National Clinical Guideline Centre

Final, August 2015

Type 1 diabetes in adults

Type 1 diabetes: diagnosis and management

Clinical guideline NG17

Appendices A – F

August 2015

2015 update

Commissioned by the National Institute for Health and Care Excellence

Royal College of Physicians
The Royal College of Surgeons of England
RCGP Royal College of General Practitioners
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Disclaimer
Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

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National Institute for Health and Care Excellence

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Appendix A: Scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Type 1 diabetes: diagnosis and management of type 1 diabetes in adults

1.1 Short title

Type 1 diabetes in adults

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. 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.

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.

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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

a) Type 1 diabetes is a long-term hormonal deficiency disorder, in which there is loss of insulin secretion. This results in high blood glucose concentrations and other metabolic and haematological abnormalities. It is usually caused by autoimmune destruction of the insulin-secreting beta cells of the pancreas. In the short term, people with type 1 diabetes may face significant challenges to daily living, for example, hyperglycaemia (high blood glucose) and hypoglycaemia (low blood glucose), the need for daily administration of insulin and frequent self-monitoring of blood glucose, and to plan daily activities such as eating and exercising. Over the long term, type1 diabetes is associated with major complications and reduced life expectancy. The condition is treated with insulin replacement therapy and at present there is no cure.

b) Approximately 10% of adults diagnosed with diabetes have type 1 diabetes. Currently, it is estimated that 0.34-0.55% of the population of England and Wales are known to have type 1

diabetes. Among people aged between 10 and 80 years, there is little difference in prevalence across age groups.

c) Type 1 diabetes can present at any age. Although it commonly presents in children and adolescents, the condition persists into and can start in adult life. Treatment regimens used to manage diabetes and the demands of living with diabetes are as complex in adults as in younger people.

d) Effective insulin management requires detailed knowledge of its actions.

e) Life expectancy for people with type 1 diabetes has increased. In one study from the USA, life expectancy among people diagnosed with type 1 diabetes between 1965 and 1980 improved by 15 years compared with people diagnosed between 1950 and 1964. Nevertheless, having type 1 diabetes typically reduces life expectancy in the UK by 20 years. People with type 1 diabetes in England are 2.6 times more likely to die than people without diabetes of the same age. Most of the deaths are due to chronic complications, although death in acute hypoglycaemia or diabetic ketoacidosis may occur.

f) The Diabetes Control and Complications Trial Research Group[1] confirmed that strict blood glucose control reduces risk of long-term complications and is associated with increased life expectancy among people with type 1 diabetes. Effective insulin management requires detailed knowledge of its actions. The insulin user needs to acquire skill in insulin management. Control of blood pressure also reduces risk of complications in people with type 1 diabetes. Controlling lipids within recommended targets for other forms of diabetes is expected to reduce excess cardiovascular risk associated with type 1 diabetes.

[1] The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993;329:977-986.

g) Early detection and effective management of type 1 diabetes and its complications are important to prevent or limit disability in people with type1 diabetes.

3.2 Current practice

a) People with type 1 diabetes manage many aspects of their own care, including administering insulin by injection or infusion, monitoring their blood glucose levels, and adjusting insulin doses accordingly. Glucose levels should be assessed regularly to guide insulin dose adjustment and to ensure they remain within target levels known to minimise risk of complications, while avoiding problems such as hypoglycaemia or ketosis.

b) People with type 1 diabetes need education and support from healthcare professionals with expertise in insulin physiology and therapeutics to manage their diabetes effectively. Hypoglycaemia remains a problem for people using insulin.

c) Fewer than 1 third of people with type 1 diabetes achieve the NICE-recommended target for blood glucose control, which is haemoglobin A1c (HbA_{1c}) of 59 mmol/mol or lower, or below 7.5%. In the last 4 audit cycles, there has been no significant improvement in the proportion of people who meet this target.

d) People with type 1 diabetes need regular monitoring for complications of diabetes. Where these occur, active management is needed. However, only 31.9% of people with type 1 diabetes in England and Wales have records of receiving all 9 of the care processes recommended by NICE. More than 30% of people with type 1 diabetes miss their annual eye and foot checks for early complications and almost 1 half miss screening appointments for kidney complications.

e) Two thirds of people with type 1 diabetes achieve the NICE-recommended target for blood pressure control. Among people

who are morbidly obese this figure is 45%. Approximately 1 third of people with type 1 diabetes achieve the current stringent target for total cholesterol, which is below 4 mmol/litre.

f) Rates of diabetic ketoacidosis appear to be increasing in the UK. There has also been an increase in the number of people with type 1 diabetes needing treatment for end-stage kidney disease.

g) Diabetes management in hospitals and other places for professional health care remains suboptimal. Insulin regimens are the most common cause of drug errors in inpatient prescribing

h) People with type 1 diabetes have traditionally received care primarily from specialist services. However, 15–20% of adults with type 1 diabetes have little or no contact with secondary care services, or are offered only infrequent appointments focussed on annual review.

i) A small number of people with type 1 diabetes experiencing life-threatening episodes of hypoglycaemia undergo pancreatic transplant or islet cell transplantation. Around 200 pancreas transplants are performed in the UK each year[2]. Around 95 islet transplants have been performed in 65 people in the UK to date[3].

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.

[2] NHS Choices http://www.nhs.uk/conditions/pancreastransplant/Pages/Introduction.aspx (accessed 23 July 2013)
[3] Diabetes UK http://www.diabetes.org.uk/Guide-to-diabetes/Treatments/Islet-transplants/ (accessed 23 July 2013)

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) Adults (aged 18 years and older) with type 1 diabetes.

b) Where the evidence supports it, the following subgroups will be given special consideration

- Ethnic groups
- People who are unable to inject themselves for whatever reason
- People whose religious beliefs may affect the management of their diabetes
- People with literacy or numeracy difficulties

4.1.2 Groups that will not be covered

a) Children and young people with type 1 diabetes (this will be addressed in a separate guideline).

b) Adults with type 2 diabetes (this will be addressed in a separate guideline).

c) Diabetes in pregnancy (this will be addressed in a separate guideline).

d) Monogenic and other rarer forms of diabetes

4.2 Healthcare setting

a) All settings in which NHS care is received or commissioned.

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 by an evidence review

a) Diagnosis of type 1 diabetes: differentiation from type 2 diabetes and other forms of diabetes using c-peptides and antibody testing.

b) Education programmes and self-care: structured educational programmes.

c) Clinical monitoring of glucose control:

- HbA_{1c}:
  - targets
  - frequency of monitoring.
- Self-monitoring of blood glucose (finger pricks):
  - targets
  - frequency of monitoring
  - timing
  - benefit of technologies (bolus calculators and downloads).
- Continuous glucose monitoring (CGM):
  - self-monitoring blood glucose versus real-time CGM
  - self-monitoring blood glucose versus retrospective CGM
  - intermittent real-time monitoring versus continuous real-time monitoring.
- Ketone monitoring (see 4.3.1.m).

d) Insulin regimens, particularly rapid-acting insulins and new background insulins (see also 4.3.1.j).

- Detemir versus degludec versus degludec-aspart combinations versus glargine versus NPH.
- Once-daily basal versus twice-daily basal.

- Rapid-acting insulins for meal times: analogues versus human soluble.

e) Non-insulin pharmacological agents in combination with insulin (specifically, metformin).

f) Needle length and injection site for insulin administration.

g) Aspirin for the primary prevention of cardiovascular disease.

h) Treatment of specific late-stage complications:

- Insulin-induced neuritis.
- Gastroparesis.
- Erectile dysfunction.

i) Inpatient management in relation to insulin replacement:

- Intravenous regimens.
- Dose-adjustment devices.

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

j) New insulin formulations, including insulin degludec, insulin degludec-aspart combinations and insulin detemir (see 4.3.1.d).

k) Hypoglycaemia unawareness.

l) Monitoring for thyroid disease.

m) The role of ketone monitoring:

- Self-monitoring for the prevention of diabetic ketoacidosis.
- Monitoring of diabetic ketoacidosis

n) Carbohydrate counting and glycaemic index taking into account balancing protein and lipid intake

o) Referral criteria for pancreas transplant and islet cell transplantation.

4.3.2 Clinical issues that will not be covered

Areas from the original guideline that will not be updated by an evidence review

a) The care process and support: topics such as multidisciplinary support, individual care plans, use of technology, and support groups will not be included.

b) Aspects of education programmes and self-management not listed in section 4.3.1: topics such as physical activity, cultural and individual lifestyle and dietary management (with the exception of carbohydrate counting) will not be included.

c) Aspects of blood glucose control and insulin therapy not listed in section 4.3.1: topics such as the management of symptomatic hypoglycaemia will not be included.

d) Arterial risk control, with the exception of aspirin.

e) Management of late complications: topics such as diabetic eye disease, diabetic kidney disease, diabetes foot, diabetic nerve damage (other than erectile dysfunction, insulin-induced neuritis and gastroparesis) will not be included.

f) Management of special situations not listed in section 4.3.1: topics such as the management of diabetic ketoacidosis (with the exception of blood ketone measurement), management of intercurrent illness, and psychological problems will not be included.

g) Inpatient management not listed in section 4.3.1.i.

