6; 12 months post-intervention HbA1 education support mean 9.5% ± 1.5% versus standard care mean 9.6% ± 1.7;

K.4 Type 1 diabetes – multiple daily injections

Review question: What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

Table 38: Evidence profile for effectiveness of multiple daily injections in improving glycaemic control in children and young people newly diagnosed with type 1 diabetes when compared with mixed insulin injections

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Multiple daily injections	Fewer than 4 injections per day	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c (%) change from baseline after 1 year											
1 (Abid	29	88	NA	MD 1.2 lower	Very low	Retrospect	Serious	NA	No serious	Serious	None

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Multiple daily injections	Fewer than 4 injections per day	Relative (95% confidence interval)	Absolute (95% confidence interval)							
2011)	(changed from 9.1 at baseline to 7.9 at 1 year)	(changed from 11.4 at baseline to 9.1 at 1 year)		CI NC		ive cohort study	risk of bias ¹		indirectness ²	imprecision ^c	
1 (Adhikari 2009)	212 (changed from 11.4 ± 1.9 at baseline to 7.5 ± 1.6 at 1 year)	247 (changed from 11.6 ± 1.8 at baseline to 8.2 ± 1.8 at 1 year)	NA	MD 0.7 lower (1.01 lower to 0.39 lower)	Very low	Retrospective cohort study	Serious risk of bias ⁴	NA	No serious indirectness ⁵	Serious imprecision ^f	None
HbA1c (%) change from baseline after 9 months											
1 (Adhikari 2009)	212 (changed from 11.4 ± 1.9 at baseline to 7.2 ± 1.7 at 9 months)	247 (changed from 11.6 ± 1.8 at baseline to 7.9 ± 1.4 at 9 months)	NA	MD 0.7 lower (0.98 lower to 0.42 lower)	Very low	Retrospective cohort study	Serious risk of bias ⁷	NA	No serious indirectness ⁵	Serious imprecision ^f	None
HbA1c (%) change from baseline after 6 months											
1 (Adhikari 2009)	212 (changed from 11.4 ± 1.9 at baseline to 6.6 ± 1.4 at 6 months)	247 (changed from 11.6 ± 1.8 at baseline to 7.3 ± 1.4 at 6 months)	NA	MD 0.7 lower (1.96 lower to 0.44 lower)	Very low	Retrospective cohort study	Serious risk of bias ⁸	NA	No serious indirectness ⁵	Serious imprecision ⁶	None
BMI standard deviation score (SDS) change from baseline after 1 year											
1 (Abid 2011)	29 (changed from 0.28 at baseline to 0.56 at 1 year)	88 (changed from 0.41 at baseline to 0.9 at 1 year)	NA	MD 0.34 lower CI NC	Very low	Retrospective cohort study	Serious risk of bias ¹	NA	No serious indirectness ²	Serious imprecision ³	None

BMI body mass index, CI confidence interval, MD mean difference, NA not applicable, NC not calculable

1 Multiple daily injections offered only to older children and young people

2 Comparison is between twice-daily injections and multiple daily injections

3 No estimates of precision reported

4 Participants allocated to treatment based on family or physician preference and high drop-out rate at 12 months reported in both thrice-daily injection cohort (44%) and multiple daily injections cohort (25%)

5 Comparison is between thrice-daily injections and multiple daily injections

6 Range of MD in HbA1c crosses two zones related to precision (see 'Methodology for 2015 update')

7 Participants allocated to treatment based on family or physician preference and high drop-out rate at 9 months in both thrice-daily injection cohort (36%) and multiple daily injections cohort (31%)

8 Participants allocated to treatment based on family or physician preference and high drop-out rate at 6 months in both thrice-daily injection cohort (26%) and multiple daily injections cohort (27%)

Table 39: Evidence profile for effectiveness of multiple daily injections in improving glycaemic control in children and young people with type 1 diabetes of at least 1 year’s duration when compared with mixed insulin injections

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Multiple daily injections	Fewer than 4 injections per day	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c (%) change from baseline after 2 years											
1 (Al-Fifi 2003)	24 (changed from 9.34 ± 1.55 at baseline to 9.49 ± 1.55 at 2 years)	57 (changed from 9.37 ± 1.8 at baseline to 9.59 ± 1.59 at 2 years)	NA	MD 0.1 lower (0.86 lower to 0.66 higher)	Very low	Retrospective cohort study	No serious risk of bias ¹	NA	Serious indirectness ^{2,3}	Serious imprecision ⁴	None
HbA1c (%) change from baseline after 1 year											
1 (Al-Fifi 2003)	24 (changed from 9.34 ± 1.55 at baseline to 9.2 ± 1.7 at 1 year)	57 (changed from 9.37 ± 1.8 at baseline to 9.46 ± 1.61 at 1 year)	NA	MD 0.26 lower (1.05 lower to 0.53 higher)	Very low	Retrospective cohort study	No serious risk of bias ¹	NA	Serious indirectness ^{2,3}	Serious imprecision ^d	None
1 (Abid 2011)	36 (9.2 at 1 year)	36 (8.9 at treatment switch)	NA	MD 0.3 higher CI NC	Very low	Interrupted time series	Serious risk of bias ⁵	NA	No serious indirectness ³	Serious imprecision ^f	None
1 (Adhikari 2009)	118 (8.5 ± 1.6 at 1 year)	198 (8.4 ± 1.5 at treatment switch)	NA	MD 0.1 higher (0.25 lower to 0.45 higher)	Very low	Interrupted time series	Serious risk of bias ⁷	NA	No serious indirectness ⁸	No serious imprecision	None
1 (Alemzadeh 2003)	44 (8.1 ± 1.0 at 1 year)	44 (9.2 ± 1.1 at treatment switch)	NA	MD 1.1 lower (1.55 lower to 0.65 lower)	Very low	Interrupted time series	No serious risk of bias	NA	No serious indirectness ⁹	No serious imprecision	None
1 (Karaguzel 2005)	25 (8.2 ± 1.5 at 1 year)	25 (9.3 ± 2.5 at treatment switch)	NA	MD 1.1 lower (2.27 lower to 0.07 higher)	Very low	Interrupted time series	No serious risk of bias	NA	Serious indirectness ^{3,10,11}	Serious imprecision ⁴	None
HbA1c (%) change from baseline after 9 months											
1 (Adhikari 2009)	129 (8.5 ± 1.6 at 9 months)	198 (8.4 ± 1.5 at treatment switch)	NA	MD 0.1 higher (0.24 lower to 0.44 higher)	Very low	Interrupted time series	Serious risk of bias ¹²	NA	no serious indirectness ⁸	No serious imprecision	None
HbA1c (%) change from baseline after 6 months											
1 (Adhikari 2009)	142 (8.3 ± 1.4 at 6 months)	198 (8.4 ± 1.5 at treatment switch)	NA	MD 0.1 lower (0.42 lower to 0.22 higher)	Very low	Interrupted time series	Serious risk of bias ¹³	NA	no serious indirectness ⁸	No serious imprecision	None

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Multiple daily injections	Fewer than 4 injections per day	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Bin-Abbas 2007)	10 (8.4 ± 0.7 at endpoint)	10 (8.6 ± 1.2 at treatment switch)	NA	MD 0.2 lower (1.12 lower to 0.72 higher)	Very low	Interrupted time series	No serious risk of bias	NA	Serious indirectness ^{c,n,o}	Serious imprecision ⁴	None
1 (Bin-Abbas 2006)	10 (8.6 ± 0.5 at endpoint)	10 (10.6 ± 1.2 at treatment switch)	NA	MD 2.0 lower (2.86 lower to 1.14 lower)	Very low	Interrupted time series	No serious risk of bias	NA	Serious indirectness ^{3,16,17}	No serious imprecision	None
1 (Karaguzel 2005)	25 (8.3 ± 1.6 at 6 months)	25 (9.3 ± 2.5 at treatment switch)	NA	MD 1.0 lower (2.19 lower to 0.19 higher)	Very low	Interrupted time series	No serious risk of bias	NA	Serious indirectness ^{3,10,11}	Serious imprecision ⁴	None
HbA1c (%) during study period (cross-sectional observational data)											
1 (Alexander 2001)	30 (9.79 ± 1.77)	1573 (9.04 ± 1.53)	NA	MD 0.75 higher (0.20 higher to 1.30 higher)	Very low	Cross-sectional survey	No serious risk of bias	NA	Serious indirectness ^{18,19,20}	Serious imprecision ⁴	None
1 (de Beaufort 2007)	926 (8.2 ± 0.0)	524 (8.2 ± 0.1)	NA	MD 0.0 (0.01 lower to 0.01 higher)	Low	Cross-sectional survey	No serious risk of bias ²¹	NA	No serious indirectness ²²	No serious imprecision	None
1 (Dorchy 1997)	15 (6.6 ± 1.1)	129 (6.6 ± 1.2)	NA	MD 0.0 (0.64 lower to 0.64 higher)	Very low	Cross-sectional survey	No serious risk of bias	NA	Serious indirectness ^{3,23}	Serious imprecision ⁴	None
1 (Vanelli 2005)	1911 (8.7 ± 0.2)	1608 (8.3 ± 0.1)	NA	MD 0.4 higher (0.39 higher to 0.41 higher)	Low	Cross-sectional survey	No serious risk of bias	NA	No serious indirectness ²⁰	No serious imprecision	None
Proportion achieving ADA age-specific HbA1c target²⁴ (cross-sectional observational data)											
1 (Mohammad 2012)	31/42 (73.8%)	192/373 (51.5%)	RR 1.43 (1.17 to 1.76)	211 more per 1000 (from 88 more to 391 more)	Very low	Cross-sectional survey	No serious risk of bias	NA	No serious indirectness ²⁵	Serious imprecision ^{2,6}	None
Number of severe hypoglycaemic episodes (ISPAD 2000 grades 2-3 or ISPAD 2009 'severe')											
1 (Al-Fifi 2003)	4/24 (16.7%)	16/57 (28.1%)	RR 0.59 (0.22 to 1.59)	115 fewer per 1000 (from 219 fewer to 166 more)	Very low	Retrospective cohort study	No serious risk of bias ¹	NA	Serious indirectness ^{3,27}	Very serious imprecision ²⁸	None
1 (Alemzadeh 2003)	7/44 (15.9%)	17/44 (38.6%)	RR 0.41 (0.19 to 0.89)	228 fewer per 1000 (from 43 fewer to 313 fewer)	Very low	Interrupted time series	No serious risk of bias	NA	no serious indirectness ^{9,29}	Serious imprecision ²⁶	None
Number of episodes of DKA											
1 (Al-Fifi 2003)	6/24 (25%)	17/57 (29.8%)	RR 0.84 (0.38 to 1.86)	48 fewer per 1000 (from	Very low	Retrospective	No serious risk of bias ¹	NA	No serious indirectness	Very serious imprecision ²⁸	None

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Multiple daily injections	Fewer than 4 injections per day	Relative (95% confidence interval)	Absolute (95% confidence interval)							
				185 fewer to 256 more)		cohort study			S ^{3,30}		
1 (Alemzadeh 2003)	0/44 (0%)	2/44 (4.5%)	RR 0.2 (0.01 to 4.05) ³²	36 fewer per 1000 (from 45 fewer to 139 more)	Very low	Interrupted time series	No serious risk of bias	NA	No serious indirectness ^{9,31}	Very serious imprecision ^{ab}	None
1 (Bin Abbas 2007)	0/10 (0%)	0/10 (0%)	NC	NC	Very low	Interrupted time series	No serious risk of bias	NA	Serious indirectness ^{3,33,34}	NA	None
1 (Bin Abbas 2006)	0/10 (0%)	0/10 (0%)	NC	NC	Very low	Interrupted time series	No serious risk of bias	NA	Serious indirectness ^{3,34,35}	NA	None

ADA American Diabetes Association, CI confidence interval, DKA diabetic ketoacidosis, ISPAD International Society for Pediatric and Adolescent Diabetes, MD mean difference, NA not applicable, NC not calculable, RR relative risk

1 Participants matched for age, sex, body mass index (BMI), insulin dose and compliance

2 All participants enrolled into adolescent education programme at baseline

3 Comparison is between twice-daily injections and multiple daily injections

4 Range of MD in HbA1c crosses two zones related to precision (see 'Methodology for 2015 update')

5 Multiple daily injections offered only to older children and young people

6 No estimates of precision reported

7 Participants allocated to treatment according to family or physician preference and high drop-out rate at 12 months (40%)

8 Comparison is between thrice-daily injections and multiple daily injections

9 Comparison is between 2-3 injections per day and multiple daily injections

10 Length of time on twice-daily injections not reported

11 Participants had poor or moderate diabetes control before treatment switch

12 Participants allocated to treatment according to family or physician preference and high drop-out rate at 9 months (35%)

13 Participants allocated to treatment according to family or physician preference and high drop-out rate at 6 months (28%)

14 HbA1c measured at different time points before and after treatment switch; mean during 3 months before switch and in last month after switch (6-10 months after switch)

15 Participants had poor diabetes control (HbA1c > 8.5%) and recurrent daytime and nocturnal hypoglycaemia (> 4 episodes per month) before treatment switch

16 HbA1c measured at different time points before and after treatment switch; mean during 6 months before switch, time point/span of measurement after switch not reported; follow-up 6-9 months

17 Participants had poor diabetes control (HbA1c > 8.5%) and recurrent daytime and nocturnal hypoglycaemia (> 8 episodes per month) before treatment switch

18 Study had only 2% participants using multiple daily injections

19 Duration of diabetes of participants was < 6 months to > 5 years

20 Participants had 1, 2 or 3 injections per day or multiple daily injections

21 Study had 11% loss to follow-up, duration of diabetes longer in those providing HbA1c data

22 Participants had 2 or 3 injections per day or a basal-bolus regimen (multiple daily injections)

23 Study had only 10% participants using multiple daily injections and included children and young people with duration of diabetes 5 months to 15 years

24 ADA age-specific targets: age < 6 years, HbA1c 7.5 - 8.5%; age 6-12 years, HbA1c ≤ 8%; age 13-18 years, HbA1c ≤ 7.5%

25 Participants had multiple daily injections, twice-daily injections, or a regimen of twice-daily intermediate-acting insulin plus 1 or more injections of regular-acting insulin (classified as < 4 injections per day)

26 RR crosses two zones related to precision (see 'Methodology for 2015 update')

27 Severe hypoglycaemia defined in study methods as hypoglycaemia requiring assistance or leading to coma or convulsion but figures reported are for admissions for hypoglycaemia over 2 year study period

28 RR crosses three zones related to precision (see 'Methodology for 2015 update')

29 Severe hypoglycaemia defined as episodes of blood glucose < 2.8 mmol/l with unconsciousness and with or without seizure

30 Outcome defined as number of admissions for DKA and length of follow-up 2 years

31 Length of follow-up 1 year

32 RR calculated by adding 0.5 to events in each arm

33 Frequency of DKA episodes measured at different times; 3 months before switch and 6-10 months after treatment switch

34 Length of follow-up 6 months

35 Frequency of DKA episodes may be measured at different times before and after treatment switch; follow-up 6-9 months after treatment switch and not reported before treatment switch

K.5 Type 1 diabetes – HbA1c targets

Review question: What is the optimal haemoglobin A1c (HbA1c) target for children and young people with type 1 diabetes?

There are no evidence profiles for this review question because no studies were identified for inclusion.

K.6 Type 1 diabetes – blood glucose targets

Review question: What are the optimal blood glucose targets for children and young people with type 1 diabetes?

There are no evidence profiles for this review question because no studies were identified for inclusion.

K.7 Type 1 diabetes – blood glucose monitoring

Review question: How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?