Areas not covered by the original guideline or the update

h) Preconception care in women with type 1 diabetes (this will be addressed by the diabetes in pregnancy guideline).

i) Contraceptive advice in women with type 1 diabetes (this will be addressed by the diabetes in pregnancy guideline).

The following NICE guidance will be cross referred to

j) Insulin pumps:

- Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus. NICE technology appraisal 151 (2008).

k) Identification of arterial risk, interventions to reduce risk (with the exception of aspirin), and blood pressure management:

- Hypertension. NICE clinical guideline 127 (2011).
- Lipid modification. NICE clinical guideline 67 (2007). (An update of this guideline is currently in progress)
- Statins for the prevention of cardiovascular events. NICE technology appraisal 94 (2006).

l) Painful neuropathy:

- Neuropathic pain. NICE clinical guideline 96 (2010). (An update of this guideline is currently in progress)
- Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin. NICE technology appraisal 159 (2008).

m) Diabetic kidney disease:

- Chronic kidney disease (update). NICE clinical guideline 73 (2008). (An update of this guideline is currently in progress)

n) Diabetic foot problems:

- Diabetic foot problems - inpatient management. NICE clinical guideline 119 (2011).
- Type 2 diabetes - footcare. NICE clinical guideline 10 (2004).

o) Monitoring and management of special situations including eating disorders, depression, or other psychological problems:

- Anxiety. NICE clinical guideline 113 (2011).
- Depression with a chronic physical health problem. NICE clinical guideline 91 (2009).
- Depression in adults (update). NICE clinical guideline 90 (2009).
- Nutrition support in adults. NICE clinical guideline 32 (2006).
- Eating disorders. NICE clinical guideline 9 (2004).

4.4 Main outcomes

a) Health-related quality of life.

b) Adverse events and complications.

c) Mortality.

d) $HbA_{1c.}$

e) Hypoglycaemia.

4.5 Review questions

Diagnosis

- In adults and young people with diabetes, what is the best diagnostic test(s) (c-peptides plus or minus antibodies) to distinguish between a diagnosis of type 1 diabetes, type 2 diabetes and other forms of diabetes?

Education programmes and self-care

- In adults with type 1 diabetes, what is the most effective structured education programme?

Clinical monitoring of glucose control

- HbA_{1c}
  - In adults with type 1 diabetes, what is the optimum target HbA_{1c} level that should be achieved to reduce the risk of complications?

  - In adults with type 1 diabetes, what is optimum frequency of HbA_{1c} monitoring for effective diabetic control?
- Self-monitoring of blood glucose (finger pricks)
  - In adults with type 1 diabetes, what is the optimum glucose target for self-monitoring of blood glucose for effective diabetic control?
  - In adults with type 1 diabetes, what is optimum timing and frequency to self-monitor blood glucose for effective diabetic control?
  - In adults with type 1 diabetes, what are the benefits of technologies (bolus calculators,downloads and smartphone apps) for self-monitoring of blood glucose?
- Continuous glucose monitoring (CGM)
  - In adults with type 1 diabetes, is real-time CGM more effective than self-monitoring blood glucose for optimal diabetic control?
  - In adults with type 1 diabetes, is retrospective CGM more effective than care without CGM (with SMBG) for improving diabetic control?
  - In adults with type 1 diabetes, is continuous real-time monitoring more effective than intermittent real-time monitoring for optimal diabetic control?
- Ketone monitoring
  - In adults with T1D (including atypical ketosis-prone diabetes), does patient self-monitoring of blood (and urine) ketones reduce the incidence of diabetic ketoacidosis and hospital admissions?
  - In adults with type 1 diabetes does inpatient monitoring of blood ketones by the healthcare professional reduce the length of hospital stay, exposure to iv insulin and the development of in-hospital complications : a) in patients with suspected diabetic ketoacidosis; b) in patients admitted with diabetic ketoacidosis and / or those who get it in hospital

Insulin regimens

- In adults with type 1 diabetes, what are the most effective long-acting insulins (detemir versus degludec versus glargine versus NPH) for optimal diabetic control?

- In adults with type 1 diabetes, is once-daily basal insulin more effective than twice-daily basal insulin for optimal diabetic control?
- In adults with type 1 diabetes, what are the most effective mixed insulins (degludec-aspart versus glargine versus NPH) for optimal diabetic control?
- In adults with type 1 diabetes, which are the most effective rapid-acting insulins for meal times: analogues versus human (intermediate NPH), for optimal diabetic control?

Insulin combination with non-insulin pharmacological agents

- In adults with type 1 diabetes, aremetformin (with or without insulin) or GLP1-agonists (with or without insulin) as effective as insulin alone for optimal diabetic control?

Insulin administration

- In adults with type 1 diabetes, what is the optimum needle length for insulin delivery?
- In adults with type 1 diabetes, what is the optimum injection site and rotation for insulin delivery?

Prevention of cardiovascular disease (aspirin)

- In adults with type 1 diabetes, is aspirin an effective anti-platelet agent for the primary prevention of cardiovascular events?

Treatment of specific late-stage complications

- In adults with type 1 diabetes, what is the most effective treatment for insulin-induced neuropathy?
- In adults with type 1 diabetes, what is the most effective treatment for gastroparesis?

Inpatient management (in relation to insulin replacement)

- In adults with type 1 diabetes who have been admitted to hospital, what is the most effective intravenous insulin regimen for optimal diabetic control?
- In adults with type 1 diabetes who have been admitted to hospital, what are the most effective dose-adjustment devices for optimal diabetic control?

Hypoglycaemia unawareness

- In adults with type 1 diabetes, what is the most effective strategy for recovering hypoglycaemia awareness?
- In adults with type 1 diabetes, how is problematic hypoglycaemia identified and quantified?

Monitoring for thyroid disease

- Should adults with type 1 diabetes be monitored for thyroid disease, and if so, for how long?

Carbohydrate counting and glycaemic index

- In adults with type 1 diabetes, what is the clinical and cost-effectiveness of a diet based on carbohydrate counting or restriction for optimal diabetic control?
- In adults with type 1 diabetes, what is the clinical and cost-effectiveness of a diet based on the glycaemic index for optimal diabetic control?

Referral criteria for pancreas transplant and pancreatic islet cell transplantation

- In adults with type 1 diabetes, what are the referral criteria that indicate a person should be considered for a pancreas transplant, or pancreatic islet cell transplantation?

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

4.7.1 Scope

This is the final version of the scope.

4.7.2 Timing

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

5 Related NICE guidance

5.1 Published guidance

5.1.1 NICE guidance to be updated

Depending on the evidence, this guideline might update and replace parts of the following NICE guidance:

- Type 1 diabetes. NICE clinical guideline 15 (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).

5.1.2 Other related NICE guidance

- Patient experience in adult NHS services. NICE clinical guideline 138 (2012).
- Lower limb peripheral arterial disease. NICE clinical guideline 147 (2012).
- Preventing type 2 diabetes: population and community-level interventions. NICE public health guidance 35 (2011).
- Hyperglycaemia in acute coronary syndromes. NICE clinical guideline 130 (2011).
- Hypertension. NICE clinical guideline 127 (2011).
- Ranibizumab for the treatment of diabetic macular oedema. NICE technology appraisal 237 (2011).

- Dexamethasone intravitreal implant for the treatment of macular oedema secondary to retinal vein occlusion. NICE technology appraisal 229 (2011).
- Ranibizumab for the treatment of diabetic macular oedema. NICE technology appraisal 237 (2011).
- Clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events. NICE technology appraisal guidance 210 (2010).
- Depression with a chronic physical health problem. NICE clinical guideline 91 (2009).
- Depression in adults. NICE clinical guideline 90 (2009).
- Medicines adherence. NICE clinical guideline 76 (2009).
- Coeliac disease. NICE clinical guideline 86 (2009).
- Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus. NICE technology appraisal 151 (2008).
- Allogeneic pancreatic islet cell transplantation for type 1 diabetes mellitus. NICE interventional procedure guideline 257 (2008).
- Inhaled insulin for the treatment of type 1 and type 2 diabetes. NICE technology appraisal 113 (2006).
- Smoking cessation services. NICE public health guidance 1 (2006).
- Obesity. NICE clinical guideline 43 (2006).
- Nutrition support in adults. NICE clinical guideline 32 (2006).
- Four commonly used methods to increase physical activity. NICE public health guidance 2 (2006).
- Statins for the prevention of cardiovascular events. NICE technology appraisal 94 (2006).
- Gastroelectrical stimulation for gastroparesis. NICE interventional procedure guide 103 (2004).

5.2 Guidance under development

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

- Diabetic macular oedema - fluocinolone acetonide intravitreal implant. NICE technology appraisal. Publication expected November 2012.
- Type 2 diabetes (update). NICE clinical guideline. Publication date to be confirmed.
- Diabetes in children (update). NICE clinical guideline. Publication date to be confirmed.
- Diabetes in pregnancy. NICE clinical guideline. Publication date to be confirmed.
- Diabetes - buccal insulin. NICE technology appraisal. Publication date to be confirmed.
- Macular oedema (diabetic) - pegaptanib sodium. NICE technology appraisal. Publication date to be confirmed.
- Macular oedema (diabetic) ranibizumab. NICE technology appraisal. Publication date to be confirmed.
- Lipid modification (update). NICE clinical guideline. Publication date to be confirmed.
- Chronic kidney disease (update). NICE clinical guideline. 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 B: Declarations of interest

B.1 Stephanie Amiel (chair)

GDG meeting	Declaration of Interests	Action taken
On appointment 13 January 2012	Personal pecuniary: I have served on advisory boards for Medtronic, Cell Novo, Novo Nordisk, MSD, Eli Lilly. I have received honoraria for lecturing/teaching from (or have spoken at meetings sponsored by) Abbott, Medtronic, Lifescan, Roche, Sanofi-Aventis. Non-personal pecuniary: I am co-head of a Clinical Academic Group and an academic division in my institutions (King's College London and King's College Hospital). They have received funding for research or service development from Novo Nordisk. Personal non-pecuniary interest: I am a member of the scientific advisory boards of the Juvenile Diabetes Research Foundation and Diabetes UK I am on the editorial board for the Diabetes and Wellness Foundation. I am academic representative to the Executive Committee of the Association of British Clinical Diabetologists. Until last year, I was the Chairman of the National Dose adjustment for normal eating (DAFNE) Executive. I have published both as named author or as part of a consensus group, reviews, papers and guidelines concerning diabetes management and particularly hypoglycaemia in diabetes, including involvement in local/national/international guidelines on insulin pump therapy (including for NTAC); bariatric surgery in diabetes; use of glucose monitoring.	Stephanie Amiel's declaration of interest in relation to DAFNE was discussed with the Guideline Lead and it was deemed to be reasonable for Stephanie to take part in the discussions. Several of the healthcare professionals on the GDG are trained educators. Wherever the interest was of relevance, the GDG were reminded of it.
GDG 1 23 October 2012	Personal pecuniary: I append a list of advisory boards attended and single (industry) sponsor educational meetings where I have been a speaker. I have resigned from all this work since my appointment to the NICE GDG chair position and have refused all subsequent invitations to such activities. Personal family interest: My husband is Chairman of Diabetes UK and Chairman of King's College Hospital NHS Foundation Trust. I am not aware of but do not keep information on his other professional activities. Non-personal pecuniary interest: I am co-lead of a Clinical Academic Group in Diabetes, Endocrinology and metabolism, Nutrition, Obesity, Vision and Related Surgeries (DENOVaRS) at King's Health	None

GDG meeting	Declaration of Interests	Action taken
	Partners (the Academic Health Sciences Centre comprising King's College Hospital and Guy's and St Thomas' Hospitals NHS Foundations Trusts, the South London and the Maudsley Mental Health Trust and King's College London). DENOVaRS is currently undertaking a project 'Changing Diabetes at KHP' which is reviewing diabetes services provided by the KHP institutions with a view to service re-design. Phase one of this project (data collection) is supported by Novo Nordisk. My current research is supported by NIHR and Diabetes UK. I am a co-investigator on a collaborative research grant from Medtronic. Please see attached publication list. I am Chairman of the EFSD/China Diabetes Society/Lilly Programme, an EFSD body that awards research grants and fellowships and organises educational visits with CDS; I am Editor of the International Diabetes Federation's journal Diabetes Voice; I participate in the National Director for Diabetes' insulin pump working party. I am on the Juvenile Diabetes Research Foundations' international scientific advisory board; academic member of the committee of the Association of British Clinical Diabetologist and a member of Diabetes UKs research committee.	
GDG 2 27 November 2012	No personal pecuniary interests within the last 12 months.	None
GDG 3 8 January 2013	Non-personal pecuniary: A named investigator on a research study being run by a colleague here at King's, Dr Pratik Choudhary, that is a collaboration with Medtronic, the insulin pump and glucose sensor manufacturer. The study is an investigation into the efficacy and safety of their overnight closed loop insulin delivery device and has been 3 years in coming to fruition, which is why it is now being activated. Dr Choudhary is the grant awardee. I did have input into the study design - again without pecuniary advantage - and will be involved in its delivery. The grant is made to KCL in Dr Choudhary's name and he is the Chief and Principal investigator, and no money comes to me.	Declare and participate.
GDG 4 5 March 2013	None declared	None
GDG 5 9 April 2013	Serving on the international working party on hypoglycaemia but there is no remuneration.	None
GDG 6 14 May 2013	None declared	None
GDG 7 18 June 2013	None declared	None
GDG 8 3 September 2013	Speaker at the SE/SW Diabetes Specialist Nurses forum on 22 November 2013. No remuneration.	Declare and participate

GDG meeting	Declaration of Interests	Action taken
GDG 9 14 October 2013	None declared	None
GDG 10 15 October 2013	None declared	None
GDG 11 26 November 2013	None declared	None
GDG 12 14 January 2014	None declared	None
GDG 13 15 January 2014	None declared	None
GDG 14 4 March 2014	None declared	None
GDG 15 15 April 2014	None declared	None
GDG 16 20 May 2014	Personal non-pecuniary: This European Association for the study of Diabetes (EASD) satellite symposium is being held by the International Hypoglycaemia Study Group (IHSG). It is funded and run by Six Degrees, which is funded by an unrestricted educational grant from Novo Nordisk. Six degrees is independent and has funding for different projects from many different sponsors. I accept travel costs and accommodation but no honorarium. Personal non-pecuniary: I am giving the Jeff Goulder Memorial lecture at the Oxford Diabetes Symposium in June. The Oxford symposium is an annual event of high repute sponsored by Novo Nordisk but run independently by the Oxford Centre for Diabetes Endocrinology and Metabolism (OCDEM). I will receive travel expenses and accommodation in an Oxford College but no other pecuniary gain.	Declare and participate
GDG 17 27 June 2014	None declared	None
GDG 18 29 July 2014	Personal non-pecuniary interest: Participation continuing in Six degrees hypoglycaemia study (as previously declared). Non-personal pecuniary interest: Academic representative on King's Health Partners project with Novo Nordisk (as previously declared). Personal non-pecuniary interest: will deliver a talk at the Diabetes Specialist Nurses forum on 6 November 2014. Non-promotional meeting. I will not receive any payment. Personal non-pecuniary: gave permission and details for Kings College Hospital for the Accu-Chek DiaPort (Roche product - intraperitoneal insulin infusion port) brochure on centres of excellence for	Declare and participate.

GDG meeting	Declaration of Interests	Action taken
	healthcare professionals.	
GDG 19 24 September 2014	Personal pecuniary interest: I attended the EASD (European Association for the Study of Diabetes) meeting which was paid for by six degrees (hypoglycaemia study group). Travel and accommodation expenses were received.	Declare and participate
GDG 20 24 March 2015	Personal non-pecuniary interest: I continue to work with the international hypoglycaemia study group organised by the Six Degrees who are providing financial support for the group.	Declare and participate

B.2 Augustin Brooks

GDG meeting	Declaration of Interests	Action taken
On appointment 8 August 2012	None declared	None
GDG 1 23 October 2012	None declared	None
GDG 2 27 November 2012	None declared	None
GDG 3 8 January 2013	None declared	None
GDG 4 5 March 2013	None declared	None
GDG 5 9 April 2013	None declared	None
GDG 6 14 May 2013	None declared	None
GDG 7 18 June 2013	None declared	None
GDG 8 3 September 2013	None declared	None
GDG 9 14 October 2013	None declared	None
GDG 10 15 October 2013	None declared	None
GDG 11 26 November 2013	None declared	None
GDG 12 14 January 2014	None declared	None
GDG 13 15 January 2014	None declared	None
GDG 14 4 March 2014	None declared	None
GDG 15 15 April 2014	None declared	None
GDG 16 20 May 2014	None declared	None

GDG meeting	Declaration of Interests	Action taken
GDG 17 27 June 2014	None declared	None
GDG 18 29 July 2014	None declared	None
GDG 19 24 September 2014	None declared	None
GDG 20 24 March 2015	None declared	None

B.3 Arthur Durrant

GDG meeting	Declaration of Interests	Action taken
On appointment 8 August 2012	None declared	None
GDG 1 23 October 2012	Lifelong membership of Diabetes UK.	None
GDG 2 27 November 2012	None declared	None
GDG 3 8 January 2013	None declared	None
GDG 4 5 March 2013	None declared	None
GDG 5 9 April 2013	None declared	None
GDG 6 14 May 2013	None declared	None
GDG 7 18 June 2013	None declared	None
GDG 8 3 September 2013	None declared	None
GDG 9 14 October 2013	Arthur declared that he has joined the lay advisory panel for diabetes and endocrinology research at Sheffield Teaching Hospitals NHS Foundation Trust.	None
GDG 10 15 October 2013	None declared	None
GDG 11 26 November 2013	None declared	None
GDG 12 14 January 2014	None declared	None
GDG 13 15 January 2014	None declared	None
GDG 14 4 March 2014	None declared	None
GDG 15 15 April 2014	None declared	None
GDG 16 20 May 2014	I have recently been appointed as the chair of the Sheffield Teaching Hospitals' Lay Panel for Diabetes	None