Table 40: Evidence profile for frequency of self-monitoring of blood glucose in children and young people with type 1 diabetes

Number of studies	Number of children and young people	Relative effect	Absolute effect	Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
Association between frequency of SMBG and HbA1c, reported as coefficients of associations										

Number of studies	Number of children and young people	Relative effect	Absolute effect	Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
5 (de Beaufort 2013; Haller 2004; Ingerski 2011; Levine 2001; Moreland 2004)	4,794	NA	Increased frequency of SMBG was inversely correlated with HbA1c independent of other variables $r = -0.17$ ($p < 0.0001$) to $r = -0.45$ ($p < 0.001$)	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Association between frequency of SMBG and HbA1c, reported as the probability of frequency of SMBG being associated with excellent control of HbA1c in the previous 12 months compared with the poor control group, SMBG performed 3-4 times per day versus 0-2 times per day										
1 (Campbell 2014)	3,272	Adjusted OR 1.7 (0.7 to 3.9)	NA	Very Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	Very serious imprecision ⁵	None
Association between frequency of SMBG and HbA1c, reported as the probability of frequency of SMBG being associated with excellent control of HbA1c in the previous 12 months compared with the poor control group, SMBG performed 5-9 times per day versus 0-2 times per day										
1 (Campbell 2014)	3,272	Adjusted OR 2.3 (1.0 to 5.1)	NA	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	Serious imprecision ⁶	None
Association between frequency of SMBG and HbA1c, reported as the probability of frequency of SMBG being associated with excellent control of HbA1c in the previous 12 months compared with the poor control group, SMBG performed ≥ 10 times per day versus 0-2 times per day										
1 (Campbell 2014)	3,272	Adjusted OR 7.0 (2.9 to 17.0)	NA	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 1 to 6 years, SMBG performed 3-4 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.5%	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 1 to 6 years, SMBG performed 5-6 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.4%	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 1 to 6 years, SMBG performed 7-9 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.1%	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 1 to 6 years, SMBG performed ≥ 10 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 7.8%	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 6 to 13 years, SMBG performed 3-4 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.7%	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 6 to 13 years, SMBG performed 5-6 times per day										
1 (Miller 2013)	NA	NA	Unadjusted	Low	Observatio	No serious	Not	No serious	No serious	None

Number of studies	Number of children and young people	Relative effect	Absolute effect mean HbA1c level 8.4%	Quality	Design	Limitations (risk of bias) risk of bias ¹	Inconsistency calculated ²	Indirectness indirectness ³	Imprecision imprecision ⁴	Other considerations
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 6 to 13 years, SMBG performed 7-9 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.1%	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 6 to 13 years, SMBG performed ≥ 10 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 7.8%	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 13 to 18 years, SMBG performed 0-3 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 10.3%	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 13 to 18 years, SMBG performed 3-4 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 9.0%	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 13 to 18 years, SMBG performed 5-6 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.5%	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 13 to 18 years, SMBG performed 7-9 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.2%	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c levels among children aged 13 to 18 years, SMBG performed ≥ 10 times per day										
1 (Miller 2013)	NA	NA	Unadjusted mean HbA1c level 8.0%	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Change in HbA1c for 1 additional test per day										
8 (Dorcy 1997; Haller 2004; Helgeson 2011; Levine 2001; McGrady 2009; Nordly 2005; Svensson 2009; Ziegler 2011)	31,083	NA	HbA1c decreased by between 0.056 percentage points and 0.4 percentage points for each additional test	Low	Observational	No serious risk of bias ¹	Not calculated ²	No serious indirectness ³	No serious imprecision ⁴	None
Association between frequency of SMBG and severe hypoglycaemic episodes										
1 (Ziegler 2011)	26,723	NA	2.38 (± 0.54) additional events per 100 patient years for every 1 additional test	Low	Observational	No serious risk of bias ¹	No serious inconsistency	No serious indirectness ³	No serious imprecision ⁴	None

CI confidence interval, MID minimally important difference, NA not applicable, OR odds ratio, r correlation coefficient, SMBG self-monitoring of blood glucose

- 1 No apparent risk of bias in the included studies
- 2 No calculation of inconsistency performed
- 3 Population, intervention and outcome as specified in the review protocol
- 4 No MID specified by the GDG
- 5 Confidence interval crosses three zones related to precision (see 'Methodology for 2015 update')
- 6 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')
- 7 Single-study analysis

Review question: What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?

Table 41: Evidence profile for effectiveness of self-monitoring of blood glucose against continuous glucose monitoring systems in children and young people diagnosed with type 1 diabetes at least 1 year before enrolment to the study

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	CGMS	SMBG	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Change in HbA1c level – at 6 months (real-time CGMS)											
2 (Langendam 2012; Mauras 2012)	146	152	NA	MD 0.09 lower in CGMS group (0.24 lower to 0.07 higher)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁴	None
Change in HbA1c level - at 6 months (retrospective CGMS)											
2 (Bukara-Radujković 2011; Langendam 2012)	59	57	NA	MD 0.3 lower (0.67 lower to 0.07 higher)	Low	RCT	Serious ⁵	No serious inconsistency ⁶	No serious indirectness ³	Serious ⁷	None
Mean blood glucose level – at 6 months											
1 (Bukara-Radujković 2011)	40	40	NA	MD 0.7 lower (1.56 lower to 0.16 higher)	Very low	RCT	Serious ⁸	No serious inconsistency ⁹	No serious indirectness ³	Very serious ¹⁰	Yes ¹¹
Severe hypoglycaemic episodes – at 6 months											
2 (Langendam 2012; Mauras 2012)	8/148 (5.4%)	13/146 (8.9%)	RR 0.63 (0.27 to 1.46)	33 fewer per 1000 (from 65 fewer to 41 more)	Low	RCT	No serious risk of bias ¹	No serious inconsistency ⁶	No serious indirectness ³	Very serious ¹⁰	None
Parental satisfaction with the intervention – change over 6 months (scale 1 to 3; higher score means greater satisfaction)											
1 (Mauras)	69	68	NA	MD 0.3 higher (0.21 to 0.39)	High	RCT	No serious risk of	No serious inconsistency	No serious indirectness	No serious imprecision ⁴	None

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	CGMS	SMBG	Relative (95% confidence interval)	Absolute (95% confidence interval)							
2012)				higher)			bias ¹	ncy ⁹	s ³		
CGMS continuous glucose monitoring system, CI confidence interval, MD mean difference, NA not applicable, QoL quality of life, RCT randomised controlled trial, RR relative risk, SMBG self-monitoring of blood glucose, SMD standardised mean difference											
1 No apparent risk of bias in the included studies											
2 Heterogeneity amongst the studies was low (I ² = 26%)											
3 Population, intervention and outcome as specified in the review protocol											
4 Confidence interval is entirely within one zone related to precision (see 'Methodology for 2015 update')											
5 In one of the included studies methods of randomisation and allocation concealment were unclear and the groups were not altogether comparable at baseline											
6 No heterogeneity found between studies (I ² = 0%)											
7 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')											
8 Methods of randomisation and allocation concealment were unclear and the groups were not altogether comparable at baseline											
9 Single-study analysis											
10 Confidence interval crosses three zones related to precision (see 'Methodology for 2015 update')											
11 There were statistically significant differences between the intervention and control groups at baseline in terms of age (p=0.016), diabetes duration (p=0.013), insulin dose (p=0.005) and mean blood glucose (p=0.031)											

Table 42: Evidence profile for effectiveness of self-monitoring of blood glucose against continuous glucose monitoring systems in children and young people recently diagnosed with type 1 diabetes (less than 1 year before enrolment to the study)

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	CGMS	SMBG	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Change in HbA1c level - at 6 months (real-time CGMS)											
1 (Langendam 2012)	76	78	NA	MD 0.10 lower in CGMS group (0.46 lower to 0.66 higher)	Moderate	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	Serious ⁴	None
Change in HbA1c level - at 12 months (real-time CGMS)											
1 (Langendam 2012)	76	78	NA	MD 0.10 higher (0.46 lower to 0.66 higher)	Moderate	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	Serious ⁴	None
Severe hypoglycaemic episodes – at 12 months											
1 (Langendam 2012)	0/76 (0%)	4/78 (5.1%)	RR 0.11 (0.01 to 2.08)	46 fewer per 1000 (from 51 fewer to 55 more)	Low	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	Very serious ⁵	None
Quality of life of parents – at 6 months (scale 1 to 100; higher score means better quality of life)											

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	CGMS	SMBG	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Langendam 2012)	76	78	NA	MD 0.5 lower (7.64 lower to 6.64 higher)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None
Quality of life of parents – at 12 months (scale 1 to 100; higher score means better quality of life)											
1 (Langendam 2012)	76	78	NA	MD 1.9 higher (4.13 lower to 7.93 higher)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None

CGMS continuous glucose monitoring system, CI confidence interval, MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk, SMBG self-monitoring of blood glucose, SMD standardised mean difference

1 No apparent risk of bias in the included studies

2 Single-study analysis

3 Population, intervention and outcome as specified in the review protocol

4 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')

5 Confidence interval crosses three zones related to precision (see 'Methodology for 2015 update')

6 Confidence interval is entirely within one zone related to precision (see 'Methodology for 2015 update')

Review question: What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?

Table 43: Evidence profile for effectiveness of continuous glucose monitoring performed in real-time compared with continuous glucose monitoring performed intermittently in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Real-time continuous glucose monitoring	Intermittent continuous glucose monitoring	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c value (%) - at 6 months											
1 (Battelino 2011)	27 (changed from 6.92 ± 0.56 at baseline to 6.92 ± 0.98 at 6 months)	26 (changed from 6.91 ± 0.67 at baseline to 7.15 ± 0.98 at 6 months)	NA	MD 0.23 lower in the real-time CGMS group (0.76 lower to 0.3 higher)	Low	RCT	No serious risk of bias ¹	No serious inconsistency ²	Serious indirectness ³	Serious imprecision ⁴	None
Severe hypoglycaemic episodes – at 6 months											
1 (Battelino 2011)	0/27 (0%)	0/26 (0%)	NC5	NA	Moderate	RCT	No serious risk of bias ¹	No serious inconsistency ²	Serious indirectness ³	NA	None

CGMS continuous glucose monitoring system, MD mean difference, NA not applicable, NC not calculable, RCT randomised controlled trial, RR relative risk,

- 1 No apparent risk of bias in the included study
2 Single-study analysis
3 Intervention and comparison not as specified in the review protocol
4 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')
5 Cannot be calculated as number of events in both intervention and control group is zero

K.8 Type 1 diabetes – blood ketone monitoring

Review question: What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis?

Table 44: Evidence profile for effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Blood ketone monitoring	Urine ketone monitoring	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Hospital admission rates: incidence of acute complications as a proxy for admission rates											
1 (Laffel 2005)	62	61	NA	MD 0.37 lower (0.74 lower to 0.00)	Low	RCT	Serious ¹	No serious inconsistency ²	Serious indirectness ³	No serious imprecision ⁴	None
Adherence to ketone monitoring: percentage of time ketones checked on sick days											
1 (Laffel 2005)	62	61	NA	90.8% of time for blood ketone monitoring and 61.3% of time for urine ketone monitoring ⁵	Low	RCT	Serious ¹	No serious inconsistency ²	Serious indirectness ³	Serious imprecision ⁶	None

NA not applicable, MD mean difference, RCT randomised controlled trial

1 Several limitations identified which amounted to a serious risk of bias but these did not negate the study findings

2 Single-study analysis

3 People aged 18 years and over were included in the study but this did not negate the study findings

4 The guideline development group (GDG) did not set a minimally important difference (MID) for this outcome

5 The study authors reported statistical significance of $p < 0.001$

K.9 Type 1 diabetes – dietary advice

Review questions: What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?

Table 45: Evidence profile for effectiveness of dietary advice based on carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes

	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Carbohydrate counting	Treatment as usual	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c value (%) - at 12 months											
2 (Enander 2012; Goksen 2014)	78	46	NA	WMD 0.38 lower (0.77 lower to 0.01 higher)	Moderate	RCT	Serious risk of bias ¹	No serious inconsistency	No serious indirectness ⁴	Serious ⁴	None
HbA1c value (%) - at 24 months											
1 (Goksen 2014)	52	32	NA	MD 0.89 lower (1.61 to 0.17 lower)	Moderate	RCT	Serious risk of bias ¹	No serious inconsistency ³	No serious indirectness ⁴	Serious ⁴	None
BMI-SDS – at 12 months											
2 (Enander 2012; Goksen 2014)	78	46	NA	WMD 0.28 lower (0.68 lower to 0.12 higher)	Moderate	RCT	No serious risk of bias ²	No serious inconsistency	No serious indirectness ⁴	Serious ⁴	None
BMI-SDS – at 24 months											
1 (Goksen 2014)	52	32	NA	MD 0.14 lower (0.66 lower to 0.38 higher)	Moderate	RCT	Serious risk of bias ¹	No serious inconsistency ³	No serious indirectness ⁴	Serious ⁴	None
Severe hypoglycaemic episodes (over the 12-month study)											
1 (Enander 2012)	0/30 (0%)	0/15 (0%)	NA ^a	MD 0.00 (NC)	Moderate	RCT	No serious risk of bias ¹	No serious inconsistency ³	No serious indirectness ⁴	No serious imprecision ⁵	None

BMI-SDS body mass index standard deviation score, MD mean difference, NA not applicable, NC not calculable, RCT randomised controlled trial, RR relative risk, WMD weighted mean difference

^a Unknown as no events reported in either treatment group

¹ Moderate risk of bias in the included studies

² No apparent risk of bias in the included study

³ Single-study analysis

⁴ Population, intervention and outcome as specified in the review protocol

⁵ Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')

Review question: What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?

Table 46: Evidence profile for effectiveness of dietary advice based on glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes, glycaemic index diet versus standard diet

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Glycaemic index	Standard diet	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Postprandial hyperglycaemia											
1 (Collier 1988)	7	7	Blood glucose after standard meal reduced from baseline in low glycaemic index phase ($p < 0.05$) No significant change in blood glucose after standard meal when compared with baseline in normal diet phase.		Moderate	RCT	No Serious risk of bias ¹	No Serious inconsistency ²	No Serious indirectness ³	Serious ⁴	None

RCT randomised controlled trial

1 No apparent risk of bias in the included study

2 Single-study analysis

3 Population, intervention and outcome as specified in the review protocol

4 Data reported only graphically with an accompanying p value, therefore unable to calculate mean difference between the intervention and comparator groups – not currently reported in table

Table 47: Evidence profile for effectiveness of dietary advice based on glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes, glycaemic index diet versus carbohydrate exchange diet

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Glycaemic Index	Carbohydrate exchange	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c value (%) change from baseline to 12 months											
1 (Gilbert 2001)	51 (changed from 8.3 ± 1.4 at baseline)	38 (no change, was 8.6 ± 1.4 at baseline and at 12)	NA	MD in change in values between groups 0.3 lower	Moderate	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	Serious ⁴	None

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Glycaemic Index	Carbohydrate exchange	Relative (95% confidence interval)	Absolute (95% confidence interval)							
	to 8.0 ± 1.0 at 12 months)	months)		(0.89 lower to 0.29 higher)							
Mean number of hypoglycaemic episodes (preprandial blood glucose < 3.5 mmol/l) per month											
1 (Gilbertson 2001)	51 (6.9 ± 6.8 episodes at 12 months)	38 (5.8 ± 5.5 episodes at 12 months)	NA	MD 1.1 more (1.46 more to 3.66 fewer)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No Serious indirectness ³	No serious imprecision ⁵	None
Mean number of hyperglycaemic episodes (preprandial blood glucose > 15 mmol/l) per month											
1 (Gilbertson 2001)	51 (11.2 ± 9.8 episodes at 12 months)	38 (16.8 ± 11.8 episodes at 12 months)	NA	MD 5.6 fewer (10.22 to 0.98 fewer)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No Serious indirectness ³	Serious ⁵	None
Number adhering to treatment (up to 12 months)											
1 (Gilbertson 2001)	46/55 (83.6%)	32/49 (65.3%)	RR 1.28 (1.01 to 1.62)	183 more per 1000 (from 7 more to 405 more)	Moderate	RCT	No Serious risk of bias ¹	No Serious inconsistency ²	No Serious indirectness ³	Serious ⁵	None

MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk

1 No apparent risk of bias in the included study

2 Single-study analysis

3 Population, intervention and outcome as specified in the review protocol

4 Findings do not meet the GDG agreed minimally important difference (MID) of 0.5 percentage points for the change in HbA1c level

5 Confidence intervals cross two zones related to precision (see the 2015 methods section of the full guideline)

K.10 Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

Review question: What is the predictive value of symptoms, signs and biochemical abnormalities as indicators of diabetic ketoacidosis in children and young people?

Table 48: Evidence profile for diagnostic test accuracy of serum beta-hydroxybutyrate and end-tidal carbon dioxide as indicators of diabetic ketoacidosis

Number of	Number	Measure of diagnostic test accuracy (95% CI)	Quality	Quality assessment
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studies	of children and young people	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
Serum beta-hydroxybutyrate (cut-off ≥ 3 mmol/l) for detecting DKA (defined by serum bicarbonate ≤ 18 mEq/l)												
1 (Sheikh-Ali 2008)	129	0.92 (0.87 to 0.97) ^a	0.84 (0.70 to 0.91) ^a	5.86 (2.96 to 11.61) ^a	0.08 (0.04 to 0.18) ^a	Very low	Retrospective	Serious ¹	NA	No serious	Very serious ²	None
Serum beta-hydroxybutyrate (cut-off ≥ 3 mmol/l) for detecting DKA (defined by venous pH of < 7.3)												
1 (Prisco 2006)	90	0.83 (NC) ^b	0.68 (NC) ^b	2.59 (NC) ^b	0.25 (NC) ^b	Moderate	Prospective	No serious	NA	No serious	Serious ³	None
Serum beta-hydroxybutyrate (cut-off ≥ 3 mmol/l) for detecting DKA (defined by blood glucose > 13.9 mmol/l)												
1 (Prisco 2006)	110	0.57 (NC) ^b	0.83 (NC) ^b	3.35 (NC) ^b	0.52 (NC) ^b	Moderate	Prospective	No serious	NA	No serious	Serious ³	None
End-tidal carbon dioxide (cut-point ≤ 29 mmHg) for detecting DKA												
1 (Fearon 2002)	44	0.83 (0.52 to 0.98)	1.0 (0.88 to 1.0)	NC	0.17 (0.05 to 0.59) ^a	Low	Prospective	No serious	NA	No serious	Very serious	Used 29 torr (≈ 29 mmHg)
1 (Gilhotra 2007)	63	0.93 (0.70 to 0.99)	0.91 (0.78 to 0.96)	10.03 (3.91 to 25.76)	0.07 (0.01 to 0.49) ^a	Low	Prospective	No serious	NA	No serious	Very serious	
End-tidal carbon dioxide (cut-point ≤ 30 mmHg) for detecting DKA												
1 (Gilhotra 2007)	58	1.0 (0.78 to 1.0) ^c	0.86 (0.72 to 0.95) ^c	7.17 (3.41 to 15.05) ^a	0 (NC) ^{a,d}	Low	Prospective	Low	NA	No serious	Very serious ²	None
End-tidal carbon dioxide (cut-point < 36 mmHg) for detecting DKA												
1 (Fearon 2002)	42	1.0 (0.74 to 1.0) ^a	0.67 (0.47 to 0.83) ^a	3.0 (1.81 to 4.98) ^a	0 (NC) ^{a,d}	High	Prospective	Low	NA	No serious	No serious	Used 36 torr (≈ 36 mmHg)

CI confidence interval, DKA diabetic ketoacidosis, NA not applicable, NC not calculable,

a Calculated by the NCC-WCH technical team from data reported in the article

b Point estimate reported only; unable to calculate 95% CI from data reported

c Point estimate reported only, CI calculated by NCC-WCH technical team from data reported in the article

d Sensitivity = 1.0 therefore negative likelihood ratio = 0, and CI not calculable

1 Highly selected population – only included participants where medical records stated ‘diabetes with ketoacidosis’

2 Confidence interval for positive likelihood ratio ranges from not useful to definitely useful

K.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions:

What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?

Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:

- **general observations (for example, heart and respiratory rate and blood pressure)**
- **body weight**
- **hydration status**
- **fluid balance**
- **neurological observations**
- **electrocardiographic (ECG) monitoring?**

Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:

- **blood glucose**
- **blood or urine ketones**
- **serum urea or electrolytes**

- acid/base status?

Table 49: Evidence profile for comparison of blood ketone monitoring versus urine ketone monitoring during treatment of diabetic ketoacidosis

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias) ¹	Inconsistency ²	Indirectness ³	Imprecision	Other considerations
	Blood ketone monitoring	Urine ketone monitoring	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Mortality											
1 (Vanelli 2003)	0/16 (0%)	0/17 (0%)	NC	NC	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁴	None
Time to resolution of ketosis (proxy measure for duration of treatment)											
1 (Vanelli 2003)	16	17	NA	MD 6.5 hours fewer (from 4 to 9.4 hours fewer)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁵	None
1 (Prisco 2006)	99	NA	NA	MD 2.3 hours fewer (from 9.42 hours fewer to 4.82 hours more)	Very low	Case series	No serious risk of bias ¹	No serious inconsistency ²	Serious indirectness ⁶	Serious imprecision ⁷	None
1 (Noyes 2007)	28 episodes of DKA	NA	NA	Median difference 11 hours fewer (range 1 hour fewer to 36 hours fewer)	Low	Case series	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁵	Yes ⁸

DKA diabetic ketoacidosis, MD mean difference, NA not applicable, NC not calculable, RCT randomised controlled trial

1 No apparent risk of bias

2 Single-study analysis

3 Population, intervention and outcome as specified in the review protocol

4 No events reported

5 No minimally important difference specified by the GDG

6 Population includes a majority of participants without DKA

7 Confidence interval crosses the line of no effect

8 The 25 participants experienced a total of 40 episodes of DKA during the study period; 28 of the episodes which were followed up until negative ketonuria was obtained and included in this analysis

K.12 Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

Review question: What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis?

There are no evidence profiles for this review question because no studies were identified for inclusion.

Review question: At what rate should children and young people with diabetic ketoacidosis be rehydrated?

Table 50: Evidence profile for an increased rate of fluid administration in children and young people with diabetic ketoacidosis – case-control studies

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment					
	Cases (cerebral oedema)	Controls (no cerebral oedema)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
Effect of a per 5 ml/kg/hour increase in fluids												
1 (Glaser 2001)	61	183	RR 1.1 (0.4 to 3.0) ^{a,b}	NA	Low	Retrospective case control	No serious bias ¹	NA ²	No serious indirectness	Very serious ³	None	
Effect of a per 1ml/kg/hour increase in fluids												
1 (Lawrence 2005)	21	42	NA	MD 3.96 (0.80 to 7.12) ^c	Low	Prospective surveillance with retrospective case control	Serious ⁴	NA ²	No serious indirectness ⁵	Serious ⁶	Yes ⁷	
Effect of per tertile increases in fluids within the first 4 hours of treatment												
1 (Edge 2006)	43	169	OR 3.30 (0.71 to 15.27) ^{d,e,g}	NA	Low	Matched case control	No serious bias ⁸	NA ²	Serious ⁹	Very serious ¹⁰	None	
1 (Edge 2006)	43	169	OR 6.55 (1.38 to 30.97) ^{d,f,g}	NA	Moderate	Matched case control	No serious bias ⁸	NA ²	Serious ⁹	No serious imprecision ¹¹	None	
Effect of the rate of fluid administration in the first 4 hours of treatment												
1 (Mahoney 1999)	9	186	NA	MD 36.4 (8.9 to 63.9) ^h	Very low	Retrospective chart review	Very serious ^{12,13,14}	NA ²	No serious indirectness	No serious imprecision ¹⁵	None	

CI confidence interval, DKA diabetic ketoacidosis, MD mean difference, MID minimally important difference, NA not applicable, OR odds ratio, RR risk ratio

a Study used both matched and unmatched controls; results presented are for matched controls as unmatched analyses did not include treatment-related variables

b Reported as RR by study authors based on the rare disease assumption; effect estimate actually derived from conditional multivariate logistic regression; controls were matched to cases by age, onset of diabetes, venous pH at presentation and serum glucose at presentation

- c Calculated by the NCC-WCH technical team using a standard deviation based on the t-distribution due to a small sample size
- d Adjusted for matching variables: age, sex and whether diabetes was newly diagnosed as well as baseline acidosis
- e OR represents the increase in risk of cerebral oedema for tertile 2 (512 ml to 879 ml) versus tertile 1 (referent category: 76 ml to 511 ml) of fluids administered
- f OR represents the increase in risk of cerebral oedema for tertile 3 (892 ml to 4090 ml) versus tertile 1 (referent category: 76 ml to 511 ml) of fluids administered
- g Evidence for an overall trend for the effect of increasing fluid administration was also tested, adjusted for age, sex, new or known diabetes and baseline acidosis; the p-value for this test was < 0.02 indicating that increasing volumes of fluid increased the risk of cerebral oedema
- h Calculated by the NCC-WCH technical team based on the normal distribution
- 1 Imputation of 12% of continuous variables due to missing data; method of imputation was not described
- 2 Single-study analysis
- 3 Confidence interval for the RR crosses all three zones related to precision (see 'Methodology for 2015 update')
- 4 To increase the numbers of cases identified a retrospective medical records search was undertaken and data combined with that from prospective surveillance
- 5 Diagnosis of cerebral oedema allowed inclusion of participants with normal neuroimaging based on the premise that clinical diagnosis is often sufficient
- 6 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update') based on an MID of 2.31 calculated by the NCC-WCH technical team using sample means and standard deviations
- 7 Diabetes type was not reported
- 8 Retrospective review of case reports led to matching being ineffective and therefore broken for analysis as controls were unavailable for a large proportion of cases within matched sets
- 9 Indirectness due to the use of tertiles of fluid administration
- 10 Confidence interval for the OR cross all three zones related to precision (see 'Methodology for 2015 update')
- 11 Confidence interval for the OR is entirely within one zone related to precision (see 'Methodology for 2015 update')
- 12 More than one episode of DKA per participant was included in analyses for participants without cerebral oedema or brain herniation
- 13 Selection bias is likely as groups were not comparable for baseline characteristics
- 14 Groups did not receive the same care
- 15 Confidence interval is entirely within one zone related to precision (see 'Methodology for 2015 update') based on an MID of 3.85 calculated by the NCC-WCH technical team using sample means and standard deviations

Table 51: Evidence profile for a slower rate of fluid administration compared with a faster rate of fluid administration in children and young people with diabetic ketoacidosis – randomised study

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Intervention (slower rate)	Comparator (faster rate)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Risk of mild cerebral oedema (brain swelling) ^a											
1 (Glaser 2013)	10/18	8/18	NA	Two-tailed p-value 0.63 ^b	Very low ^c	Randomised controlled trial pilot study	No serious bias	NA ¹	Serious ²	Very serious ^{3,4,5}	None

ADC apparent brain diffusion coefficient, CI confidence interval, MID minimally important difference, NA not applicable, RCT randomised controlled trial
 a One group received a bolus of 0.9% saline of 20 ml/kg with two-thirds of fluid deficit replaced over the first 24 hours and the remaining third replaced over the next 24 hours (a fluid deficit of 10% was assumed); the other treatment group received a bolus of 0.9% saline of 10 ml/kg with fluid deficit replaced evenly over 48 hours (a fluid deficit of 7% was assumed)

b Calculated by the NCC-WCH technical team using the Wilcoxon rank sum test for non-parametric data using an online calculator at cs.fairfield.edu/~sawin/stats/templates/wilcoxon.xls; individual patient data were obtained from study authors as results were presented graphically in the original article

c Starting point of moderate quality as the study is a pilot study for an RCT

1 Single-study analysis

2 ADC to detect brain swelling was used as a proxy for mild cerebral oedema

3 Not sufficiently powered to detect small differences and power calculations were not aimed at detecting between-group differences; calculations were to detect a 1.3 standard deviation change in ADC between treatment and post-recovery

4 No confidence interval was calculable as data were not normally distributed

5 MID not calculable

Table 52: Evidence profile for a slower rate of fluid administration compared with a faster rate of fluid administration in children and young people with diabetic ketoacidosis – partially randomised study

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Slower rate ^{a,b}	Faster rate ^{a,b}	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Time to resolution of acidosis, hours											
1 (Felner 2001)	30	60	NA	MD -4.10 (-5.88 to -2.32) ^c	Very low	Partially randomised cohort study	Serious ¹	No serious inconsistency ²	No serious indirectness	Serious ³	Yes ⁴
Change in serum sodium, mmol/l											
1 (Felner 2001)	30	60	NA	MD 0.00 (-1.78 to 1.78) ^c	Very low	Partially randomised cohort study	Very serious ^{5,6}	No serious inconsistency ²	Serious ⁷	No serious imprecision ⁸	Yes ⁴
Change in serum chloride, mmol/l											
1 (Felner 2001)	30	60	NA	MD 1.95 (-0.78 to 4.68) ^c	Very low	Partially randomised cohort study	Very serious ^{5,6}	No serious inconsistency ²	Serious ⁷	Serious ⁹	Yes ⁴
Admission to ICU ^d											
1 (Felner 2001)	30	60	RR 0.95 (0.48 to 1.86) ^c	NA	Very low	Partially randomised cohort study	No serious bias	No serious inconsistency ²	No serious indirectness	Very serious ¹⁰	Yes ⁴

CI confidence interval, ICU intensive care unit, MD mean difference, NA not applicable

a Treatment groups were assigned based on the introduction of a new treatment protocol in 1997; for the faster rate group fluid deficit was calculated based on the percentage of dehydration (7 to 10%) by weight in kg and added to 1.5 times the required maintenance rate (50% of the fluids were administered in the first 12 hours and the remaining 50% over the next 24 hours); the slower rate group received total fluids at a rate of 2.5 times the required maintenance rate regardless of the degree of dehydration (fluids were decreased to 1 to 1.5 times the maintenance rate after 24 hours of treatment)

b The total mean volumes of fluid (l/m²/24 hours) were 5.3 ± 1.4 and 5.4 ± 1.2 for the faster rate group, depending on whether a two- or three-bag protocol was used, and 4.1 ± 1.1 for the slower rate group

c Calculated by the NCC-WCH technical team using the t-distribution due to a small sample size

d Admission to ICU was defined according to symptoms and signs including altered level of consciousness, severe acidosis (pH < 7.00), haemodynamic instability, or very young age (< 3 years)

1 Resolution of acidosis was not defined

2 Single-study analysis

3 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update') based on an MID of 3.70 calculated by the NCC-WCH technical team using sample means and standard deviations

4 The study authors conducted retrospective analyses on non-randomised participants to compare groups 1A and 1B due to subtle differences in the treatment protocols (three-versus two-bag rehydration); no statistically significant differences were observed therefore data were pooled by the NCC-WCH technical team

5 The amount of sodium chloride varied slightly between treatment groups (0.45% for the faster rate group and 0.675% for the slower rate group)

6 The time over which the change in serum levels of biochemical variables was assessed was not reported

7 Serum levels were reported as change scores not actual values after treatment

8 Confidence interval is entirely within one zone related to precision (see 'Methodology for 2015 update') based on an MID of 2.26 calculated by the NCC-WCH technical team using sample means and standard deviations

9 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update') based on an MID of 3.33 calculated by the NCC-WCH technical team using sample means and standard deviations

10 Confidence interval for the RR crosses all three zones related to precision (see 'Methodology for 2015 update')

Review question: What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

Table 53: Evidence profile for comparison of 75 mEq/l concentration of sodium with 100 mEq/l concentration of sodium for the treatment of diabetic ketoacidosis in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment					
	Intervention (75 mEq/l)	Comparator (100 mEq/l)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
Plasma sodium (corrected)												
<i>Baseline</i>												
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD 0.7 (-3.1 to 4.5) ^a	Very low	Retrospective chart review	Serious ¹	NA ²	No serious indirectness	Very serious ³	None	
<i>4 hours' follow-up</i>												
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD 0.6 (-3.0 to 4.2) ^a	Very low	Retrospective chart review	Serious ¹	NA ²	No serious indirectness	Very serious ⁴	None	
<i>8 hours' follow-up</i>												
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -1.5 (-5.3 to 2.3) ^a	Very low	Retrospective chart review	Serious ¹	NA ²	No serious indirectness	Serious ⁵	None	
<i>16 hours' follow-up</i>												
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -0.2 (-2.7 to 2.3) ^a	Very low	Retrospective chart review	Serious ¹	NA ²	No serious indirectness	Very serious ⁶	None	
<i>24 hours' follow-up</i>												
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -0.6 (-3.1 to 1.9) ^a	Very low	Retrospective chart review	Serious ¹	NA ²	No serious indirectness	Very serious ⁷	None	
Plasma carbon dioxide												
<i>Baseline</i>												
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -0.9 (-4.8 to 3.0) ^a	Very low	Retrospective chart review	Serious ¹	NA ²	No serious indirectness	Very serious ⁸	None	
<i>4 hours' follow-up</i>												
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -0.2	Very	Retrospective	Serious ¹	NA ²	No serious	Very serious ⁹	None	

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment					
	Intervention (75 mEq/l)	Comparator (100 mEq/l)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
Erdeve 2011)				(-4.8 to 4.4) ^a	low	chart review			indirectness			
8 hours' follow-up												
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -0.8 (-5.5 to 3.9) ^a	Very low	Retrospective chart review	Serious ¹	NA ²	No serious indirectness	Very serious ¹⁰	None	
16 hours' follow-up												
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD 0.4 (-3.5 to 4.3) ^a	Very low	Retrospective chart review	Serious ¹	NA ²	No serious indirectness	Very serious ¹¹	None	
24 hours' follow-up												
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -1.2 (-5.9 to 3.5) ^a	Very low	Retrospective chart review	Serious ¹	NA ²	No serious indirectness	Very serious ¹²	None	
pH												
Baseline												
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD -0.10 (-0.21 to 0.01) ^a	Very low	Retrospective chart review	Serious ¹	NA ²	No serious indirectness	Serious ¹³	None	
4 hours' follow-up												
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD 0.00 (-0.07 to 0.07) ^a	Very low	Retrospective chart review	Serious ¹	NA ²	No serious indirectness	Very serious ¹⁴	None	
8 hours' follow-up												
1 (Savas-Erdeve et al., 2011)	19/32	13/32	NA	MD -0.06 (-0.13 to 0.01) ^a	Very low	Retrospective chart review	Serious ¹	NA ²	No serious indirectness	Serious ¹⁵	None	
16 hours' follow-up												
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD 0.0 (-0.7 to 0.7) ^a	Very low	Retrospective chart review	Serious ¹	NA ²	No serious indirectness	Very serious ¹⁶	None	
24 hours' follow-up												
1 (Savas-Erdeve 2011)	19/32	13/32	NA	MD 0.0 (-0.7 to 0.7) ^a	Very low	Retrospective chart review	Serious ¹	NA ²	No serious indirectness	Very serious ¹⁶	None	

ANOVA analysis of variance, CI confidence interval, MD mean difference, MID minimally important difference, NA not applicable

a Calculated by the NCC-WCH technical team using confidence intervals based on the t-distribution due to a small sample size

1 Analysis used ANOVA however there is no mention of potential confounders being accounted for in the analysis

2 Single-study analysis

3 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 2.48 calculated by the NCC-WCH technical team using sample means and standard deviations

4 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 2.37 calculated by the NCC-WCH technical team using sample means and standard deviations

- 5 Confidence interval crosses more than one zone related to precision (see 'Methodology for 2015 update') based on an MID of 2.42 calculated by the NCC-WCH technical team using sample means and standard deviations
- 6 Confidence interval spans crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 1.57 calculated by the NCC-WCH technical team using sample means and standard deviations
- 7 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 1.49 calculated by the NCC-WCH technical team using sample means and standard deviations
- 8 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 2.59 calculated by the NCC-WCH technical team using sample means and standard deviations
- 9 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 3.03 calculated by the NCC-WCH technical team using sample means and standard deviations
- 10 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 3.08 calculated by the NCC-WCH technical team using sample means and standard deviations
- 11 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 2.63 calculated by the NCC-WCH technical team using sample means and standard deviations
- 12 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') zones based on an MID of 3.19 calculated by the NCC-WCH technical team using sample means and standard deviations
- 13 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 0.09 calculated by the NCC-WCH technical team using sample means and standard deviations
- 14 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 0.05 calculated by the NCC-WCH technical team using sample means and standard deviations
- 15 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update') based on an MID of 0.05 calculated by the NCC-WCH technical team using sample means and standard deviations
- 16 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 0.46 calculated by the NCC-WCH technical team using sample means and standard deviations

Table 54: Evidence profile for comparison of bicarbonate with no bicarbonate for the treatment of diabetic ketoacidosis in children and young people