GDG meeting	Declaration of Interests	Action taken
	& Endocrinology Research.	
GDG 17 27 June 2014	None declared	None
GDG 18 29 July 2014	None declared	None
GDG 19 24 September 2014	None declared	None
GDG 20 24 March 2015	None declared	None

B.4 Michael Flynn

GDG meeting	Declaration of Interests	Action taken
On appointment 12 July 2012	None declared	None
GDG 1 23 October 2012	Attended meetings supported by pharmaceutical companies. Reasonable expenses only.	Declare and participate
GDG 2 27 November 2012	None declared	None
GDG 3 8 January 2013	None declared	None
GDG 4 5 March 2013	None declared	None
GDG 5 9 April 2013	None declared	None
GDG 6 14 May 2013	None declared	None
GDG 7 18 June 2013	None declared	None
GDG 8 3 September 2013	None declared	None
GDG 9 14 October 2013	None declared	None
GDG 10 15 October 2013	None declared	None
GDG 11 26 November 2013	None declared	None
GDG 12 14 January 2014	None declared	None
GDG 13 15 January 2014	None declared	None
GDG 14 4 March 2014	None declared	None
GDG 15 15 April 2014	None declared	None
GDG 16	None declared	None

GDG meeting	Declaration of Interests	Action taken
20 May 2014		
GDG 17 27 June 2014	None declared	None
GDG 18 29 July 2014	None declared	None
GDG 19 24 September 2014	TBC	-
GDG 20 24 March 2015	TBC	

B.5 Roger Gadsby

GDG meeting	Declaration of Interests	Action taken
On appointment 29 January 2012	My current industry work involves advisory boards for MSD (sitagliptin), NovoNordisk (Insulin degludec) and Janssen (canagliflozin). Insulin degludec is the only one that I think has possible impacts on Type 1 diabetes. Dr Roger Gadsby has received funding over the past 28 years for attending symposia and other educational events, for speaking at meetings, and for participating in advisory committees, from a variety of diabetes and cardiovascular pharmaceutical companies. These include AstraZeneca, Boehringer Ingelheim, Janssen-Cilag GlaxoSmithKline, Servier, Sanofi-Aventis, Takeda, Bristol Myers Squibb, NovoNordisk, Roche, Roche Diagnostics, MSD, Merck-Serono, Grunenthal, Solvay and Novartis. He holds no shares in any companies. From 1 Sept 2009 to 31 Dec 2011 two sessions per week of his time at Warwick Medical School were supported by an unrestricted educational grant from the two pharmaceutical companies NovoNordisk and Takeda. Personal family interest: None Non-personal pecuniary interest: In 2000 he helped to set up Warwick Diabetes Care (WDC), an organisation at Warwick University providing diabetes education programmes across the UK in 2000. WDC received support from 14 diabetes pharmaceutical companies who as foundation sponsors provided educational grants to assist its launch and initial development. Several of the current diabetes education programmes at Warwick Medical School are supported by educational grants from	Declare and withdraw from discussions of all types of insulin.

GDG meeting	Declaration of Interests	Action taken
	pharmaceutical companies. He is chairman of the Trustees of a small charity called Pregnancy Sickness Support Trust (Registered Charity No 1094788) which gives information and support to women with pregnancy sickness symptoms. The charity has received support from a number of organisations and companies including Vitabiotics Ltd, Duchesnay Inc. (Canada) and the charity committee of Land Rover plc.	
GDG 1 23 October 2012	Not a member of the GDG	None
GDG 2 27 November 2012	Not a member of the GDG	None
GDG 3 8 January 2013	Not a member of the GDG	None
GDG 4 5 March 2013	Did not attend	None
GDG 5 9 April 2013	Doing advisory work paid for by Novo Nordisk	Declare and withdraw from discussions on insulin.
GDG 6 14 May 2013	I was a member of the NovoNordisk Diabetes Primary Care Advisory Board for Degludec which met on 23 October 2012. That is the only paid work that could possibly constitute a conflict of interest. Other Advisory boards were for Janssen on 9 Nov 2012 and 2 May 2013 but these are for canagloflozin a drug for type 2 diabetes, so no conflict with the type 1 guideline I think. My other strands of paid work in the past year are through my work at the Universities of Warwick and Bedfordshire, My work as GP lead for the National Diabetes Audit, and as Primary care lead for NHS Diabetes (finished on 31 March 2013). I have also done lots of work for NICE, most of it unpaid apart from 3 days paid as chairman of the Annual Evidence Update panel for CG 119.	Declare and withdraw from discussions on insulin.
GDG 7 18 June 2013	None declared	None
GDG 8 3 September 2013	None declared	None
GDG 9 14 October 2013	None declared	None
GDG 10 15 October 2013	Did not attend meeting.	None
GDG 11 26 November 2013	Did not attend meeting.	None
GDG 12 14 January 2014	None declared	None

GDG meeting	Declaration of Interests	Action taken
GDG 13 15 January 2014	None declared	None
GDG 14 4 March 2014	None declared	None
GDG 15 15 April 2014	Since the last GDG meeting I have been asked to attend and have attended a first meeting of an advisory group for the Eli Lilly / Boehringer Alliance looking at a new insulin which is not licensed or launched yet in the UK. It is likely to come to market sometime in 2015.	Declare and participate.
GDG 16 20 May 2014	None declared	None
GDG 17 27 June 2014	Did not attend meeting.	None
GDG 18 29 July 2014	None declared	None
GDG 19 24 September 2014	None declared	
GDG 20 17 March 2015	I have been member of the International Advisory Board for Eli Lily from April 2014, advising on new insulin (biosimilar glargine) which is likely to be launched in the UK in 2015. I am a member of the advisory board for MSD on a project to plan to co-ordinate primary and secondary healthcare data in January 2015. This project is a generic data project and is not planned to deal in any specific products. I have spoken at local meetings on type 2 diabetes and SGLT2 inhibitors for Janssen. I work one day a week for the National Diabetes Audit, and 1.5 days a week for Warwick Medical School, University of Warwick. Courses from Warwick are sometimes sponsored by Diabetes Pharma companies, but I am not aware of any sponsorship in the relevant time periods for this declaration.	Declare and participate

B.6 Peter Hammond

GDG meeting	Declaration of Interests	Action taken
On appointment 11 July 2012	Personal Pecuniary: In the last 12 months I have received honoraria for lecturing from Novo Nordisk, Lilly, Sanofi (ELIXA trial), Medtronic and Animas; and for attending advisory boards from Sanofi (ELIXA study) and Medtronic.	Declare and withdraw from discussing recommendations for insulin, continuous glucose monitoring and pumps (valid until October 2013).
GDG 1 23 October 2012	Sanofi sponsored attendance at the EASD October 2012 (reasonable expenses).	Declare and withdraw from discussing recommendations for insulin, continuous glucose

GDG meeting	Declaration of Interests	Action taken
	I lectured for both Animas and Medtronic in October (16th and 24th respectively). I have future commitments lecturing for Medtronic but have advised them that I will no longer be paid for this work. I have not been paid for lecturing this year by Novo, Sanofi or Lilly, so my last paid activity was an advisory board for Sanofi at Diabetes UK in March (8th I believe), although this was specifically an update meeting for researchers on the ELIXA study (lixisenatide - GLP1 agonist). My unit is a centre for the ELIXA study. (Sanofi) NHS Diabetes Lead for Insulin Pump Therapy	monitoring and pumps (valid until October 2013).
GDG 2 27 November 2012	Personal Pecuniary: In the last 12 months I have received honoraria for lecturing from Novo Nordisk, Lilly, Roche, Medtronic and Animas; and for attending advisory boards from Sanofi (ELIXA trial) and Medtronic. Sanofi sponsored my attendance at the EASD October 2012.	Declare and withdraw from discussing recommendations for insulin, continuous glucose monitoring and pumps (valid until October 2013).
GDG 3 8 January 2013	None declared	None
GDG 4 5 March 2013	Roche provided sponsorship to attend Advanced Technology and Therapeutics in Diabetes meeting, Paris 27th February - 2nd March 2013.	Declare and participate.
GDG 5 9 April 2013	None declared	None
GDG 6 14 May 2013	None declared	None
GDG 7 18 June 2013	None declared	None
GDG 8 3 September 2013	None declared	None
GDG 9 14 October 2013	None declared	None
GDG 10 15 October 2013	None declared	None
GDG 11 26 November 2013	None declared	None
GDG 12 14 January 2014	None declared	None
GDG 13 15 January 2014	None declared	None
GDG 14 4 March 2014	None declared	None
GDG 15 15 April 2014	None declared	None
GDG 16	Personal non-pecuniary interest: attended an	Declare and participate

GDG meeting	Declaration of Interests	Action taken
20 May 2014	advisory panel for the flash glucose sensor. His attendance fee was donated to charity by Abbott.	
GDG 17 27 June 2014	None declared	None
GDG 18 29 July 2014	None declared	None
GDG 19 24 September 2014	Personal non-pecuniary interest: I did a video-workshop on diabetes and pregnancy for Medtronic to various centres in Eastern Europe.	Declare and participate
GDG 20 24 March 2015	Personal pecuniary interest: I have again accepted sponsorship from Roche to attend the Advanced Technology and Therapeutics in Diabetes meeting in Paris in February.	

B.7 Michael Kendall

GDG meeting	Declaration of Interests	Action taken
On appointment 14 August 2012	None declared	None
GDG 1 23 October 2012	Reasonable expenses received to attend a presentation by C8 Medisensors for new glucose monitor (currently unavailable and in development)	Declare and participate
GDG 2 27 November 2012	None declared	None
GDG 3 8 January 2013	None declared	None
GDG 4 5 March 2013	None declared	None
GDG 5 9 April 2013	None declared	None
GDG 6 14 May 2013	Acted as an unpaid / voluntary 'Alpha tester' between February 2013 and May 2013 for the new version (V2.0) of the mySugr diabetes logging app for iPhone http://mysugr.com which I have been using since September 2012.	Declare and participate
GDG 7 18 June 2013	None declared	None
GDG 8 3 September 2013	None declared	None
GDG 9 14 October 2013	None declared	None
GDG 10 15 October 2013	None declared	None
GDG 11 26 November 2013	None declared	None
GDG 12 14 January 2014	None declared	None
GDG 13	None declared	None

GDG meeting	Declaration of Interests	Action taken
15 January 2014		
GDG 14 4 March 2014	None declared	None
GDG 15 15 April 2014	None declared	None
GDG 16 20 May 2014	None declared	None
GDG 17 27 June 2014	None declared	None
GDG 18 29 July 2014	None declared	None
GDG 19 24 September 2014	I was invited by Abbott to attend a pre-launch event for the Libre Flash glucose monitoring system prior to its launch at the European Association for the Study of Diabetes meeting in September 2014. I was given a starter pack to allow a trial of the system for 28 days which has a retail value of £150. Reasonable travel expenses only were paid.	Declare and withdraw from further discussions about continuous glucose monitoring.
GDG 20 16 March 2015	I was invited to trial the Abbott Freestyle Libre immediately before launch at EASD 2014. I was invited to the 'Bloggers Breakfast'. My travel expenses were paid for and breakfast provided. I also received a starter pack worth approximately £150. I have been invited to join the Medtronic 'Bloggers and Patient Advocate' group. Travel expenses are paid for and lunch is provided for occasional (6 monthly or annual) meetings. There is also a chance (as yet unconfirmed) that I might be invited to trial the MiniMed 640 G pump/CGM system for 64 days in May. I will let you know if that happens. I have been invited to attend Diabetes UK's Professional Conference 2015 as part of Diabetes UK's Blogger/Social Media	Declare and withdraw from further discussions about continuous glucose monitoring

B.8 Vibhuti Mistry

GDG meeting	Declaration of Interests	Action taken
On appointment 20 July 2012	None declared	None
GDG 1 23 October 2012	1. Sponsored by Animas to attend 2 day insulin pump conference delivered by the Cambridge Diabetes Team. 2. Sponsored by Lilly to do an MSc module 'Insulin Management' at Leicester University. 3. 'Year of Care' Trainer (Care Planning part of NHS	None

GDG meeting	Declaration of Interests	Action taken
	Diabetes). Teaching for Lilly and Novo over a year ago.	
GDG 2 27 November 2012	None declared	None
GDG 3 8 January 2013	None declared	None
GDG 4 5 March 2013	None declared	None
GDG 5 9 April 2013	Non-personal pecuniary: Vibhuti has been asked by Lilly to do some teaching for which she would not be paid directly (her department would receive the payment).	No action required for this meeting
GDG 6 14 May 2013	None declared	None
GDG 7 18 June 2013	None declared	None
GDG 8 3 September 2013	None declared	None
GDG 9 14 October 2013	Did not attend meeting.	None
GDG 10 15 October 2013	None declared	None
GDG 11 26 November 2013	None declared	None
GDG 12 14 January 2014	None declared	None
GDG 13 15 January 2014	None declared	None
GDG 14 4 March 2014	None declared	None
GDG 15 15 April 2014	None declared	None
GDG 16 20 May 2014	None declared	None
GDG 17 27 June 2014	None declared	None
GDG 18 29 July 2014	None declared	None
GDG 19 24 September 2014	TBC	-
GDG 20 24 March 2015	Did not attend the meeting	

B.9 Henrietta Mulnier

GDG meeting	Declaration of Interests	Action taken
On appointment	Novo Nordisk - Nurse advisory board. One-off	Declare and withdraw from

GDG meeting	Declaration of Interests	Action taken
13 August 2012	consultancy. Lilly - occasional paid teaching sessions which may continue.	discussions about insulin and needles.
GDG 1 23 October 2012	Personal Pecuniary: In the past 12 months I have received honoraria from Novo Nordisk, for attending a nurse advisory board, and from Lilly for teaching. I have also been paid a very modest fee for writing editorials and for the diabetes journals published by SB communications.	Declare and withdraw from discussions about insulin and needles
GDG 2 27 November 2012	Novo Nordisk, nurse advisory board. One-off consultancy on 3rd July 2012. I will decline to attend any further boards Occasional paid teaching for Lilly. Most recent and last was on 2nd November 2012. I will decline future teaching. Occasional writing for SB communications who publish diabetes journals such as the Journal of Diabetes Nursing. I will write these without payment from now on. In summary In the past 12 months I have received honoraria from Novo Nordisk, for attending a nurse advisory board, and from Lilly for teaching. I have also been paid a very modest fee for writing editorials and for the diabetes journals published by SB communications.	Declare and withdraw from discussions about insulin and needle lengths. Conflict for questions comparing Insulin types (expires 2/11/2013) and needle length (expires 3/7/2013). Agreed to give up paid work for industry for the duration of the guideline.
GDG 3 8 January 2013	None declared	None
GDG 4 5 March 2013	None declared	None
GDG 5 9 April 2013	None declared	None
GDG 6 14 May 2013	None. Did not attend meeting.	None
GDG 7 18 June 2013	None declared	None
GDG 8 3 September 2013	Personal non-pecuniary interest: invited to join a working group funded by Novo Nordisk to develop a new education and support programme. I will decline payment and accept only reasonable travel and accommodation expenses.	Declare and participate at chair's discretion (pending expiry of prior conflict for insulin).
GDG 9 14 October 2013	None declared	None
GDG 10 15 October 2013	None declared	None
GDG 11 26 November 2013	None declared	None
GDG 12 14 January 2014	None declared	None
GDG 13	None declared	None

GDG meeting	Declaration of Interests	Action taken
15 January 2014		
GDG 14 4 March 2014	None declared	None
GDG 15 15 April 2014	None declared	None
GDG 16 20 May 2014	None declared	None
GDG 17 27 June 2014	None declared	None
GDG 18 29 July 2014	None declared	None
GDG 19 24 September 2014	Non-personal pecuniary interest: I delivered a module on behalf of Kings College London to East Lancashire Health Trust. The funding for the module came from Lilly; she did not receive a direct payment and carried out the teaching according to her role as Lecturer King's College London.	Declare and participate.
GDG 20 24 March 2015		

B.10 Victoria Ruszala

GDG meeting	Declaration of Interests	Action taken
On appointment 13 August 2012	Personal Pecuniary: I have received consultancy fees from the following companies for sponsored road shows and teaching sessions related to diabetes (predominantly Type 2 diabetes): Lilly, Sanofi Aventis, Merck Sharpe Dohme, Novo Nordisk, Boehringer Ingelheim. UKCPA teaching at sponsored study days.	Declare and withdraw from discussions about insulin, CGM and needles.
GDG 1 23 October 2012	None declared	None
GDG 2 27 November 2012	UKCPA teaching at sponsored study days. 19/11/2012 Sanofi Free attendance at UKCPA Symposium 16/02/2012 Pharmacy Management/ Novo Nordisk Steering Group (next meeting Jan 2013) 19/03/2012 Boehringer / Lilly Progression of Type 2 diabetes: Workshop 09/05/2012 MSD SMART update in Type 2 Diabetes: Workshop 28/06/2012 Boehringer / Lily Addressing Kidney Health in Type 2 Diabetes: GP teaching 05/12/2012 Boehringer / Lily Complexity of Type 2 diabetes: Workshop (Last paid meeting)	Declare and withdraw from discussions about insulin, CGM and needles.
GDG 3 8 January 2013	None declared	None
GDG 4 5 March 2013	Did not attend meeting	None