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment					
	Intervention (bicarbonate)	Comparator (no bicarbonate)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
Duration of hospitalisation, hours												
1 (Green 1998)	57/106 Mean duration 85 (75 to 95)	49/106 Mean duration 69 (58 to 60)	NA	Adjusted R2 0.23, p-value 0.07 ^{a,b}	Very low	Retrospective case series	Serious ¹	NA ²	Serious ³	No serious imprecision ⁴	Yes ^{5,6}	
1 (Marr 1981) ^c	45	33	NA	MD 1.75 (0.04 to 3.46) ^d	Very low	Retrospective chart review	Serious ⁷	NA ²	Serious ⁸	Serious ⁹	Yes ⁵	
Risk of cerebral oedema												
1 (Lawrence 2005)	4/17 cases 1/34 controls	13/17 cases 33/34 controls	OR 10.15 (1.03 to 99.57) ^e	NA	Very low	Surveillance and retrospective case control	Serious ¹⁰	NA ²	No serious indirectness	Serious ¹¹	Yes ⁵	

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Intervention (bicarbonate)	Comparator (no bicarbonate)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
1 (Edge 2006)	5/43 cases 6/169 controls	38/43 cases 163/169 controls	OR 3.70 (1.02 to 13.10)	NA	Very low	Matched case control	No serious bias ¹²	NA ²	No serious indirectness	Serious ¹¹	None
Risk of cerebral oedema adjusted for baseline acidosis											
1 (Edge 2006)	5/43 cases 6/169 controls	38/43 cases 163/169 controls	OR 1.50 (0.39 to 5.76) ^f	NA	Very low	Matched case control	No serious bias ¹²	NA ²	No serious indirectness	Very serious ¹³	None
Duration of acidosis, hours											
1 (Marr 1981) ^c	45	33	NA	MD -2.70 (-5.20 to -0.20) ^d	Very low	Retrospective chart review	Very serious ^{5,14}	NA ²	Serious ⁶	Serious ¹⁵	Yes ⁵

CI confidence interval, DKA diabetic ketoacidosis, MD mean difference, MID minimally important difference, NA not applicable, OR odds ratio, RR relative risk

a R² represents the correlation between duration of hospitalisation and the administration of bicarbonate

b Adjusted for calendar year, pH, base deficit, creatinine and haemoglobin because treatment groups were not comparable at baseline for these variables

c Comparison of children and young people who received sodium as either sodium bicarbonate, or sodium bicarbonate plus saline, or sodium bicarbonate and saline and lactate Ringers, or sodium bicarbonate and lactate Ringers with children and young people who received saline alone, lactate Ringers, or lactate Ringers with saline

d Calculated by the NCC-WCH technical team

e Crude effect estimate calculated by the NCC-WCH technical team

f The OR was also adjusted for age, sex and whether diabetes was newly diagnosed

1 Missing data were present for 124 out of 486 admissions reviewed for inclusion and these admissions were, therefore, excluded from analyses; high risk of bias

2 Single-study analysis

3 Only severe cases of DKA were included in the study; generalisability is reduced

4 MID not calculable.

5 Diabetes type not reported

6 Data from matched analyses were not used by the NCC-WCH technical team due to the high percentage of missing data (41%) generated by the matching process (49 participants per group, reduced to 29 participants per group after matching)

7 No baseline characteristics were reported; selection bias is likely

8 Treatments were grouped according to data extracted from medical records and combined by the NCC-WCH technical team to derive comparisons which best matched the review protocol

9 Confidence interval crosses more than one zone related to precision (see 'Methodology for 2015 update') based on an MID of 2.41 calculated by the NCC-WCH technical team using sample means and standard deviations

10 Results are from only 17 of 21 cases and 34 of 42 controls; loss of information is likely to have caused bias

11 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')

12 Retrospective review of case reports led to matching being ineffective and therefore broken for analysis as controls were unavailable for a large proportion of cases within matched sets

13 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update')

14 Acidosis was not defined

15 Confidence interval crosses more than one zone related to precision (see 'Methodology for 2015 update') based on an MID of 3.48 calculated by the NCC-WCH technical team using sample means and standard deviations

Table 55: Evidence profile for the use of bicarbonate in treating diabetic ketoacidosis in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Cases (cerebral oedema)	Controls (no cerebral oedema)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Treatment with bicarbonate											
1 (Glaser 2001)	61	183	RR 4.2 (1.5 to 12.1) ^a	NA	Moderate ^b	Retrospective case control	No serious bias	NA ¹	No serious indirectness	No serious imprecision ²	None

CI confidence interval, NA not applicable, RR relative risk

a Reported as RR by study authors based on the rare disease assumption; effect estimate actually derived from conditional multivariate logistic regression; controls were matched to cases by age, onset of diabetes, venous pH at presentation and serum glucose at presentation

b Quality upgraded due to a large effect size

1 Single-study analysis

2 Confidence interval is entirely in one zone related to precision (see 'Methodology for 2015 update')

Table 56: Evidence profile for comparison of phosphate with no phosphate for the treatment of diabetic ketoacidosis in children and young people

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Intervention (phosphate)	Comparator (no phosphate)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Serum calcium											
1 (Becker 1983)	13	9	NA	MD -1.1 (-1.7 to -0.5) ^{a,b}	Very low	Partially randomised prospective cohort	Very serious ^{1,2,3,4}	NA ⁵	No serious indirectness	No serious imprecision ⁶	Yes ⁷

CI confidence interval, MD mean difference, NA not applicable

a Calculated by the NCC-WCH technical team using confidence intervals based on the t-distribution due to a small sample size

b The intervention group received potassium replacement as mono- or di-basic phosphate salts versus controls who received no phosphate

1 Controls were not allocated using randomisation; randomisation method for the treatment groups is not described

2 Controls were less severe cases and received substantially different treatment compared with the two randomised treatment groups

3 Groups were not comparable at baseline

4 Data were presented graphically in the original article; numerical data were reported only for values at 12 hours' follow-up because results were significant for phosphate versus controls; high risk of reporting bias

5 Single-study analysis

6 Confidence interval crosses all three zones related to precision (see 'Methodology for 2015 update') based on an MID of 0.29 calculated by the NCC-WCH technical team using sample means and standard deviations

7 Diabetes type is not reported

K.13 Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents

Review question: What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?

Table 57: Effectiveness of intravenous osmotic agents in the treatment of cerebral oedema associated with diabetic ketoacidosis in children and young people with type 1 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment					
	Mannitol	Hypertonic saline	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
Adjusted odds ratio of mortality for hypertonic saline alone versus mannitol alone												
1 (DeCoursey 2013)	NA	NA	2.71 (1.01 to 7.26) ^{5,6}	NA	Very low	Retrospective cohort	Serious ¹	NA ²	Serious indirectness ³	Very serious imprecision ⁴	None	
Healthcare utilisation: brain imaging with CT scan (%)												
1 (DeCoursey 2013)	525/1202 (43.7)	109/299 (36.5)	NA	NA	Very low	Retrospective cohort	Serious ¹	NA ²	Serious indirectness ³	Very serious imprecision ⁴	None	
Healthcare utilisation: mechanical ventilation (%)												
1 (DeCoursey 2013)	184/1202 (15.3)	43/299 (14.4)	NA	NA	Very low	Retrospective cohort	Serious ¹	NA ²	Serious indirectness ³	Very serious imprecision ⁴	None	
Healthcare utilisation: intensive care unit admission (%)												
1 (DeCoursey 2013)	784/1202 (65.2)	269/299 (90)	NA	NA	Very low	Retrospective cohort	Serious ¹	NA ²	Serious indirectness ³	Very serious imprecision ⁴	None	

CI confidence interval, NA not applicable

1 More participants in the hypertonic saline group were admitted to intensive care unit (ICU) than those in the mannitol group

2 Single-study analysis

3 Upper age limit is slightly higher than the guideline population and a small number of participants (< 1.5% total) who may not have had cerebral oedema associated with diabetic ketoacidosis (DKA) were included in the analysis

4 Confidence interval crosses three zones related to precision (see 'Methodology for 2015 update')

5 Adjusted for discharge year, hospital clustering, gender, mechanical ventilation, brain imaging with CT scan, ICD-9 code (diabetes with hyperosmolar state (250.2) or diabetes with coma (250.3))

6 Treatment group with both hypertonic saline and mannitol was excluded from further analysis as participants treated with both agents would have been switched to the alternative agent once the initial therapy failed and the study database did not allow for the order of therapy intervention to be determined

K.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

Review question: When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?

Table 58: Evidence profile for the effect of insulin administered within 1 hour of fluid replacement compared to insulin administered at least 1 hour after fluid administration on the risk of cerebral oedema

Number of studies	Number of patients		Effect		Quality	Design	Quality assessment				
	Cases (cerebral oedema)	Controls (no cerebral oedema)	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Association between timing of insulin therapy and risk of cerebral oedema											
1 (Edge 2006)	43	169	Adjusted OR: 4.7 (1.5 to 13.9) ^{a,b}	NA	Moderate	Matched case control	No serious bias ^{1,2,3}	Not relevant	No serious indirectness	No serious imprecision ^{4,5}	None
Association between timing of insulin therapy and risk of cerebral oedema, adjusted for baseline biochemical measures to account for severity of acidosis											
1 (Edge 2006)	43	169	Adjusted OR: 12.7 (1.41 to 114.5) ^{a,b,c}	NA	Moderate	Matched case control	No serious bias ^{1,2,3}	Not relevant	No serious indirectness	No serious imprecision ^{4,5}	None

CI confidence interval, OR odds ratio, NA not applicable

a OR is for participants who received insulin therapy within 1 hour of fluid replacement compared to those who did not

b Adjusted for matching variables: age, sex and whether diabetes was newly diagnosed as well as baseline acidosis

c Baseline biochemical measures included in the multivariate model included: plasma glucose, potassium, urea, sodium and paCO₂

1 Retrospective review of case reports led to matching being ineffective and therefore broken for analysis as controls were unavailable for a large proportion of cases within matched sets

2 Whether controls were clearly established as not being cases was not reported

3 Standardisation of exposure measurement was not clear

4 Large effect size

5 Wide CI suggests imprecision but CI is entirely within one zone related to precision (see 'Methodology for 2015 update') therefore not downgraded

Review question: How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

Table 59: Comparison of insulin dosage of 0.025 U/kg/hour or 0.05 U/kg/hour with a dosage of 0.1 U/kg/hour in children and young people with type 1 diabetes and DKA

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment					
	Low dosage insulin	Standard dosage insulin	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
Change in blood glucose from admission (low dosage 0.05 U/kg/hour)												
<i>Children of all ages</i>												
1 (Al Hanshi 2011)	N = 33 Median difference: -17 mmol/l (IQR: -26 to -12)	N = 34 Median difference: -21 mmol/l (IQR: -52 to -15)	NA	P-value = 0.004, adjusted R = 0.62 ^a	Very low	Retrospective cohort	Serious ¹	NA ⁵	No serious indirectness	No serious imprecision ⁸		
1 (Puttha 2010)	N = 41 MD: 11.3 mmol/l (8.6 to 13.9)	N = 52 MD: 11.8 mmol/l (8.4 to 15.2)	NA	MD: -0.50 (-4.75 to 3.75) ^b	Very low	Retrospective cohort	Very serious ^{2,3}	NA ⁵	No serious indirectness	No serious imprecision ⁸	Short follow-up period	
<i>Subgroup analysis: children aged less than 5 years</i>												
1 (Puttha 2010)	N = 6 MD: 15.9 mmol/l (2.2 to 29.5)	N = 5 MD: 20.1 mmol/l (10.6 to 29.6)	NA	MD: -4.20 (-20.61 to 12.21) ^b	Very low	Retrospective cohort	Very serious ^{2,3}	NA ⁵	No serious indirectness ⁶	No serious imprecision ⁸	Short follow-up period	
Incidence of hypoglycaemia (low dosage 0.025 U/kg/hour)												
1 (Kapellen 2012)	8/23	2/41	RR: 7.13 (1.65 to 30.79) ^c	NA	Very low	Retrospective cohort	Very serious ^{2,3}	NA ⁵	No serious indirectness ⁶	No serious imprecision ⁹		
Incidence of hypoglycaemia (low dosage 0.05 U/kg/hour)												
1 (Puttha 2010)	0/41	7/80	RR: 0.13 (0.008 to 2.22) ^c	NA	Very low	Retrospective cohort	Very serious ^{2,3}	NA ⁵	No serious indirectness ^{6,7}	Very serious ¹⁰		
Incidence of hypokalaemia (low dosage 0.025 U/kg/hour)												
1 (Kapellen 2012)	3/23	15/41	RR: 0.36 (0.12 to 1.10) ^c	NA	Very low	Retrospective cohort	Very serious ^{2,3,4}	NA ⁵	No serious indirectness ⁶	Serious ¹¹		
Change in blood pH from admission (low dosage 0.05 U/kg/hour)												
<i>Children of all ages</i>												
1 (Puttha 2010)	N = 41 MD: 0.13 (0.09 to 0.18)	N = 52 MD: 0.11 (0.07 to 0.15)	NA	MD: 0.02 (-0.04 to 0.08) ^b	Very low	Retrospective cohort	Very serious ^{2,3}	NA ⁵	No serious indirectness ⁶	No serious imprecision ⁸	Short follow-up period	
<i>Subgroup analysis: children aged less than 5 years</i>												

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Low dosage insulin	Standard dosage insulin	Relative (95% CI)	Absolute (95% CI)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
1 (Puttha 2010)	N = 6 MD: 0.17 (-0.01 to 0.31)	N = 5 MD: 0.15 (-0.8 to 0.40)	NA	MD: 0.02 (-0.26 to 0.30) ^b	Very low	Retrospective cohort	Very serious ^{2,3}	NA ⁵	No serious indirectness ⁶	No serious imprecision ⁸	Short follow-up period
Time to pH > 7.3 (resolution of acidosis)											
1 (Puttha 2010)	N = 41	N = 52	NA	MD: -1.3 (-4.4 to 1.8) ^b	Very low	Retrospective cohort	Very serious ^{2,3}	NA ⁵	No serious indirectness ⁶	No serious imprecision ⁸	Short follow-up period

CI confidence interval, IQR interquartile range, MD mean difference, MID minimally important difference, NA not applicable, RR relative risk
a R represents the correlation between insulin dose and plasma glucose at 12 hours' follow-up, adjusted for the baseline value and age
b Confidence intervals calculated by the NCC-WCH technical team using a standard deviation based on the t-distribution due to small sample size
c Calculated by the NCC-WCH technical team
 1 Dosages were changed from initial values in some participants
 2 Failure to adequately control for confounding
 3 Participants not selected from the same population
 4 Differences between groups may be due to differences in treatment protocols for management of blood potassium
 5 Single-study analysis
 6 Population and measurement outcome match the protocol
 7 Participants from 1 PICU centre were included in the analysis; this may have reduced generalisability or skewed results due to the inclusion of more severe cases
 8 The GDG did not specify a MID for this outcome
 9 Confidence interval entirely within one zone related to precision (see 'Methodology for 2015 update')
 10 Confidence interval cross all three zones related to precision (see 'Methodology for 2015 update')
 11 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')

K.15 Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis

Review question: What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?

There are no evidence profiles for this review question because no studies were identified for inclusion.

K.16 Type 1 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?