GDG meeting	Declaration of Interests	Action taken
GDG 5 9 April 2013	None declared	None
GDG 6 14 May 2013	None declared	None
GDG 7 18 June 2013	None declared	None
GDG 8 3 September 2013	None declared	None
GDG 9 14 October 2013	Personal non-pecuniary: Vicky is the pharmacy lead for NHS England Endocrinology clinical reference group.	Declare and participate
GDG 10 15 October 2013	None. Did not attend meeting.	None
GDG 11 26 November 2013	None. Did not attend meeting.	None
GDG 12 14 January 2014	None declared	None
GDG 13 15 January 2014	None declared	None
GDG 14 4 March 2014	None declared	None
GDG 15 15 April 2014	None declared	None
GDG 16 20 May 2014	None declared	None
GDG 17 27 June 2014	None declared	None
GDG 18 29 July 2014	Personal pecuniary: Vicky Ruszala declared that she has recently attended an advisory board for Sanofi, thus extending the active period for the interest already declared in relation to Sanofi. Vicky is conflicted for insulin and the chair agreed that she could not participate in reviewing these recommendations.	Declare and withdraw from discussions on insulin.
GDG 19 24 September 2014	None declared	-
GDG 20 24 March 2015	TBC	

B.11 Stuart Smellie

GDG meeting	Declaration of Interests	Action taken
On appointment 13 July 2012	None	None
GDG 1 23 October 2012	Occasional educational talks to GPs funded by a AstraZeneca, MSD, Schering Plough and Sanofi Aventis. Talks given twice a year, most years, about cholesterol lowering (standard rate of £300 per talk).	Declare and participate

GDG meeting	Declaration of Interests	Action taken
	MSD, Schering Plough and Sanofi were all more than 12 months ago. AstraZeneca was within the last 6 months. Stuart was paid for attending an advisory board for tredaptive (MSD), which predated the GDG. Visiting professorship programme for Australian Royal College of Pathologists -travel and accommodation provided for visit in 2014. Taught on BMJ Masterclasses - educational and paid but no industry involvement. Clinical Director, Association of Clinical Biochemists. Vice President, Association of Clinical Pathologists.	
GDG 2 27 November 2012	Did not attend meeting.	None
GDG 3 8 January 2013	None	None
GDG 4 5 March 2013	None	None
GDG 5 9 April 2013	None	None
GDG 6 14 May 2013	None	None
GDG 7 18 June 2013	Did not attend meeting.	None
GDG 8 3 September 2013	None	None
GDG 9 14 October 2013	None	None
GDG 10 15 October 2013	None	None
GDG 11 26 November 2013	None	None
GDG 12 14 January 2014	Did not attend meeting.	None
GDG 13 15 January 2014	Did not attend meeting.	None
GDG 14 4 March 2014	None declared.	None
GDG 15 15 April 2014	None declared.	None
GDG 16 20 May 2014	None declared.	None

GDG meeting	Declaration of Interests	Action taken
GDG 17 27 June 2014	Did not attend meeting.	None
GDG 18 29 July 2014	None declared.	None
GDG 19 24 September 2014	TBC	-
GDG 20 24 March 2015	Did not attend the meeting	

B.12 Perdy van den Berg

GDG meeting	Declaration of Interests	Action taken
On appointment 13 July 2012	None	None
GDG 1 23 October 2012	Sponsorship from Novo Nordisk for £250 to cover costs of travel, registration and overnight accommodation for PCOS annual conference in Birmingham 16-17th November.	No action required
GDG 2 27 November 2012	None	None
GDG 3 8 January 2013	Will receive reasonable expenses to attend Diabetes UK conference	No action required
GDG 4 5 March 2013	None declared	None
GDG 5 9 April 2013	Did not attend meeting.	None
GDG 6 14 May 2013	None declared	None
GDG 7 18 June 2013	None declared	None
GDG 8 3 September 2013	None declared	None
GDG 9 14 October 2013	Did not attend meeting.	None
GDG 10 15 October 2013	None declared	None
GDG 11 26 November 2013	Did not attend meeting.	None
GDG 12 14 January 2014	None declared	None
GDG 13 15 January 2014	None declared	None
GDG 14 4 March 2014	None declared	None
GDG 15 15 April 2014	None declared	None
GDG 16	Did not attend meeting.	None

GDG meeting	Declaration of Interests	Action taken
20 May 2014		
GDG 17 27 June 2014	None declared	None
GDG 18 29 July 2014	None declared	None
GDG 19 24 September 2014	TBC	-
GDG 20 24 March 2015	Did not attend the meeting	None

B.13 Rayaz Malik (co-opted expert)

GDG meeting	Declaration of Interests	Action taken
On appointment 13 July 2012	None declared	No action required
GDG 12 14 January 2014	None declared	No action required
GDG 16 20 May 2014	None declared	No action required

B.14 NCGC members

GDG meeting	Declaration of Interests	Action taken
On appointment 13 July 2012	Bernard Higgins: Non-personal pecuniary interest: The department in which I work has taken part in multi-centre studies over the past 12 months, sponsored by the following companies: Novartis, Pro-pharma, Schering-Plough, Aradigm, GSK, ResMed, Astra-Zeneca, Nycomed, Gilead and Chiesi. I do not receive any personal payment or gratuity, and I do not have administrative responsibility for the fund into which payments are made. Personal non-pecuniary interest: I am the chair-elect of BTS executive. Elisabetta Fenu: Personal pecuniary interest: I was an employee of Novartis UK where I held the position of Health Economics and Outcomes Manager in May and June 2012. I was involved in the NICE TA submission of the product Xolair for the treatment of asthma. Nancy Turnball: Personal pecuniary interest: I do consultancy work for WHO and other departments of the RCP.	Declare and participate Declare and participate Declare and participate Declare and participate
GDG 1 23 October 2012	None declared	No action required
GDG 2 27 November 2012	None declared	No action required
GDG 3	None declared	No action required

GDG meeting	Declaration of Interests	Action taken
8 January 2013		
GDG 4 5 March 2013	None declared	No action required
GDG 5 9 April 2013	None declared	No action required
GDG 6 14 May 2013	None declared	No action required
GDG 7 18 June 2013	Non e declared	No action required
GDG 8 3 September 2013	None declared	No action required
GDG 9 14 October 2013	None declared	No action required
GDG 10 15 October 2013	None declared	No action required
GDG 11 26 November 2013	None declared	No action required
GDG 12 14 January 2014	None declared	No action required
GDG 13 15 January 2014	None declared	No action required
GDG 14 4 March 2014	None declared	No action required
GDG 15 15 April 2014	None declared	No action required
GDG 16 20 May 2014	None declared	No action required
GDG 17 27 June 2014	None declared	No action required
GDG 18 29 July 2014	None declared	No action required
GDG 19 24 September 2014	None declared	No action required
GDG 20 24 March 2015	TBC	

Appendix C: Review protocols

C.1 Clinical protocols

C.1.1 Diagnosis/markers for distinguishing types of diabetes

C.1.1.1 Distinguishing between different types of diabetes

Component	Description
Review question	In adults 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?
Objectives	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/concentration of each of these markers is present and distinguishes the types. • 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? • When is there uncertainty, and what should be done when uncertainty exists?
Population	Adults with all types of diabetes • Adult is defined as aged ≥18 years • Diabetes types are: type 1 diabetes, type 2 diabetes, LADA and MODY.
Subgroups	The following groups will be considered separately if data are available: • Adults
Diagnostic tests	• C-peptide ○ Plasma C-peptide (stimulated) ○ Urinary C-peptide ○ Urinary C-peptide/creatinine ratio • Antibody tests: ○ anti-islet cell antibody (ICA) ○ anti-glutamic acid decarboxylase 65 antibody or anti-glutamic acid decarboxylase antibody (GADA) ○ insulinoma-associated (IA-2/ICA512) autoantibody ○ zinc transporter 8 (ZnT8) ○ islet-specific glucose-6-phosphatase catalytic subunit (IGRP)
Outcomes	• Presence of marker (No. or % of patients with marker) • Concentration/titre of marker • Change in marker over time (No. or % of patients with marker) • Change in concentration/titre of marker over time (micrograms/ml)
Importance of outcomes	Critical outcomes • N/A
Study design	• Observational studies
Population size and directness	• Studies will be excluded if: ○ The population is mixed, with no adult subgroup analyses. Mixed populations excluded are: - 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 • Sample size restrictions. We will exclude studies in: ○ Adults and young people with sample size of N<50, if we retrieve >20 studies that have been conducted in adults and young people separately ○ Adults with a sample size of N<50, if there are >20 adult studies retrieved.
Setting	• All settings (as per Scope)
Search Strategy	See appendix F Search will be restricted to studies published since the original GL (2003). If only a few studies are found, then we will extend the search to all years.
Review Strategy	Appraisal of methodological quality/evidence synthesis • The methodological quality of each study will be assessed using NICE checklists and a narrative synthesis of the evidence will be provided.
Notes	If no/insufficient evidence is found we will (in order of preference): • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.2 Educating programmes and self-care