Table 60: Evidence profile for prevalence of retinopathy according to age

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Age < 9 years									
8 (Frank 1982, Cerutti 1989, Johansen 1994, Klein 1984, Kernell 1997, Joner 1992, Flack 1996, Donaghue 1999)	NC	0.0 to 9.0 (4.5)	Moderate	Cross sectional and prospective cohort	No serious risk of bias	No serious inconsistency	No serious indirectness	NA ¹	None
Age 9 years									
8 (Frank 1982, Cerutti 1989, Johansen 1994, Klein 1984, Kernell 1997, Joner 1992, Flack 1996, Donaghue 1999)	NC	0.0 to 9.0 (4.5)	Moderate	Cross sectional and prospective cohort	No serious risk of bias	No serious inconsistency	No serious indirectness	NA ¹	None
Age 10 years									
9 (Cerutti 1989, Massin 2007, Kernell 1997, Johansen 1994, Joner 1992, Flack 1996, Frank 1982, Donaghue 1999, Klein 1984)	NC	0.0 to 15.0 (6.7)	Low ^a	Cross sectional and prospective cohort	No serious risk of bias	Serious inconsistency ²	No serious indirectness	NA ¹	None
Age 11 years									
8 (Cerutti 1989, Massin 2007, Johansen I 1994, Cho 2011, Joner 1992, Flack 1996, Frank 1982, Klein 1984)	NC	0.0 to 15.0 (6.4)	Low ^a	Cross sectional and prospective cohort	No serious risk of bias	Serious inconsistency ²	No serious indirectness	NA ¹	None
Age 12 years									
9 (Massin 2007, Johansen 1994, Cho 2011, Joner 1992, Flack 1996, Frank 1982, Cerutti 1989, Klein 1984, Olsen I 2004)	NC	1.0 to 19.0 (7.7)	Low ^a	Cross sectional and prospective cohort	No serious risk of bias	Serious inconsistency ²	No serious indirectness	NA ¹	None
Age 13 years									

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
8 (Massin 2007, Johansen 1994, Frank 1982, Cho 2011, Klein 1984, Olsen 2004, Flack 1996, Cerutti 1989)	NC	1.0 to 25.0 (13.0)	Low ^a	Cross sectional and prospective cohort	No serious risk of bias	Serious inconsistency ²	No serious indirectness	NA ¹	None
Age 14 years									
8 (Massin 2007, Johansen 1994, Frank 1982, Cho 2011, Klein 1984, Olsen 2004, Flack 1996, Cerutti 1989)	NC	5.8 to 44.0 (13.0)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ¹	None
Age 15 years									
8 (Massin 2007, Johansen 1994, Cho 2011, Olsen 2004, Flack 1996, Cerutti 1989, Frank 1982, Klein 1984)	NC	5.8 to 54.0 (28.7)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ¹	None
Age 16 years									
6 (Cho 2011, Massin 2007, Flack 1996, Cerutti 1989, Frank 1982, Klein 1984)	NC	11.0 to 54.0 (42.8)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ¹	None
Age 17 years									
5 (Massin 2007, Cerutti 1989, Flack 1996, Frank 1982, Klein 1984)	NC	17.7 to 54.0 (45.7)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ¹	None
Age 18 years									
5 (Massin 2007, Flack 1996, Frank 1982, Klein 1984, Cerutti 1989)	NC	17.7 to 60.0 (48.0)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ¹	None

NA not applicable, NC not calculable

a Serious inconsistency between point estimates

b Very serious inconsistency between point estimates

1 Unable to comment on imprecision as no confidence intervals reported for ranges

2 Serious inconsistency as range of point estimates varies between 10 and 20 percentage points

3 Very serious inconsistency as range of point estimates varies by more than 20 percentage points

Table 61: Evidence profile for prevalence of retinopathy according to duration of diabetes

Number of studies	Number of	Range of	Quality	Design	Quality assessment
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Appendix K: GRADE tables

	children and young people	prevalence, % (median, %)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Duration < 2 years									
6 (Frank 1982, Massin 2007, Kernell 1997, Flack 1996, Lobefalo 1997, Murphy 1990)	NC	1.0 to 21.0 (7.9)	Low ^a	Cross sectional and prospective cohort	No serious risk of bias	Serious inconsistency ¹	No serious indirectness	NA ²	None
Duration 2 years									
6 (Frank 1982, Massin 2007, Cho 2011, Flack 1996, Lobefalo 1997, Murphy 1990)	NC	1.0 to 21.0 (10.9)	Low ^a	Cross sectional and prospective cohort	No serious risk of bias	Serious inconsistency ¹	No serious indirectness	NA ²	None
Duration 3 years									
7 (Frank 1982, Massin 2007, Cho 2011, Flack 1996, Lobefalo 1997, Murphy 1990, Cerutti 1989)	NC	1.0 to 23.0 (10.5)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ²	None
Duration 4 years									
7 (Frank 1982, Massin 2007, Cho 2011, Flack 1996, Lobefalo 1997, Murphy 1990, Cerutti 1989)	NC	1.0 to 23.0 (10.5)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ²	None
Duration 5 years									
7 (Massin 2007, Cho 2011, Flack 1996, Lobefalo 1997, Cerutti 1989, Frank 1982, Murphy 1990)	NC	6.2 to 50.0 (13.6)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ²	None
Duration 6 years									
6 (Massin 2007, Flack 1996, Lobefalo 1997, Frank 1982, Cerutti 1989, Murphy 1990)	NC	6.2 to 50.0 (19.3)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ²	None
Duration 7 years									
6 (Massin 2007, Flack 1996, Lobefalo 1997, Frank 1982, Cerutti 1989, Murphy 1990)	NC	6.2 to 50.0 (22.9)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ²	None
Duration 8 years									
7 (Massin 2007, Joner 1992, Flack 1996, Lobefalo 1997, Frank 1982, Cerutti 1989, Murphy 1990)	NC	6.2 to 50.0 (20.7)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ²	None
Duration 9 years									
6 (Massin 2007, Lobefalo 1997, Frank 1990)	NC	6.2 to 59.0 (37.0)	Very low ^b	Cross sectional and prospective	No serious	Very serious inconsistency ³	No serious indirectness	NA ²	None

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Appendix K: GRADE tables

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment					
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
1982, Goldstein 1993, Murphy 1990, Flack 1996)				cohort	risk of bias					
Duration 10 years										
6 (Massin 2007, Lobefalo 1997, Kernell 1997, Murphy 1990, Flack 1996, Frank 1982)	NC	6.2 to 67.0 (41.0)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ²	None	
Duration 11 years										
7 (Massin 2007, Lobefalo 1997, Kernell 1997, Cerutti 1989, Flack 1996, Frank 1982, Murphy 1990)	NC	13.0 to 75.0 (57.5)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ²	None	
Duration 12 years										
7 (Massin 2007, Lobefalo 1997, Kernell 1997, Flack 1996, Cerutti 1989, Frank 1982, Murphy 1990)	NC	13.0 to 75.0 (57.1)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ²	None	
Duration 13 years										
6 (Massin 2007, Lobefalo 1997, Flack 1996, Cerutti 1989, Frank 1982, 1990)	NC	13.0 to 75.0 (57.3)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ²	None	
Duration 14 years										
6 (Massin 2007, Lobefalo 1997, Joner 1992, Flack 1996, Cerutti 1989, Murphy 1990)	NC	13.0 to 75.0 (53.1)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ²	None	
Duration 15 years										
7 (Massin 2007, Lobefalo 1997, Flack 1996, Cerutti 1989, Frank 1982, Murphy 1990, Goldstein 1993)	NC	13.0 to 92.0 (57.5)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ²	None	
Duration 16 years										
6 (Massin 2007, Lobefalo 1997, Flack 1996, Cerutti 1989, Frank 1982, Murphy 1990)	NC	13.0 to 75.0 (57.3)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ²	None	
Duration 17 years										
5 (Massin 2007,	NC	13.0 to 75.0	Very low ^b	Cross sectional	No	Very serious	No serious	NA ²	None	

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Lobefalo 1997, Flack 1996, Cerutti 1989, Murphy 1990)		(57.1)		and prospective cohort	serious risk of bias	inconsistency ³	indirectness		
Duration 18 years									
4 (Massin 2007, Lobefalo 1997, Flack 1996, Murphy 1990)	NC	13.0 to 75.0 (38.9)	Very low ^b	Cross sectional and prospective cohort	No serious risk of bias	Very serious inconsistency ³	No serious indirectness	NA ²	None

NA not applicable, NC not calculable

a Serious inconsistency between point estimates

b Very serious inconsistency between point estimates

1 Serious inconsistency as range of point estimates varies between 10 and 20 percentage points

2 Unable to comment on imprecision as no confidence intervals reported for ranges

3 Very serious inconsistency as range of point estimates varies by more than 20 percentage points

Table 62: Evidence profile for incidence of retinopathy

Number of studies	Number of children and young people	Incidence per hundred person years	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Any sustained retinopathy									
1 (DCCT Research Group 1994)	55	18	High	Randomised controlled trial	No serious risk of bias	NA	No serious indirectness	No serious imprecision	Intensive treatment group; no participant had retinopathy at baseline
1 (DCCT Research Group 1994)	70	23	High	Randomised controlled trial	No serious risk of bias	NA	No serious indirectness	No serious imprecision	Conventional treatment group; no participant had retinopathy at baseline
≥ 3 step worsening of retinopathy									
1 (DCCT Research Group 1994)	55	3.2	High	Randomised controlled trial	No serious risk of bias	NA	No serious indirectness	No serious imprecision	Intensive treatment group; no participant had retinopathy at baseline
1 (DCCT Research Group 1994)	70	6.3	High	Randomised controlled trial	No serious risk of bias	NA	No serious indirectness	No serious imprecision	Conventional treatment group; no participant had retinopathy at baseline
Any retinopathy									
1 (Cheung 2008)	645	14.8	Moderate	Prospective cohort study	No serious	NA	No serious indirectness	No serious imprecision	No participant had retinopathy at

Number of studies	Number of children and young people	Incidence per hundred person years	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
					risk of bias				baseline
1 (Flack 1996)	182	7	Moderate	Prospective cohort study	No serious risk of bias	NA	No serious indirectness	No serious imprecision	Incidence estimated by subtracting prevalence at start of study from prevalence at end of stud.
Any retinopathy in age group 0 to 9 years									
1 (Klein 1989)	26	3.85	Moderate	Prospective cohort study	No serious risk of bias	NA	No serious indirectness	No serious imprecision	No participant had retinopathy at baseline
1 (Klein 1997)	14	0	Moderate	Prospective cohort study	No serious risk of bias	NA	No serious indirectness	No serious imprecision	No participant had retinopathy at baseline
Any retinopathy in age group 10 to 12 years									
1 (Klein 1989)	42	13.7	Moderate	Prospective cohort study	No serious risk of bias	NA	No serious indirectness	No serious imprecision	No participant had retinopathy at baseline
Any retinopathy in age group 13 – 14 years									
1 (Klein 1989)	25	12	Moderate	Prospective cohort study	No serious risk of bias	NA	No serious indirectness	No serious imprecision	No participant had retinopathy at baseline
Any retinopathy in age group 10 to 14 years									
1 (Klein 1997)	47	1.08	Moderate	Prospective cohort study	No serious risk of bias	NA	No serious indirectness	No serious imprecision	No participant had retinopathy at baseline

DCCT Diabetes Control and Complications Trial, NA not applicable

K.17 Type 1 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?

Table 63: Evidence profile for prevalence of low-level albuminuria by age (albumin:creatinine ratio ranging from > 3.39 mg/mmol to > 3.5 mg/mmol in males, and from > 3.39 mg/mmol to > 4.0 mg/mmol in females, in at least 2 out of 3 urine collections)

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Age < 10 years									
5 (Daniels 2013; Donaghue 1999; Dunger 2014 dos Santos 2002; Yoo 2004)	NC	0 to 66.7 (0)	Very low	Cross sectional	Very serious risk of bias ^{1,2,3}	No serious inconsistency	No serious indirectness	NA ⁴	None
Age 10 years									
8 (Bognetti 1997; Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Gallego 2006; Galler 2012; Yoo 2004)	NC	0 to 9 (0)	Very low	Cross sectional and prospective cohort	Very serious risk of bias ^{1,2,3}	No serious inconsistency	No serious indirectness	NA ⁴	None
Age 11 years									
5 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002)	NC	0 to 10 (2.4)	Very low	Cross sectional	Very serious risk of bias ^{1,2,3}	No serious inconsistency	No serious indirectness	NA ⁴	None
Age 12 years									
6 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen et al. 2004)	NC	0 to 15.4 (2.2)	Very low	Cross sectional and prospective cohort	Very serious risk of bias ^{1,2,3}	No serious inconsistency	No serious indirectness	NA ⁴	None
Age 13 years									
6 (Cho 2011; Daniels 2013;	NC	0 to 67 (5)	Very low	Cross sectional and prospective cohort	Very serious risk of	Very serious inconsistency ⁵	No serious indirectness	NA ⁴	None

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen 2004)					bias ^{1,2,3}				
Age 14 years									
6 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen 2004)	NC	0 to 67 (4.7)	Very low	Cross sectional and prospective cohort	Very serious risk of bias ^{1,2,3}	Very serious inconsistency ⁵	No serious indirectness	NA ⁴	None
Age 15 years									
7 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; Dos Santos 2002; Galler 2012; Olsen 2004)	NC	0 to 75 (5)	Very low	Cross sectional and prospective	Very serious risk of bias ^{1,2,3}	Very serious inconsistency ⁶	No serious indirectness	NA ⁴	None
Age 16 years									
6 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen 2004)	NC	3 to 75 (9.9)	Very low	Cross sectional and prospective cohort	Very serious risk of bias ^{1,2,3}	Very serious inconsistency ⁷	No serious indirectness	NA ⁴	None
Age 17 years									
5 (Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen 2004)	NC	5 to 67 (14)	Very low	Cross sectional and prospective cohort	Very serious risk of bias ^{1,2,3}	Very serious inconsistency ⁸	No serious indirectness	NA ⁴	None
Age 18 years									
5 (Daniels 2013; Donaghue 1999; Dunger 2014; Dos Santos 2002; Olsen 2004)	NC	5 to 67 (14)	Very low	Cross sectional and prospective cohort	Very serious risk of bias ^{1,2,3}	Very serious inconsistency ⁸	No serious indirectness	NA ⁴	None

NA not applicable, NC not calculable

1. Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for in the majority of studies

2. Small sample size (28 participants) in 1 study (dos Santos 2002)
3. Reasons for losses to follow-up (ranging from 11% to 69%) not reported in most studies
4. Not applicable as no confidence intervals were reported
5. Range of prevalence estimates varied between 0% and 67% (prevalence of 67% calculated by NCC-WCH from a study of only 28 patients)
6. Range of prevalence estimates varied between 0% and 75% (prevalence of 75% calculated by NCC-WCH from a study of only 28 patients)
7. Range of prevalence estimates varied between 3% and 75% (prevalence of 75% calculated by NCC-WCH from a study of only 28 patients)
8. Range of prevalence estimates varied between 5% and 67% (prevalence of 67% calculated by NCC-WCH from a study of only 28 patients)

Table 64: Evidence profile for prevalence of low-level albuminuria by age (albumin:creatinine ratio > 4.59 in males, and > 5.24 mg/mmol in females, in at least 2 out of 3 urine collections)

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
<i>Age ≤ 10 years</i>									
1 (Karavanaki 1999)	NC	0 to 0 (0)	Low	Prospective cohort	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ²	None

NA not applicable, NC not calculable

1. Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for in the study
2. Not applicable as no confidence intervals were reported

Table 65: Evidence profile for prevalence of low-level albuminuria by duration of diabetes (albumin:creatinine ratio ranging from > 3.39 mg/mmol to > 3.5 mg/mmol in males, and from > 3.39 mg/mmol to > 4.0 mg/mmol in females, in at least 2 out of 3 urine collections)

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
<i>Duration < 2 years</i>									
5 (Donaghue 1999; dos Santos 2002; Dunger 2014; Nicoloff 2001; Yoo 2004)	NC	0 to 0 (0)	Very low	Cross sectional and prospective	Very serious risk of bias ^{1,2,3}	No serious inconsistency	No serious indirectness	NA ⁴	None
<i>Duration 2 years</i>									
5 (Donaghue 1999; dos Santos . 2002; Dunger 2014; Nicoloff 2001; Yoo 2004)	NC	0 to 16.7 (1)	Very low	Cross sectional and prospective	Very serious risk of bias ^{1,2,3}	No serious inconsistency	No serious indirectness	NA ⁴	None
<i>Duration 3 years</i>									
4	NC	0 to 2	Very low	Cross sectional	Very serious	No serious	No serious	NA ⁴	None

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Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
(Donaghue 1999; Dos Santos 2002; Dunger 2014; Nicoloff 2001)		(0)		and prospective	risk of bias ^{1,2,3}	inconsistency	indirectness		
Duration 4 years									
5 (Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Nicoloff 2001)	NC	0 to 16.7 (2)	Very low	Cross sectional and prospective	Very serious risk of bias ^{1,2,3}	No serious inconsistency	No serious indirectness	NA ⁴	None
Duration 5 years									
6 (Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005; Nicoloff 2001)	NC	0 to 25 (2.8)	Very low	Cross sectional and prospective	Very serious risk of bias ^{1,2,3}	No serious inconsistency	No serious indirectness	NA ⁴	None
Duration 6 years									
6 (Bognetti 1997; Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005)	NC	0 to 50 (4.4)	Very low	Cross sectional	Very serious risk of bias ^{1,2,3}	Very serious inconsistency ⁵	No serious indirectness	NA ⁴	None
Duration 7 years									
5 (Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005)	NC	1.9 to 26.1 (5)	Very low	Cross sectional	Very serious risk of bias ^{1,2,3}	Very serious inconsistency ⁶	No serious indirectness	NA ⁴	None
Duration 8 years									
5 (Daniels 2013; Donaghue 1999; dos Santos 2002; Kong 2005)	NC	1.9 to 22.2 (5)	Very low	Cross sectional	Very serious risk of bias ^{1,2,3}	Very serious inconsistency ⁶	No serious indirectness	NA ⁴	None
Duration 9 years									
5 (Daniels 2013; Donaghue 1999; dos Santos 2002;)	NC	1.9 to 29 (5)	Very low	Cross sectional	Very serious risk of bias ^{1,2,3}	Very serious inconsistency ⁷	No serious indirectness	NA ⁴	None

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Dunger 2014; Kong 2005)									
<i>Duration 10 years</i>									
5 (Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005)	NC	1.9 to 31.8 (6.9)	Very low	Cross sectional	Very serious risk of bias ^{1,2,3}	Very serious inconsistency ⁷	No serious indirectness	NA ⁴	None
<i>Duration 11 years</i>									
4 (Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005)	NC	1 to 28.3 (20.2)	Very low	Cross sectional	Very serious risk of bias ^{1,2,3}	Very serious inconsistency ⁸	No serious indirectness	NA ⁴	None
<i>Duration 12 years</i>									
2 (Dunger 2014; Kong 2005)	NC	1 to 16.3 (8.66)	Low	Cross sectional	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ⁴	None
<i>Duration 13 years</i>									
2 (Dunger 2014; Kong 2005)	NC	1 to 31.9 (16.5)	Low	Cross sectional	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ⁴	None
<i>Duration 14 years</i>									
2 (Dunger 2014; Kong 2005)	NC	1 to 35.9 (18.5)	Low	Cross sectional	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ⁴	None
<i>Duration 15 years</i>									
2 (Dunger 2014; Kong 2005)	NC	1 to 20 (10.5)	Low	Cross sectional	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ⁴	None

NA not applicable, NC not calculable

1. Unclear whether important confounders for low-level oalbuminuria prevalence estimates were accounted for in the majority of studies

2. Small sample size (28 participants) in 1 study (dos Santos 2002)

3. Reasons for losses to follow-up (ranging from 11% to 69%) not reported in most studies

4. Not applicable as no confidence intervals were reported

5. Range of prevalence estimates varied between 0% and 50% (prevalence of 50% calculated by NCC-WCH technical team from a study of only 28 participants)

6. Range of prevalence estimates varied between 1.87% and 20% (prevalence of 20% calculated by NCC-WCH technical team from a study of only 28 participants)

7. Range of prevalence estimates varied between 1.87% and 28.6% (prevalence of 28.6% calculated by NCC-WCH technical team from a study of only 28 participants)

8. Range of prevalence estimates varied between 1.02% and 80% (prevalence of 80% calculated by NCC-WCH technical team from a study of only 28 participants)

Table 66: Evidence profile for incidence of low-level albuminuria by duration of diabetes (albumin:creatinine ratio > 3.5 mg/mmol in males, and > 4.0 mg/mmol in females, in at least 2 out of 3 urine collections)

Number of studies	Number of children and young people	Range of incidence, % (median, %)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Duration < 1 year									
1 (Rudberg 1993)	NC	8 (NA)	Low	Prospective	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ²	None
Duration 1 year									
1 (Rudberg 1993)	NC	8 (NA)	Low	Prospective	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ²	None
Duration 2 years									
1 (Rudberg 1993)	NC	8 (NA)	Low	Prospective	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ²	None
Duration 3 years									
1 (Rudberg 1993)	NC	8 (NA)	Low	Prospective	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ²	None
Duration 4 years									
1 (Rudberg 1993)	NC	8 (NA)	Low	Prospective	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ²	None
Duration 5 years									
1 (Rudberg 1993)	NC	14 (NA)	Low	Prospective	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ²	None
Duration 6 years									
1 (Rudberg 1993)	NC	14 (NA)	Low	Prospective	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ²	None
Duration 7 years									
1 (Rudberg 1993)	NC	14 (NA)	Low	Prospective	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ²	None
Duration 8 years									
1 (Rudberg 1993)	NC	14 (NA)	Low	Prospective	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ²	None
Duration 9 years									
1 (Rudberg 1993)	NC	14 (NA)	Low	Prospective	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	NA ²	None

NA not applicable, NC not calculable

1. Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for

2. Not applicable as no confidence intervals were reported

K.18 Type 2 diabetes – education

Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?

There are no evidence profiles for this review question because no studies were identified for inclusion.

K.19 Type 2 diabetes – behavioural interventions

Review question: What is the effectiveness of behavioural interventions to promote engagement with clinical services in children and young people with type 2 diabetes?

Review question: What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 2 diabetes?

There are no evidence profiles for these review questions because no studies were identified for inclusion.

K.20 Type 2 diabetes – dietary advice

Review question: What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?

Table 67: Evidence profile for comparison of a very low calorie diet with usual care in morbidly obese African-American children and young people with type 2 diabetes

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Intervention	Comparator	Relative (95% confidence interval)	Absolute (95% confidence interval)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Change in BMI by end of diet (approximately 2 months after baseline)											
1 (Willi 2004)	15	15	NA	MD -12.4 (-17.1 to -7.7) ^{a,b}	Very low	Retrospective chart review	Very serious ^{1,2,3}	NA	Serious indirectness ^{4,5}	Very serious ^{5,6}	Yes ¹
Change in BMI by 6 months' follow-up											

Number of studies	Number of children and young people		Effect		Quality	Design	Quality assessment				
	Intervention	Comparator	Relative (95% confidence interval)	Absolute (95% confidence interval)			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
1 (Willi 2004)	15	15	NA	MD -12.7 (-18.1 to -7.2) ^{a,b}	Very low	Retrospective chart review	Very serious ^{1,2,3}	NA	Serious indirectness ^{4,5}	Very serious ^{5,6}	Yes ⁱ
Change in BMI by 12 months' follow-up											
1 (Willi 2004)	15	15	NA	MD -9.5 (-16.2 to -2.8) ^{a,b}	Very low	Retrospective chart review	Very serious ^{1,2,3}	NA	Serious indirectness ^{4,5}	Very serious ^{5,6}	Yes ⁱ
Change in BMI by 18 months' follow-up											
1 (Willi 2004)	15	15	NA	MD -9.1 (-16.8 to -1.4) ^{a,b}	Very low	Retrospective chart review	Very serious ^{1,2,3}	NA	Serious indirectness ^{4,5}	Very serious ^{5,6}	Yes ⁱ
Change in BMI by 24 months' follow-up											
1 (Willi 2004)	15	15	NA	MD: -9.1 (-17.8 to -0.3) ^{a,b}	Very low	Retrospective chart review	Very serious ^{1,2,3}	NA	Serious indirectness ^{4,5}	Very serious ^{6,7}	Yes ⁱ
HbA1c levels at end of diet (approximately 2 months after baseline)											
1 (Willi 2004)	15	15	NA	MD -1.6 (-3.5 to 0.3) ^{a,b}	Very low	Retrospective chart review	Very serious ^{1,2,3}	NA	Serious indirectness ^{4,5}	Very serious ^{6,7}	None
HbA1c levels at 6 months after baseline											
1 (Willi 2004)	15	15	NA	MD -0.9 (-3.1 to 1.4) ^{a,b}	Very low	Retrospective chart review	Very serious ^{1,2,3}	NA	Serious indirectness ^{4,5}	Very serious ^{6,7}	None
HbA1c levels at 12 months after baseline											
1 (Willi 2004)	15	15	NA	MD -0.5 (-2.7 to 1.7) ^{a,b}	Very low	Retrospective chart review	Very serious ^{1,2,3}	NA	Serious indirectness ^{4,5}	Very serious ^{6,7}	None
HbA1c levels at 18 months after baseline											
1 (Willi 2004)	15	15	NA	MD -0.4 (-2.7 to 1.9) ^{a,b}	Very low	Retrospective chart review	Very serious ^{1,2,3}	NA	Serious indirectness ^{4,5}	Very serious ^{6,7}	None
HbA1c levels at 24 months after baseline											
1 (Willi 2004)	15	15	NA	MD -1.0 (-3.4 to 1.4) ^{a,b}	Very low	Retrospective chart review	Very serious ^{1,2,3}	NA	Serious indirectness ^{4,5}	Very serious ^{6,7}	None

BMI body mass index, CI confidence interval, NA not applicable, MD mean difference, SDS standard deviation score, SE standard error

a Point estimate and SE derived from graphs by NCC-WCH technical team

b CI calculated using t-distribution due to small sample size

1 No randomisation used to allocate the intervention

2 Usual care for controls is unclear; likely to differ from intervention group by more than just diet as intervention group was withdrawn from oral anti-diabetic medication before treatment

3 Attrition bias is unclear; participants who adhered to the diet for less than 6 weeks were excluded from long-term follow-up analysis

4 Population is narrow (morbidly obese African-American children and young people) therefore generalisability is reduced

5 Results for this outcome are based on BMI alone, not BMI SDS score

6 No CIs reported and none calculable (estimates derived from graphs by NCC-WCH technical team, see footnote a)

7 P-values reported as < critical value (for example, $p < 0.05$ or $p < 0.01$), not as exact values

K.21 Type 2 diabetes – weight loss

Review question: Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?

Table 68: Evidence profile for effectiveness of weight loss in children and young people with type 2 diabetes who are overweight or obese in improving glycaemic control

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Metformin and lifestyle intervention	Metformin only	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Number of glycaemic failure cases over 5 years^a											
1 (TODAY Study Group 2012)	109/234 (46.6%)	120/232 (51.7%)	RR 0.90 lower (0.75 to 1.08)	52 fewer per 1000 (from 129 fewer to 41 more)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	Serious indirectness ³	No serious imprecision ⁴	None
Median time to treatment failure (months)											
1 (TODAY Study Group 2012)	234 (median = 11.8 months)	232 (median = 10.3 months)	NA ⁵	NA ⁵	Low	RCT	No serious risk of bias ¹	No serious inconsistency ²	Serious indirectness ³	NA ⁶	None
Number of children and young people achieving a reduction of at least 7 percentage points in percent overweight											
1 (TODAY Study Group 2012)	73/234 (31.2%)	56/232 (24.3%)	RR 1.27 higher (0.95 to 1.72)	65 more per 1000 (from 12 fewer to 174 more)	Moderate	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness	Serious imprecision ⁷	

CI confidence interval, NA not applicable, RR relative risk, RCT randomised controlled trial, TODAY Treatment Options for type 2 Diabetes in Adolescents and Youth

a The study defined treatment failure as a persistently elevated glycated haemoglobin level of 8% or higher over a period of 6 months or persistent metabolic decompensation (defined as either the inability to wean the participant from insulin within 3 months of its initiation for decompensation or the occurrence of a second episode of decompensation within 3 months of discontinuation of insulin)

1 The evaluation identified no serious risk of bias

2 Single-study analysis

3 The outcomes reported in the study were not strictly pertinent to the requirements of the protocol

4The 95% CI is entirely within one zone related to precision (see 'Methodology for 2015 update')

5Median values cannot be used to assess effects

6 Imprecision cannot be assessed because median values cannot be used to assess effects

7The 95% CI crosses two zones related to precision (see 'Methodology for 2015 update')

K.22 Type 2 diabetes – metformin

Review question: What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?

Table 69: Evidence profile for effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with placebo

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias) ¹	Inconsistency ²	Indirectness ³	Imprecision	Other considerations
	Metformin	Placebo	Relative (95% confidence interval)	Absolute (95% confidence interval)							
HbA1c value (% at endpoint)											
1 (Jones 2002)	36	36	NA	MD between the groups at endpoint 1.1 lower (1.19 lower to 1.01 lower) ^a	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ^e	None
Number needing rescue medication											
1 (Jones 2002)	4/42 (9.5%)	26/40 (65%)	RR 0.15 (0.06 to 0.4)	552 fewer per 1000 (from 390 fewer to 611 fewer)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁴	None
Number reporting any adverse event (including number with DKA)											
1 (Jones 2002)	29/42 (69%)	24/40 (60%)	RR 1.15 (0.83 to 1.59)	90 more per 1000 (from 102 fewer to 354 more)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁵	None
Number of dropouts											
1 (Jones 2002)	6/42 (14.3%)	4/40 (10%)	RR 1.43 (0.42 to 3.91)	43 more per 1000 (from 58 fewer to 291 more)	High	RCT	No serious risk of bias ¹	No serious inconsistency ²	No serious indirectness ³	No serious imprecision ⁶	None
FPG concentration (change from baseline, mmol/l)											
1 (Jones 2002)	36	36	NA	MD between	High	RCT	No serious	No serious	No serious	No serious	None

Number of studies	Number of children and young people		Effect		Quality	Design	Limitations (risk of bias)	Inconsistency	Indirectness	Imprecision	Other considerations
	Metformin	Placebo	Relative (95% confidence interval)	Absolute (95% confidence interval)							
2002)				the groups 3.6 lower (3.83 lower to 3.37 lower) ^h			risk of bias ¹	inconsistency ²	indirectness ³	imprecision ⁷	

DKA diabetic ketoacidosis, FPG fasting plasma glucose, MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk
 a Adjusted mean HbA1c at baseline (%), metformin 7.2 ± 1.2, placebo 8.6 ± 0.2

1 No apparent risk of bias in the included study

2 Single-study analysis

3 Study met population, intervention and outcomes as specified in the review protocol

4 Mean difference at endpoint is greater than minimally important difference (MID) of 0.5 percentage points (5.5 mmol/mol)

5 Absolute effect is greater than default MID of 25% (250 per 1,000)

6 While the absolute effect does not meet default MID criteria, this was not considered to impact on the findings as the adverse events were spread equally across study groups

7 Change in FPG from baseline (mmol/l), metformin -2.4 ± 0.5, placebo 1.2 ± 0.5

K.23 Type 2 diabetes – HbA1c targets

Review question: What is the optimal HbA1c target for children and young people with type 2 diabetes?

There are no evidence profiles for this review question because no studies were identified for inclusion.

K.24 Type 2 diabetes – hypertension

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Table 70: Evidence profile for prevalence of hypertension by age

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment					
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
Median age of 13.2 years at diagnosis										
Hypertension (blood pressure values > 95th percentile)										
1 (Reinehr 2008)	51	44.0% (30.1 to 57.9) ^a	Very low	Prospective chart review	Serious ¹	No serious inconsistency ²	Serious ³	No serious imprecision	None	
Aged 10 to 15 years at diagnosis										

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Hypertension (systolic blood pressure > 130mmHg and diastolic blood pressure > 85mmHg)									
1 (Urakami 2009)	112	11.6% (5.6 to 17.6) ^a	Very low	Retrospective chart review	No serious bias	No serious inconsistency ²	Very serious ^{4,5,6}	No serious imprecision	None

CI confidence interval, IQR interquartile range

a Calculated by the NCC-WCH technical team.

1 Data were analysed only for participants with complete follow up (51/129, 39.5%); the study authors stated that the 78 participants who dropped out did not differ significantly at baseline from those who were successfully followed up

2 Single-study analysis

3 Prevalence estimates do not relate to a specific age; only the median age was reported (13.2 years, IQR 12.1 to 14.7)

4 Prevalence estimates do not relate to a specific age; only the mean age was reported (12.9 years ± 1.5)

5 Hypertension was defined based on absolute values and not percentiles

6 The study population comprised Japanese participants therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited

Table 71: Evidence profile for prevalence of hypertension by duration of diabetes

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Within 1 year of diagnosis									
Hypertension (systolic or diastolic > 95th percentile)									
1 (Rodriguez 2010)	176	18.2% (12.5 to 23.9) ^a	Very low	Prospective multi-centre study	Serious ¹	No serious inconsistency ²	No serious indirectness	No serious imprecision	None
One year after diagnosis									
Systolic hypertension (> 98th percentile)									
1 (Shield 2009)	59	15.7% (6.2 to 25.2) ^a	Low	Prospective follow-up of surveillance data	No serious bias	No serious inconsistency ²	No serious indirectness	No serious imprecision	None
Diastolic hypertension (> 98th percentile)									
1 (Shield 2009)	59	34.1% (21.8 to 46.4) ^a	Low	Prospective follow-up of surveillance data	No serious bias	No serious inconsistency ²	No serious indirectness	No serious imprecision	None
Within 2 years of diagnosis									
Hypertension (blood pressure values > 90th percentile)									
1 (Copeland 2011)	704	26.3% (23.0 to 29.6) ^a	Low	Analysis of baseline data from a randomised controlled trial ⁴	No serious bias	No serious inconsistency ²	Serious ³	No serious imprecision	None
Hypertension (blood pressure values > 95th percentile)									
1 (Copeland 2011)	704	13.6% (11.1 to 16.1) ^a	Low	Analysis of baseline data from a randomised controlled trial ⁴	No serious bias	No serious inconsistency ²	Serious ³	No serious imprecision	None
Two years after diagnosis									
Hypertension (blood pressure values > 95th percentile)									
1 (Reinehr 2008)	51	32.0% (18.9 to 45.1) ^a	Very low	Prospective chart review	Serious ⁵	No serious inconsistency ²	No serious indirectness	No serious imprecision	None

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Within 3 years of diagnosis									
Hypertension (blood pressure values ≥ 95th percentile)									
1 (Ettinger 2005)	26	58.0% (38.0 to 78.0) ^a	Very low	Prospective chart review	No serious bias	No serious inconsistency ²	Very serious ^{3,6}	No serious imprecision	Yes ⁷
Within 4 years of diagnosis									
Hypertension (systolic and diastolic > 95th percentile)									
1 (Eppens 2006)	265	8.0% (4.7 to 11.3) ^a	Very low	Cross-sectional survey	Very serious ^{8,9}	No serious inconsistency ²	Very serious ^{3,10}	No serious imprecision	Yes ¹¹
Hypertension (systolic > 95th percentile)									
1 (Hotu 2004)	3	28.0% (5.6 to 50.4) ^a	Very low	Cross-sectional survey	No serious bias	No serious inconsistency ²	Very serious ^{3,12,13}	No serious imprecision	None
Between 1 and 5 years after diagnosis									
Hypertension (systolic or diastolic > 95th percentile)									
1 (Rodriguez 2010)	219	27.9% (22.0 to 33.8) ^a	Very low	Prospective multi-centre study	Serious ¹⁴	No serious inconsistency ²	No serious indirectness	No serious imprecision	None
More than 5 years after diagnosis									
Hypertension (systolic or diastolic > 95th percentile)									
1 (Rodriguez 2010)	15	26.7% (2.3 to 51.1) ^a	Very low	Prospective multi-centre study	Very serious ¹⁵	No serious inconsistency ²	No serious indirectness	No serious imprecision	None

CI confidence interval, RCT randomised controlled trial

^a Calculated by the NCC-WCH technical team

1 Data for this outcome were available for only 176 (42.9%) of the 410 participants in the study

2 Single-study analysis

3 Prevalence estimates do not relate to specific times after diagnosis

4 Starting point of moderate for quality rating as baseline analysis of an RCT

5 Data were analysed only for participants with complete follow up (51/129, 39.5%); the study authors stated that the 78 participants who dropped out did not differ significantly at baseline from those who were successfully followed up

6 The population comprised non-Hispanic black or Hispanic Latino participants therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited

7 Children and young people who were taking anti-hypertensive medication were eligible for inclusion

8 Participants with missing data were excluded from analysis however the number of missing values was not reported

9 Hypertension was screened for in only 80% of participants

10 The majority of the population comprised Western Pacific Islanders therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited

11 The minimum duration of diabetes of study participants was 12 months

12 The study population comprised Maori and Pacific Islanders therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited

13 The study population comprised young people aged 18 and 19 years (age range 11 to 19 years); it is unclear at what time point after diagnosis the prevalence estimate for hypertension is based on therefore some participants may be above the age range specified in the protocol for this review

14 Data for this outcome were available for only 219 (53.4%) of the 410 participants in the study

15 Data for this outcome were available for only 15 (3.7%) of the 410 participants in the study

K.25 Type 2 diabetes – dyslipidaemia

Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?