C.1.2.1 Structured education programmes

Component	Description
Review question	In adults with type 1 diabetes, what is the most effective structured education programme in terms of clinical and cost-effectiveness?
Objectives	The aim of this review is to compare different structured educational programmes for adults with type 1 diabetes and whether they lead to an improvement in QoL and clinical outcomes
Population	Adults with type 1 diabetes • Adult is defined as aged over 18 years
Subgroups	The following groups will be considered separately if data are available: • None specified The following factors will be considered for subgroup analysis if heterogeneity is present, in the following order: • Whether patients included or recruited in the trials were solely type 1 diabetes with hypoglycaemia • Duration of diabetes (for example newly diagnosed) • Whether CHO restriction was included in the programme If heterogeneity is still not explained then we will look at: • Whether follow-up programmes were done or not • Basal insulin regimens: ○ once versus twice/day ○ analogue versus non-analogue

Intervention	• Structured education programme
Comparison	• Other education programmes • Usual care/no treatment • SMBG
Outcomes	• HbA1c (continuous) • Hypoglycaemia - preferably severe hypoglycaemia if reported (dichotomous or continuous outcome, depending how it is reported) • Hospital admissions (dichotomous or continuous, depending how it is reported) • Hypoglycaemia unawareness (dichotomous) • Quality of life – measured by DQoL, DSQoL, PAID, HADS, fear of hypoglycaemia, anxiety, depression (continuous) • Adverse events (dichotomous) • Knowledge (dichotomous or continuous, depending how it is reported) • Adherence (dichotomous or continuous, depending how it is reported)
Importance of outcomes	Critical outcomes • HbA1c • Severe hypoglycaemia • Quality of life
Study design	RCTs • Unit of randomisation: individual patient, cluster randomised trials
Population size and directness	• No restrictions on sample size • No restrictions on treatment duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will not be considered unless ≥75% are type 1 diabetes, or data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used.
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists and the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: o ≤6 months (or the one nearest to 6 months if multiple time-points are given) o >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.2.2 Carb counting

Review question	**In adults with type 1 diabetes, what is the clinical and cost-effectiveness of a diet based on carbohydrate counting/restriction for optimal diabetic control?**
Objectives	The aim of this review is to determine whether carbohydrate counting/restriction is effective for optimal diabetic blood glucose control in adults with type 1 diabetes in terms of cost and clinical effectiveness, particularly for post-prandial blood glucose control.

Population	Adults with type 1 diabetes • Adult is defined as aged ≥ 18 years
Subgroups	The following subgroups will be considered separately if data are available: • None specified The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • different methods of CHO counting/restriction • different thresholds set for CHO counting/restriction
Intervention	Carbohydrate counting /restriction (this may involve technology such as a bolus calculator)
Comparison	• Placebo • Usual care/no carbohydrate counting • Manual carbohydrate counting (if the intervention is carb counting using a technology)
Outcomes	• HbA1c (continuous) • Hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Severe hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Nocturnal hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Quality of life – measured by whatever is used in the study (continuous) • Adverse events (dichotomous)
Importance of outcomes	Critical outcomes • HbA1c • Hypoglycaemia
Study Design	RCTs, observational studies • Unit of randomisation: individual patient
Population size and directness	• No restrictions on sample size • No restrictions on treatment duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used, ○ the population contains ≥70% of type 1 diabetes patients, ○ if ≥50% of people are aged >18 years the study will be included. • Studies looking at different carbohydrate content diets will be excluded. • Studies looking at GI index will be excluded (as this is being covered in a separate review).
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists • Where possible, the quality of the evidence will be assessed by GRADE for each outcome. • Taking into consideration the advice on prognostic reviews in the NICE guidelines manual, meta-analysis or GRADE will not be undertaken for prognostic studies or qualitative studies

	Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.2.3 Glycaemic index diet – low GI versus high GI diet

Component	Description
Review question	In adults with type 1 diabetes, what is the clinical and cost-effectiveness of a diet based on the glycaemic index for optimal diabetic control?
Objectives	The aim of this review is to determine whether a low GI diet is more effective than a high GI diet for diabetic control in adults with type 1 diabetes.
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • None specified The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • different background insulin regimens
Intervention	High GI diet (this may include balancing protein and lipid intake)
Comparison	Low GI diet (this may include balancing protein and lipid intake)
Outcomes	• HbA1c (continuous) • Severe hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Nocturnal hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Quality of life – measured by DQoL or any measure used in the studies retrieved (continuous) • Patient satisfaction (dichotomous or continuous outcome, depending how it is reported) • Adherence (dichotomous)
Importance of outcomes	Critical outcomes • HbA1c • Severe hypoglycaemia
Study design	RCTs • Unit of randomisation: individual patient
Population size and directness	• No restrictions on sample size • No restrictions on treatment duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used.

	○ the population contains ≥70% of type 1 diabetes patients ○ if ≥50% of people are aged >18 years the study will be included
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists and the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.3 Blood glucose monitoring

C.1.3.1 HbA1c (targets)

Component	Description
Review question	In adults with type 1 diabetes, what is the optimum target HbA1c level that should be achieved to reduce the risk of complications?
Objectives	The aim of this review is to determine whether the current HbA1c target for adults with type 1 diabetes needs changing, as there may be evidence that lower targets lead to better diabetic control or outcomes, however there may be issues of adherence. Also to determine the risk of complications at different levels of HbA1c, and what is the optimum treatment regime that should follow to achieve this? Different targets for different groups of patients will be needed (for example, for pump users).
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years
Subgroups	None
Intervention	HbA1c target values
Comparison	• Other target values (RCTs and comparative observational studies) • No targets (prognostic studies)
Outcomes	• Number of people reaching target HbA1c (dichotomous) • Final HbA1cvalue (continuous) • Hypoglycaemia (dichotomous or continuous outcome at a particular target • Severe hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Nocturnal hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Complications/avoidance: ○ CV events (MI, IHD, Stroke, cardiac and peripheral revascularisation, major amputation)

Component	Description
	○ Retinopathy ○ Low-level (micro) albuminuria/proteinuria ○ Renal replacement therapy/end-stage renal failure ○ Neuropathy ○ Sudden death • Quality of life – (dichotomous/continuous)
Importance of outcomes	Critical outcomes • Complications • Hypoglycaemia
Study design	RCTs, observational studies, prognostic studies
Population size and directness	• No restrictions on sample size (unless >10 studies, then sample sizes of N<100 will be excluded) • No restrictions on study duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. ○ the population contains ≥70% of type 1 diabetes patients ○ if ≥ 50% of people are aged >18 years the study will be included • Studies will be excluded if they: ○ do not stratify results by different HbA1ctargets
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists • Where possible, the quality of the evidence will be assessed by GRADE for each outcome. • Taking into consideration the advice on prognostic reviews in the NICE guidelines manual, meta-analysis or GRADE will not be undertaken for prognostic studies Synthesis of data • Meta-analysis will be conducted where appropriate • Data will be synthesised in a narrative review where meta-analysis is not possible • Outcomes will be grouped into the following categories based on time-points: • ≤6 months (or the one nearest to 6 months if multiple time-points are given) • >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT, observational or prognostic evidence is found, we will (in order of preference): • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.3.2 HbA1c (frequency of monitoring)

Component	Description
Review question	In adults with type 1 diabetes, what is optimum frequency of HbA1c monitoring for effective diabetic control?
Objectives	The aim of this review is to determine how often HbA1c should be monitored in order to maintain optimum glucose/diabetic control and reduce the incidence of adverse events and hypoglycaemia episodes.

Component	Description
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • Newly diagnosed (<5 years) • Significant microvascular complications • Hypoglycaemia unawareness The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • None specified
Intervention	HbA1c monitoring
Comparison	• HbA1c monitoring (the same as the intervention but at a different frequency or delivery time) • Standard care • No comparison (non-comparative studies)
Outcomes	• Hypoglycaemia - preferably severe hypoglycaemia if reported (dichotomous or continuous outcome, depending how it is reported) • HbA1c (continuous) • Quality of life – measured by any measure reported in the study (continuous) • Adverse events (dichotomous) • Adherence (dichotomous) • Complications ○ CV events (MI, IHD, Stroke, cardiac and peripheral revascularisation, major amputation) ○ Retinopathy ○ Low-level (micro) albuminuria/proteinuria ○ Renal replacement therapy/end-stage renal failure ○ Neuropathy ○ Sudden death
Importance of outcomes	Critical outcomes • Hypoglycaemia • HbA1c Complications- retinopathy
Study design	All types
Population size and directness	• No restrictions on sample size (unless >10 studies, then sample sizes of N<100 will be excluded) • No restrictions on study duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. ○ the population contains ≥70% of type 1 diabetes patients ○ if ≥50% of people are aged >18 years the study will be included • Studies will be excluded if they: ○ do not stratify results by different monitoring frequencies
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality

Component	Description
	• The methodological quality of each study will be assessed using NICE checklists • Where possible, the quality of the evidence will be assessed by GRADE for each outcome. • Taking into consideration the advice on prognostic reviews in the NICE guidelines manual, meta-analysis or GRADE will not be undertaken for prognostic studies Synthesis of data • Meta-analysis will be conducted where appropriate • Data will be synthesised in a narrative review where meta-analysis is not possible • Outcomes will be grouped into the following categories based on time-points: • ≤6 months (or the one nearest to 6 months if multiple time-points are given) • >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT, observational or prognostic evidence is found, we will (in order of preference): • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.3.3 SMBG (timing and frequency)