Table 72: Evidence profile for prevalence of dyslipidaemia by age

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
Median age of 13.2 years at diagnosis									
Prevalence of dyslipidaemia									
1 (Reinehr 2008)	51	65.0% (51.6 to 78.4) ^b	Very low	Prospective chart review	Very Serious ^{1,2}	No serious inconsistency ³	Serious ⁴	No serious imprecision	None
Aged between 10 and 15 years at diagnosis									
Triglycerides > 150mg/dl (1.7mmol/l)									
1 (Urakami 2009)	112	33.0% (24.2 to 41.8) ^b	Very low	Retrospective chart review	No serious bias	No serious inconsistency ³	Serious ^{5,6}	No serious imprecision	None
High density lipoproteins < 40mg/dl (1.0mmol/l)									
1 (Urakami 2009)	112	21.4% (13.7 to 29.1) ^b	Very low	Retrospective chart review	No serious bias	No serious inconsistency ³	Serious ^{5,6}	No serious imprecision	None

CI confidence interval, HDL high-density lipoprotein, IQR interquartile range, LDL low-density lipoprotein, RCT randomised controlled trial

a Dyslipidaemia was defined using the following cut-offs: total cholesterol > 5.1mmol/l (200mg/dl), LDL > 3.3mmol/l (130mg/dl), HDL < 0.9mmol (35mg/dl) or triglycerides > 1.7mmol/l (150mg/dl)

b Calculated by the NCC-WCH technical team

c Based on the age range for inclusion in the study as the actual age range of participants was not reported

1 Data were analysed only for participants with complete follow-up (51/129, 39.5%); the study authors stated that the 78 participants who dropped out did not differ significantly at baseline from those who were successfully followed up

2 The study did not report whether or not total cholesterol, LDL, HDL, and triglycerides were measured using fasting samples, and this would affect the accuracy of LDL and triglyceride measurements

3 Single-study analysis

4 Prevalence estimates do not relate to a specific age; only the median age was reported (13.2 years, IQR 12.1 to 14.7)

5 Prevalence estimates do not relate to a specific age; only the mean age was reported (12.9 years ± 1.5)

6 The population comprised Japanese participants therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited

Table 73: Evidence profile for prevalence of dyslipidaemia by duration of diabetes

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
At 1 year after diagnosis									
Prevalence of LDL > 130mg/dl (3.4mmol/l)									
1 (Le 2013)	86	12.5% (5.4 to 19.6) ^a	Very low	Retrospective chart review	Serious bias ¹	No serious inconsistency ²	No serious indirectness	No serious imprecision	
Prevalence of HDL < 35mg/dl (0.9mmol/l)									

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment				
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations
1 (Le 2013)	86	25.0% (15.8 to 34.2) ^a	Very low	Retrospective chart review	No serious bias	No serious inconsistency ²	No serious indirectness	No serious imprecision	
Within 2 years of diagnosis									
Low density lipoproteins ≥ 160mg/dl (4.1mmol/l)									
1 (Copeland 2011)	704	0.4% (0.00 to 0.87) ^a	Low	Analysis of baseline data from a randomised controlled trial ^b	No serious bias	No serious inconsistency ²	Serious ³	No serious imprecision	
High density lipoproteins < 50mg/dl (1.3mmol/l, females) or < 40mg/dl (1.0mmol/l, males)									
1 (Copeland 2011)	704	79.8% (76.8 to 82.8) ^a	Low	Analysis of baseline data from a randomised controlled trial ^b	No serious bias	No serious inconsistency ²	Serious ³	No serious imprecision	
Triglycerides ≥ 200mg/dl (2.3mmol/l)									
1 (Copeland 2011)	704	10.2% (8.0 to 12.4) ^a	Low	Analysis of baseline data from a randomised controlled trial ^b	No serious bias	No serious inconsistency ²	Serious ³	No serious imprecision	
At 2 years after diagnosis									
Prevalence of dyslipidaemia									
1 (Reinehr 2008)	51	69.0% (56.0 to 82.0) ^a	Very low	Prospective chart review	Very serious ^{4,5}	No serious inconsistency ²	No serious indirectness	No serious imprecision	
Within 3 years of diagnosis									
Dyslipidaemia (not defined)									
1 (Ettinger 2005)	26	69.2% (50.5 to 87.9) ^a	Very low	Prospective chart review	Serious ⁶	No serious inconsistency ²	Very serious ^{3,7}	No serious imprecision	
Within 4 years of diagnosis									
Total cholesterol ≥ 6mmol/l									
1 (Eppens 2006)	331	12.0% (8.5 to 15.5) ^a	Very low	Cross-sectional survey	Serious ⁸	No serious inconsistency ²	Very serious ^{3,9}	No serious imprecision	Yes ¹⁰
Low density lipoproteins > 4mmol/l									
1 (Eppens 2006)	331	12.0% (8.5 to 15.5) ^a	Very low	Cross-sectional survey	Serious ⁸	No serious inconsistency ²	Very serious ^{3,9}	No serious imprecision	Yes ¹⁰
High density lipoproteins < 0.9mmol/l									
1 (Eppens 2006)	331	10.0% (6.8 to 13.2) ^a	Very low	Cross-sectional survey	Serious ⁸	No serious inconsistency ²	Very serious ^{3,9}	No serious imprecision	Yes ¹⁰
Triglycerides ≥ 2.2mmol/l									
1 (Eppens 2006)	331	16.0% (12.1 to 19.9) ^a	Very low	Cross-sectional survey	Serious ⁸	No serious inconsistency ²	Very serious ^{3,9}	No serious imprecision	Yes ¹⁰
Total cholesterol:high density lipoproteins molar ratio > 4.5 molar units									
1 (Hotu 2004)	13	85.0% (63.4 to 1.00) ^a	Very low	Cross-sectional survey	Very serious ^{5,11}	No serious inconsistency ²	Very serious ^{3,12,13}	No serious imprecision	

CI confidence interval, HDL high-density lipoprotein, IQR interquartile range, LDL low-density lipoprotein, RCT randomised controlled trial
^a Calculated by the NCC-WCH technical team

^b Starting point of moderate for quality rating as baseline analysis of an RCT

c Dyslipidaemia was defined using the following cut-offs: total cholesterol > 5.1mmol/l (200mg/dl), LDL > 3.3mmol/l (130mg/dl), HDL < 0.9mmol (35mg/dl) or triglycerides > 1.7mmol/l (150mg/dl)

1 Due to the retrospective study design, the study could not guarantee the fasting status of lipid measures, which would affect the accuracy of LDL and triglycerides

2 Single-study analysis

3 Prevalence estimates do not relate to specific times after diagnosis

4 Data were analysed only for participants with complete follow-up (51/129, 39.5%); the study authors stated that the 78 participants who dropped out did not differ significantly at baseline from those who were successfully followed up

5 The study did not report whether or not total cholesterol, LDL, HDL, and triglycerides were measured using fasting samples and this would affect the accuracy of LDL and triglyceride measurements

6 Dyslipidaemia was not defined

7 The population comprised non-Hispanic black or Hispanic Latino participants therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited

8 Participants with missing data were excluded from analysis however the number of missing values was not reported

9 The majority of the population comprised Western Pacific Islanders therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited

10 The minimum duration of diabetes of study participants was 12 months (this item was not included in evidence grading)

11 Dyslipidaemia was measured in only 72.0% (13/18) of study participants

12 The study population comprised Maori and Pacific Islanders therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited

13 The study population comprised young people aged 18 and 19 years (age range 11 to 19 years); it is unclear at what time point after diagnosis the prevalence estimate for dyslipidaemia is based on and, therefore, some participants may be above the age range specified in the protocol for this review

K.26 Type 2 diabetes – retinopathy

Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?

Table 74: Evidence profile for prevalence of retinopathy according to age

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment					
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
12 to 16 years										
1 (Levitsky 2013)	140	5.7 (2.5 to 11.0) ^a	Moderate ^b	Randomised controlled trial	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	
17 to 18 years										
1 (Levitsky 2013)	137	12.4 (7.4 to 19.1) ^a	Moderate ^b	Randomised controlled trial	No serious risk of bias	NA	No serious indirectness	No serious imprecision	None	
10.8 to 17.8 years										
1 (Shield 2009)	55	0.0 (0.0 to 6.5) ^a	Low ^c	Prospective cohort	Serious risk of bias ¹	No serious inconsistency	No serious indirectness	No serious imprecision	None	

CI confidence interval, NA not applicable, RCT randomised controlled trial
a 95% CI calculated by NCC-WCH technical team from data reported in the article

b Although the study design was an RCT, data obtained were cross-sectional and observational in nature

c Serious risk of bias

1 Study design included postal survey of clinicians therefore at risk of selection bias

Table 75: Evidence profile for prevalence of retinopathy according to duration of diabetes

Number of studies	Number of children and young people	Prevalence, % (95% CI)	Quality	Design	Quality assessment					
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
12 months										
1 (Shield 2009)	55	0.0 (0.0 to 6.5) ^a	Low ^b	Prospective cohort	Serious risk of bias ¹	NA	No serious indirectness	No serious imprecision		
24 to 49 months										
1 (Levitsky 2013)	170	5.3 (2.5 to 9.8) ^a	Low ^{c,d}	Randomised controlled trial	No serious risk of bias	NA	Serious indirectness ²	No serious imprecision		
50 to 66 months										
1 (Levitsky 2013)	172	13.4 (8.7 to 19.4) ^a	Low ^{c,d}	Randomised controlled trial	No serious risk of bias	NA	Serious indirectness ²	No serious imprecision		
67 to 101 months										
1 (Levitsky 2013)	137	22.3 (16.3 to 29.2) ^a	Low ^{c,d}	Randomised controlled trial	No serious risk of bias	NA	Serious indirectness ²	No serious imprecision		

CI confidence interval, NA not applicable, RCT randomised controlled trial

a 95% CI calculated by NCC-WCH technical team from data reported in the article

b Serious risk of bias

c Although the study design was an RCT, data obtained were cross-sectional and observational in nature

d Serious indirectness

1 Study design included postal survey of clinicians therefore at risk of selection bias

K.27 Type 2 diabetes – nephropathy

Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

Table 76: Evidence profile for prevalence of low-level albuminuria by age in children and young people with type 2 diabetes

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment					
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
Age <11										
1 (Yoo. 2004)	NC	0 (NA)	Very low	Cross sectional	Very serious risk of bias ^{1,2}	No serious inconsistency	No serious indirectness	NA ^c	None	

Low-level albuminuria defined as albumin:creatinine ratio (ACR) > 3.5 mg/mmol in males and ACR > 4.0 mg/mmol in females in at least 2 out of 3 urine collections

NC not calculable, NA not applicable

1 Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for in the study

2 Small sample size (22 participants) for type 2 diabetes

c Not applicable as confidence intervals were not reported

Table 77: Evidence profile for prevalence of low-level albuminuria by duration of diabetes in children and young people with type 2 diabetes

Number of studies	Number of children and young people	Range of prevalence, % (median, %)	Quality	Design	Quality assessment					
					Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	
Duration < 2 years										
3 (Farah 2006; Lynch 2013; Yoo 2004)	NC	0 to 29.6 (6.3)	Very low	Cross sectional	Very serious risk of bias ^{1,2}	Very serious inconsistency ³	No serious indirectness	NA ⁴	None	
Duration 2 years										
1 (Farah 2006)	NC	29.6 (NA)	Very low	Cross sectional	Very serious risk of bias ^{1,2}	No serious inconsistency	No serious indirectness	NA ⁴	None	
Duration 3 years										
1 (Farah 2006)	NC	32.3 (NA)	Very low	Cross sectional	Very serious risk of bias ^{1,2}	No serious inconsistency	No serious indirectness	NA ⁴	None	
Duration 4 years										
1 (Farah 2006)	NC	32.3 (NA)	Very low	Cross sectional	Very serious risk of bias ^{1,2}	No serious inconsistency	No serious indirectness	NA ⁴	None	
Duration 5 years										
1 (Farah 2006)	NC	32.3 (NA)	Very low	Cross sectional	Very serious risk of bias ^{1,2}	No serious inconsistency	No serious indirectness	NA ⁴	None	

Low-level albuminuria defined as albumin:creatinine ratio (ACR) > 3.5 mg/mmol in males and ACR > 4.0 mg/mmol in females in at least 2 out of 3 urine collections

NC not calculable, NA not applicable

1 Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for in studies

2 Small sample sizes in studies for type 2 diabetes (40 participants in Farah 2006 and 22 in Yoo 2004)

3 Prevalence estimates ranged from 0% to 29.6%

4 Not applicable as confidence intervals were not reported

Appendix L: Research recommendations

L.1 2015 recommendations for research

L.1.1 Type 1 diabetes – education

L.1.1.1 What is the clinical and cost effectiveness of a programme of structured education from diagnosis for children and young people with type 1 diabetes?

Why is this important

The GDG has recommended education from diagnosis for children and young people with type 1 diabetes but not specified that this should be 'structured' because there is no evidence to support structured education delivered at diagnosis. Future research should compare a structured education programme delivered from diagnosis with a non-structured education programme delivered from diagnosis (usual care). Important outcomes will include achieving the target HbA1c after 1 year and satisfaction of the child or young person and their family members or carers (as appropriate).

L.1.1.2 What is the impact of training in teaching skills for healthcare professionals on the effectiveness of education for children and young people with type 1 diabetes?

Why this is important

The GDG has recommended that children and young people with type 1 diabetes should be offered education, but has not specified that the education should be delivered by healthcare professionals trained in its delivery. Future research should use randomised controlled trials to compare diabetes education delivered by healthcare professionals who have received training in teaching skills and those who have not. Different approaches to training (such as participating in training in schools) should be considered as part of the research. Important outcomes will include the child or young person achieving their target HbA1c, satisfaction of the child or young person and their family members or carers (as appropriate), and satisfaction among healthcare professionals delivering the education.

L.1.1.3 What is the effectiveness of education programmes in which young people with type 1 diabetes provide training for their peers?

Why this is important

Training delivered by peers is effective both in healthcare and in other settings. This research should evaluate the engagement of the child or young person with type 1 diabetes and their family members or carers (as appropriate), and outcomes for the child or young person. Outcomes could include their success in achieving their target HbA1c level, engagement with diabetes care and management (for example, attendance at clinic), and satisfaction with the education programme. The impact on the young person delivering the training should also be evaluated (this could cover the impact on their diabetes care and the psychosocial impact of providing training for their peers). The research should be conducted using quantitative, qualitative and mixed methods.

This is a rephrasing of a 2004 research recommendation to comply with current NICE format and style as it was selected a key research recommendation by the GDG for the 2015 update. The justification for the selection is summarised in the table below.

Potential criterion	Explanation
Importance to patients or the population	This is of importance because there is evidence of the effectiveness of peer-delivered education in other healthcare and wider settings
Relevance to NICE guidance	Relevant to a future update of this guideline
Relevance to the NHS	Relevant to a future update of this guideline and potential reduction in costs associated with long-term complications
National priorities	Not applicable
Current evidence base	Lack of evidence specific to peer-delivered education in children and young people with diabetes
Equality	Research would need to take account of accessibility to and effectiveness of education for people with protected characteristics such as different age and ethnic groups
Feasibility	Feasible
Other comments	None

L.1.2 Type 1 diabetes – blood glucose targets

L.1.2.1 What is the optimal upper limit and timing for blood glucose measurements after meals for children and young people with type 1 diabetes to achieve an HbA1c level of 48 mmol/mol (6.5%) without unacceptable hypoglycaemia?

Why this is important

Setting an upper limit for blood glucose measurements 1–2 hours after meals of less than 8 mmol/litre (rather than the 9 mmol/litre recommended in this guideline) could potentially lead to an improvement in blood glucose control without an unacceptable risk of hypoglycaemia. The evidence reviewed for the guideline did not allow a precise evaluation of the upper limit for the target range, or the timing of blood glucose testing relative to meals. Future research should investigate the HbA1c levels of children and young people with type 1 diabetes who aim for blood glucose measurements after meals slightly lower (to ensure their safety) than 9 mmol/litre, to help decide whether lowering the upper limit is effective in improving long-term blood glucose control. Outcomes include the child or young person's satisfaction with treatment, their HbA1c levels, rates of hypoglycaemia, and the views of their family members or carers (as appropriate), and quality of life.

This was selected a key research recommendation by the GDG for the 2015 update. The justification for the selection is summarised in the table below.

Potential criterion	Explanation
Importance to patients or the population	This is of importance because it is of interest to know whether it is safe and acceptable to refine the target range for postprandial blood glucose measurements
Relevance to NICE guidance	Relevant to a future update of this guideline
Relevance to the NHS	Relevant to a future update of this guideline and potential reduction in costs associated with long-term complications
National priorities	Not applicable
Current evidence base	Further evidence is needed
Equality	Not applicable
Feasibility	Feasible
Other comments	None

L.1.3 Type 1 diabetes – intermittent continuous glucose monitoring compared with real-time continuous glucose monitoring

L.1.3.1 What is the clinical and cost effectiveness of real-time continuous glucose monitoring systems compared to 5 or more capillary blood glucose tests per day in children aged 5 years or younger with type 1 diabetes who use insulin pump therapy?

Why this is important

The GDG's recommendation was to consider ongoing real-time continuous glucose monitoring systems (CGMS) for neonates, infants and pre-school children with type 1 diabetes. This weak recommendation reflected a lack of evidence of effectiveness of CGMS in such children (only a few studies having been conducted in this age group). The GDG considered use of CGMS in this age group to be important because of the risk of adverse neurodevelopmental consequences of type 1 diabetes and parental anxiety (particularly in those with pre-school children). Further research in the form of a multi-centre randomised controlled trial comparing CGMS with 5 or more capillary blood glucose tests per day is needed to achieve a large enough sample size. Important outcomes include HbA1c levels, incidence of hypoglycaemia, satisfaction of the child and their family members or carers (as appropriate), and quality of life. Future research should ideally monitor neurodevelopmental consequences but this would require studies with long-term follow up.

L.1.4 Type 1 diabetes – dietary advice

L.1.4.1 What is the impact of educating children and young people with type 1 diabetes and their family members or carers (as appropriate) about their glycaemic index from diagnosis?

Why this is important

Very little evidence on the effectiveness of dietary advice based on glycaemic index was identified for inclusion in the guideline review, and the evidence that was identified related mostly to twice-daily insulin regimens. Research is needed to evaluate the effectiveness of teaching children and young people with type 1 diabetes and their family members or carers (as appropriate) about glycaemic index in the context of modern, intensive insulin treatment regimens (insulin pump therapy or multiple daily injections). Important outcomes include success in achieving the target HbA1c level, blood glucose levels after meals, frequency of hypoglycaemia, quality of life, food choices, and the frequency and timing of insulin administration to lower blood glucose levels after meals.

This was selected a key research recommendation by the GDG for the 2015 update. The justification for the selection is summarised in the table below.

Potential criterion	Explanation
Importance to patients or the population	This is of importance because there is very little evidence of effectiveness of dietetic advice based on glycaemic index from diagnosis in terms of improving glycaemic control
Relevance to NICE guidance	Relevant to a future update of this guideline
Relevance to the NHS	Relevant to a future update of this guideline and potential reduction in costs associated with long-term complications
National priorities	Not applicable
Current evidence base	Lack of evidence currently other than in relation to cardiovascular health and no evidence in relation to modern intensive insulin treatment regimens
Equality	Research would need to take account of accessibility to and

Potential criterion	Explanation
	effectiveness of education for children and young people with protected characteristics such as different age and ethnic groups
Feasibility	Feasible
Other comments	None

L.1.5 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

L.1.5.1 What is the optimal dosage of intravenous insulin for managing diabetic ketoacidosis (DKA) in children and young people?

Why this is important

The evidence reviewed for the guideline did not allow evaluation of the comparative effectiveness and safety of specific dosages of intravenous insulin, such as 0.025, 0.05 and 0.1 units/kg/hour. The only relevant studies conducted to date have been small retrospective cohort studies with fewer than 100 participants. A large, multi-centre randomised controlled trial is needed to undertake a comparative study of different dosages. This is because DKA is relatively uncommon and cerebral oedema (a potential adverse consequence of DKA) is rare, and there is a concern that larger dosages are associated with an increased risk of cerebral oedema. Important outcomes include rate of DKA resolution, incidence of hypoglycaemia and incidence of cerebral oedema.

This was selected a key research recommendation by the GDG for the 2015 update. The justification for the selection is summarised in the table below.

Potential criterion	Explanation
Importance to patients or the population	The GDG was able to make a recommendation about dosages of 0.05-0.1 units/kg/hour and further research would allow refinement of the recommendations
Relevance to NICE guidance	Relevant to a future update of this guideline
Relevance to the NHS	Relevant to a future update of this guideline and potential reduction in costs from avoiding prolonged hospitalisation and improving patient safety
National priorities	Not applicable
Current evidence base	Limited evidence was identified and there were no randomised controlled trials
Equality	Not applicable
Feasibility	Feasible with a large multi-centre randomised controlled trial
Other comments	None

L.1.6 Type 2 diabetes – behavioural interventions

L.1.6.1 What is the clinical and cost effectiveness of behavioural interventions for children and young people with type 2 diabetes?

Why this is important

The GDG has recommended that children and young people with type 2 diabetes and their family members or carers (as appropriate) should have access to mental health services, and this could include access to behavioural interventions. However, the evidence reviewed for the guideline was insufficient to recommend any specific behavioural intervention (no evidence at all related to behavioural interventions in children and young people with type 2

diabetes was identified for inclusion in the guideline review). The GDG recognised that for children and young people with type 2 diabetes and their family members or carers (as appropriate) lack of engagement with services (for example, non-attendance at clinic) is an important factor. Research is, therefore, needed to evaluate the effectiveness of any of the behavioural interventions prioritised by the GDG for consideration: family therapy (including behavioural family systems therapy); cognitive behavioural therapy; motivational interviewing; counselling; mentoring; and peer support. In particular, family therapy is a priority for evaluation given the social and cultural impact of type 2 diabetes in children and young people. Other behavioural interventions that are socially and culturally relevant and appropriate for children and young people with type 2 diabetes should also be evaluated. Initial research should be piloted at a local level and include process evaluation to assess cultural factors which may affect the application of interventions. Research ultimately needs to consist of multicentre, regional or national randomised controlled trials because type 2 diabetes in children and young people is still relatively rare. Any large-scale research study should include consideration of clinical and cost effectiveness.

L.1.7 Type 2 diabetes – weight loss

L.1.7.1 What is the correlation between changes in body mass index standard deviation scores and absolute HbA1c measurements or changes in HbA1c in children and young people with type 2 diabetes?

Why this is important

The GDG did not identify any evidence in children and young people with type 2 diabetes to indicate a correlation between weight loss or changes in body mass index standard deviation scores (BMISDS) and HbA1c. However, this form of correlation would be expected in children and young people and has already been demonstrated in adults. Studies in children and young people with type 2 diabetes are, therefore, needed. Such studies are likely to be observational in design and a prospective, register-based follow-up study covering all children and young people with type 2 diabetes in the UK would be ideal because type 2 diabetes is a relatively rarer condition in this age group. Changes in BMISDS and HbA1c over time would be of interest in such a study.

L.1.8 Type 2 diabetes – metformin

L.1.8.1 What is the long-term comparative clinical and cost effectiveness of different metformin preparations for treating type 2 diabetes in children and young people?

Why this is important

There is high-quality evidence for the clinical and cost effectiveness of metformin as a treatment for type 2 diabetes from diagnosis in children and young people. However, all of the relevant evidence relates to administration in tablet form and using a standard dosage, despite alternative preparations (including extended-release tablets and oral solutions) being available and having potential advantages to the standard preparation. Gastrointestinal disorders (for example, nausea, vomiting, diarrhoea, abdominal pain and loss of appetite) are very common with metformin, especially at the start of treatment, and may be reduced or avoided with alternative preparations. Extended-release tablets and oral solutions may also be easier to swallow, as standard formulation metformin consists of large tablets. Further research would preferably consist of randomised controlled trials. Outcomes should include blood glucose control (preferably using measurement of HbA1c levels) and the child or young person's satisfaction with and adherence to treatment.

This was selected a key research recommendation by the GDG for the 2015 update. The justification for the selection is summarised in the table below.

Potential criterion	Explanation
Importance to patients or the population	This is of importance because there are existing and emerging non-insulin agents (for example, metformin) which could be combined with insulin with potential benefit
Relevance to NICE guidance	Relevant to a future update of this guideline
Relevance to the NHS	Relevant to a future update of this guideline and potential reduction in costs associated with long-term complications
National priorities	Not applicable
Current evidence base	Not yet addressed in a NICE guideline
Equality	Not applicable
Feasibility	Feasible
Other comments	None

L.2 2004 recommendations for research that remain relevant in the 2015 update

Type 1 diabetes	Comments
Education	Further research is needed to evaluate the effectiveness of education programmes in which young people with type 1 diabetes provide training for their peers.
Insulin regimens	Research is needed to compare the effectiveness of continuous subcutaneous insulin infusion (or insulin pump therapy) and multiple daily injection regimens in children and young people with type 1 diabetes.
Insulin preparations	Research is needed to evaluate the effectiveness of long-acting insulin analogues in children and young people with type 1 diabetes.
Methods of delivering insulin	Further research is required to evaluate the effectiveness of insulin delivery systems in children and young people with type 1 diabetes.
	Research is needed to compare the effectiveness of insulin delivery modes (for example, dermal, nasal, oral and pulmonary) in children and young people with type 1 diabetes.
Non-insulin agents (oral antidiabetic drugs)	What is the clinical and cost effectiveness of non-insulin agents (for example, metformin) combined with insulin treatment in children and young people with type 1 diabetes?
	This research recommendation replaces the following from the 2004 guideline. Further research is needed to evaluate the effectiveness of (for example, metformin) combined with insulin treatment in children and young people with type 1 diabetes. The GDG's view was this remained an important area for research, and that non-insulin agents other than metformin could be

Type 1 diabetes		Comments
		investigated as part of the research. The GDG summarised the importance of the proposed research as follows. There are existing and emerging non-insulin agents which have potential for improving control in type 1 diabetes in children and young people (for example, metformin). Research comparing treatment with such agents combined with insulin and treatment with insulin alone should be conducted in the form of randomised controlled trials. Important outcomes to measure will include achieving HbA1c targets, tolerability and satisfaction with treatment.
Monitoring glycaemic control	Research is needed to investigate the clinical implications of alternative site monitoring (for example, the arm as opposed to the finger) in children and young people with type 1 diabetes.	
Screening for complications and associated conditions	Further research is needed to evaluate the effectiveness of screening for cardiovascular risk factors in children and young people with type 1 diabetes.	
Cognitive disorders	Further research is needed to evaluate the effects of persistent hypoglycaemia and recurrent diabetic ketoacidosis on neurocognitive function	
Adolescence	Further studies are needed to evaluate the effectiveness of behavioural and social interventions on anxiety and depression, eating disorders, behavioural and conduct disorders, and adherence to therapy in children and young people with type 1 diabetes, especially in adolescence, from diagnosis and in established diabetes.	
Communication between organisations	Further research is needed to evaluate the effects of low blood glucose levels on learning, attendance at school and educational attainment	
Transition from paediatric to adult care	Further research is needed to investigate young people's experiences of transition from paediatric to adult services for people with type 1 diabetes.	

L.3 2004 recommendations for research that were deleted as part of the 2015 update

Type 1 diabetes		Explanation
Education	Further research is needed to evaluate the effectiveness of age-specific structured education programmes	This research has been done and the intervention was ineffective. The GDG has, therefore, deleted this research

Type 1 diabetes		Explanation
	covering all aspects of care in children and young people with type 1 diabetes, their families and other carers.	recommendation as part of the update
	Further research is needed to determine the most effective way of training healthcare professionals to provide education about type 1 diabetes in children and young people.	This research recommendation was replaced by a new research recommendation related to training of healthcare professionals as part of the update
Insulin regimens	Research is needed to compare the effectiveness of multiple daily injection regimens with twice-daily injection regimens in children and young people with type 1 diabetes.	The GDG deleted this research recommendation because the update has addressed this topic and made recommendations in the section about multiple daily injections
Insulin preparations	Further research is needed to evaluate the effectiveness of once-daily injection regimens in children and young people with type 1 diabetes, and especially in pre-school children.	The GDG deleted this research recommendation because the update has addressed this topic and made recommendations in the section about multiple daily injections
Monitoring glycaemic control	Research is needed to evaluate the clinical effectiveness of the routine use of invasive and non-invasive continuous glucose monitoring systems for optimising glycaemic control in children and young people with type 1 diabetes.	This research recommendation was deleted because the update has addressed this topic and recommendations have been made in the section about continuous glucose monitoring systems
Diet	Further research is needed to evaluate the effectiveness of training in flexible, intensive insulin management to enable children and young people with type 1 diabetes to adjust insulin doses to match carbohydrate intake.	This research recommendation was deleted because the update has addressed this and recommendations have been made in the sections about multiple daily injections and dietary advice related to carbohydrate counting
Diabetic ketoacidosis	Further research is needed to evaluate the role of blood ketone monitoring in preventing diabetic ketoacidosis in children and young people with type 1 diabetes.	This research recommendation was deleted because the update has addressed this topic and made a recommendation in the section about ketone monitoring during intercurrent illness
	Further research is needed to investigate the effectiveness of different concentrations of rehydration fluid, the rate of rehydration, the use of albumin infusion and the dose of insulin infusion in the management of diabetic ketoacidosis in children and young people.	This research recommendation was replaced with a research recommendation focused specifically on identifying the optimal intravenous insulin dosage during management for diabetic ketoacidosis (the other aspects of the 2004 research recommendation have been addressed as part of the update and recommendations have been made for these topics)

Appendix M: Young people's consultation day

A young people's consultation day was organised for this guideline in collaboration with the NCB. The objective of the consultation day was to elicit the views of young people with type 1 diabetes and their carers in relation to topics considered in the guideline. Fourteen young women aged 13 to 17 years, seven young men aged 13 to 18 years, and 20 adults (14

mothers, five fathers and one older sister) participated in the consultation day. The main conclusions were³⁸ [evidence level IV]

- Young people wanted to be treated as 'normal' individuals growing towards adulthood.
- Young people wanted to be well informed about diabetes and to be involved in decisions affecting their care as they became more mature and independent.
- Young people and their parents wanted health care to be accessible, supportive and age-banded.
- Young people and their parents wanted consistent, accessible and up-to-date information about living with type 1 diabetes.
- Young people and their parents wanted schools to have consistent, but flexible, policies that offered support to young people with type 1 diabetes without treating them differently from their peers.
- More specific points identified by the NCB are summarised below and in the relevant sections of the guideline.³⁸ [evidence level IV]
- Young people with type 1 diabetes felt that healthcare professionals should be skilled in gaining the confidence of young people by educating them about diabetes in accessible language, treated them as individuals and with respect, and ensuring that they are given the opportunity to contribute to decisions about their diabetes care – see Section 3.2 (diabetes care teams).
- Young people with type 1 diabetes and their parents felt they should have 24-hour access to a named specialist nurse with whom they could speak confidentially and whom they could contact between clinic appointments – see Section 3.2 (diabetes care teams).
- Some young women with type 1 diabetes stated a preference for a female doctor who they felt they would be more comfortable with than a male doctor – see Section 3.2 (diabetes care teams).
- Young people with type 1 diabetes and their parents felt that it was important to see the same members of the diabetes care team wherever possible – see Section 3.2 (diabetes care teams).
- Young people with type 1 diabetes liked age-banded clinics – see Sections 3.2 (diabetes care teams) and 7.2 (transition from paediatric to adult care).
- Young people with type 1 diabetes were happy to miss school in order to attend clinic appointments, but their parents would prefer clinic appointments to be available outside school hours – see Section 3.2 (diabetes care teams).
- Parents suggested that clinic appointments should be flexible enough to take into account school terms and timetables and examination schedules – see Section 3.2 (diabetes care teams).
- Parents of young people with type 1 diabetes felt that there should be easy access to psychology services and suggested that paediatric diabetes care teams should include a psychologist – see Sections 3.2 (diabetes care teams) and 6.7 (psychosocial support).
- At the time of diagnosis some young people with type 1 diabetes felt they were given too much information at one time – see Section 3.4 (essential education at diagnosis).
- Young people with type 1 diabetes wanted information aimed at them rather than just at their parents although they understood that their parents also needed to know how to manage type 1 diabetes – see Section 3.4 (essential education at diagnosis).
- Young people with type 1 diabetes wanted insulin regimens that were flexible and allowed for a measure of spontaneity, and they wanted to be informed about the types of insulin that are available and given up-to-date information on insulin delivery devices and blood glucose testing monitors – see Section 4.2 (insulin regimens).
- Parents suggested annual updates from staff on the new products available – see Section 4.2 (insulin regimens).

- It was mentioned that some young people with type 1 diabetes may find four injections/day too many but they wanted to be involved in the discussion about how best to fit diabetes treatment into their chosen lifestyle while maintaining optimal metabolic control – see Section 4.2 (insulin regimens).
- Young people with type 1 diabetes and their parents wanted consistent, accessible up-to-date information on many aspects of living with type 1 diabetes, including information on what happens when you have type 1 diabetes, healthy eating, what to expect at clinic visits, types of insulin, injecting insulin and injection sites, hypoglycaemia and what to do if it occurs, complications of diabetes, how to drink alcohol safely, travelling abroad and leisure activities, becoming more independent, leaving home, implications for future careers, and new products and research – see Sections 4.2 (insulin regimens) and 4.1 (universal principles of education).
- Parents felt that education should be delivered through one-to-one or group education sessions with a specialist nurse, whereas young people with type 1 diabetes were more positive about accessing information through leaflets, CD-ROMs, videos and websites – see Section 4.1 (universal principles of education).
- Young people with type 1 diabetes, in particular young women, were sensitive about body weight and wanted weighing to be carried out in a private room – see Section 5.5 (screening for complications and associated conditions).
- Young people with type 1 diabetes valued meeting other young people with type 1 diabetes and might benefit from formalised arrangements for meeting each other – see Section 7.1 (support groups).
- Some parents suggested that age of transfer of young people with type 1 diabetes from paediatric to adult services should be standardised and that clinics should be jointly run by paediatric and adult services to provide continuity of care – see Section 7.2 (transition from paediatric to adult care).
- Other parents thought that individual young people with type 1 diabetes should be involved in the decision about when transfer should occur – see Section 7.2 (transition from paediatric to adult care).

Appendix N: Superseded text from 2004 guideline

This appendix is presented in a separate document.