Component	Description
Review question	In adults with type 1 diabetes, what is optimum timing and frequency to self-monitor blood glucose for effective diabetic control?
Objectives	The aim of this review is to determine how often SMBG should be performed in order to maintain optimum glucose/diabetic control and reduce the incidence of adverse events and hypoglycaemia episodes. Issues of adherence too?
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • significant comorbidities • hypoglycaemia problems • people with recurrent DKA • different durations of disease • different lifestyles/activity levels • people striving for tight control The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • different sites of monitoring • different times of monitoring • different technologies of monitoring • different glucose targets for monitoring
Intervention	SMBG (finger pricks)
Comparison	• SMBG (finger pricks) - the same as the intervention but at a different frequency or delivery time • No comparison (for non-comparative studies)
Outcomes	• Hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Severe hypoglycaemia (dichotomous or continuous outcome, depending how it is

	reported) • Nocturnal hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Time within range (blood glucose) (continuous) • HbA1c (continuous) • Quality of life – measured by any measure specified in the study (continuous) • DKA (dichotomous) • Adherence (dichotomous) • Unscheduled care use
Importance of outcomes	Critical outcomes • Hypoglycaemia • HbA1c
Study design	• RCTs, observational studies any
Population size and directness	• No restrictions on sample size (unless >10 studies, then sample sizes of N<100 will be excluded) • No restrictions on study duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. ○ the population contains ≥70% of type 1 diabetes patients ○ if ≥50% of people are aged >18 years the study will be included • Studies will be excluded if they: ○ do not stratify results by different monitoring frequencies
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists • Where possible, the quality of the evidence will be assessed by GRADE for each outcome. • Taking into consideration the advice on prognostic reviews in the NICE guidelines manual, meta-analysis or GRADE will not be undertaken for prognostic studies Synthesis of data • Meta-analysis will be conducted where appropriate • Data will be synthesised in a narrative review where meta-analysis is not possible • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT, observational or prognostic evidence is found, we will (in order of preference): • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.3.4 SMBG (targets)

Component	Description
Review question	In adults with type 1 diabetes, what is the optimum glucose target/profile for self-

	monitoring of blood glucose for effective diabetic control?
Objectives	The aim of this review is to determine what is the best glucose target patients should be aiming for when self-monitoring blood glucose in order to lead to optimum diabetic control, however, there may be issues of adherence. We are interested in the impact of variability on complication risk. There is some data on variability. Do clinicians and patients need to worry about post prandial glucose levels if HbA1c is OK? Does HbA1c variability for complications matter? And what extent does mean blood glucose mean anything at all, given the HbA1c values.
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • Male versus female • Age The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • Duration of diabetes • Presence of complications (do we need more monitoring if tighter control is needed?)
Intervention	SMBG (finger pricks) - Blood glucose target/profile values/glucose variabiity
Comparison	• Other target values (RCTs and comparative observational studies) • No targets (prognostic studies)
Outcomes	• HbA1c value (continuous) • Risk of hypoglycaemia (dichotomous or continuous) • Risk of severe hypoglycaemia (dichotomous or continuous) • Risk of nocturnal hypoglycaemia (dichotomous or continuous) • Risk of complications (dichotomous or continuous) • 'QoL - any measure reported in the study (continuous)
Importance of outcomes	Critical outcomes • Risk of hypoglycaemia • Risk of complications
Study design	• RCTs, observational studies, prognostic studies
Population size and directness	• No restrictions on sample size (unless >10 studies, then sample sizes of N<100 will be excluded) • No restrictions on study duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. ○ the population contains ≥70% of type 1 diabetes patients ○ if ≥50% of people are aged >18 years the study will be included • Studies will be excluded if they: ○ do not stratify results by different glucose targets
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists • Where possible , the quality of the evidence will be assessed by GRADE for each outcome. • Taking into consideration the advice on prognostic reviews in the NICE guidelines

	manual, meta-analysis or GRADE will not be undertaken for prognostic studies Synthesis of data • Meta-analysis will be conducted where appropriate • Data will be synthesised in a narrative review where meta-analysis is not possible • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT, observational or prognostic evidence is found, we will (in order of preference): • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.3.5 SMBG technologies

Component	Description
Review question	In adults with type 1 diabetes, what are the benefits of technologies (bolus calculators and downloads) for self-monitoring of blood glucose?
Objectives	The aim of this review is to determine whether new technologies (bolus calculators and downloads) improve SMBG and clinical outcomes. Issues of adherence too?
Population	Adults with type 1 diabetes • Adult is defined as aged ≥ 18 years
Subgroups	The following groups will be considered separately if data are available: • Age • Duration of diabetes • Blood glucose control (HbA1c <8% versus >8%) The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • different frequencies of monitoring • different site of monitoring • different times of monitoring • different glucose targets for monitoring
Intervention	• SMBG (finger pricks) - bolus calculators • SMBG (finger pricks) - downloads
Comparison	SMBG (finger pricks) – standard SMBG methods
Outcomes	• Hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Severe hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Nocturnal hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • HbA1c (continuous) • Quality of life – measured by whatever is reported in the paper (continuous) • Adverse events (dichotomous) • Adherence (dichotomous)
Importance of outcomes	Critical outcomes • Hypoglycaemia • HbA1c

Component	Description
Study design	RCTs
Population size and directness	• No restrictions on sample size (unless >10 studies, then sample sizes of n<100 will be excluded) • No restrictions on treatment duration. • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ Data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. ○ the population contains ≥70% of type 1 diabetes patients ○ if ≥50% of people are aged >18 years the study will be included
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists • Where possible, the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Data will be synthesised in a narrative review where meta-analysis is not possible • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT, observational or prognostic evidence is found, we will (in order of preference): • Observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.3.6 CGM (retrospective) versus SMBG

Component	Description
Review question	In adults with type 1 diabetes, is retrospective CGM more effective than care without CGM (with SMBG) for improving diabetic control?
Objectives	The aim of this review is to determine whether retrospective CGM is more effective than no CGM (that is, SMBG) for managing diabetic control in adults with type 1 diabetes. Adherence may also be an issue?
Population	Adults with type 1 diabetes • Adult is defined as aged ≥ 18 years
Subgroups	The following groups will be considered separately if data are available: • None specified The following factors will be considered for subgroup analysis if heterogeneity is present: • frequency of SMBG • Type of CGM or SMBG method/monitor
Intervention	Retrospective CGM

Comparison	Care without CGM (with SMBG) – comparison group must be on similar insulin regimen as the treatment group
Outcomes	Outcomes • HbA1c (continuous) • Hypoglycaemia - preferably severe hypoglycaemia if reported (dichotomous or continuous outcome, depending how it is reported) • Quality of life – measured by any measure stated in paper (continuous) or patient satisfaction • Adverse events – (dichotomous) • Adherence (dichotomous)
Importance of outcomes	Critical outcomes • HbA1c • Hypoglycaemia
Study design	RCTs • Unit of randomisation: individual patient
Population size and directness	• No restrictions on sample size • Exclude studies <1 week duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used, ○ the population contains ≥70% of type 1 diabetes patients, ○ if ≥50% of people are aged >18 years the study will be included.
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each outcome will be assessed using NICE checklists and the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used to assess imprecision: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.3.7 CGM (real-time) versus SMBG

Component	Description
Review question	In adults with type 1 diabetes, is real-time CGM more effective than SMBG CGM for optimum diabetic control?
Objectives	The aim of this review is to determine whether real-time CGM is more effective than care without CGM (that is, SMBG) for managing diabetic control in adults with type 1 diabetes. Adherence may also be an issue?
Population	Adults with type 1 diabetes

	• Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • None specified The following factors will be considered for subgroup analysis if heterogeneity is present: • frequency of CGM (real-time) • Type of CGM method/monitor (real-time and retrospective) • Frequency of SMBG
Intervention	Real-time CGM
Comparison	Care without CGM (with SMBG) – comparison group must be on similar insulin regimen as the treatment group
Outcomes	• HbA1c (continuous) • Hypoglycaemia - preferably severe hypoglycaemia if reported (dichotomous or continuous outcome, depending how it is reported) • Quality of life – measured by any measure stated in the paper (continuous) • Adverse events – (dichotomous) • Adherence (dichotomous)
Importance of outcomes	• Critical outcomesHbA1c • Hypoglycaemia
Study design	RCTs • Unit of randomisation: individual patient
Population size and directness	• No restrictions on sample size • Exclude studies <1 week duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used, ○ the population contains ≥70% of type 1 diabetes patients, ○ if ≥50% of people are aged >18 years the study will be included.
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists and the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.3.8 CGM (continuous) versus CGM (intermittent)

Component	Description
Review question	In adults with type 1 diabetes, is continuous real-time monitoring more effective than intermittent real-time monitoring for optimum glucose/diabetic control?
Objectives	The aim of this review is to determine whether continuous use of real-time CGM is better than intermittent use of real-time CGM for managing diabetic control in adults with type 1 diabetes. Adherence may also be an issue?
Population	Adults with type 1 diabetes • Adult is defined as aged ≥ 18 years
Subgroups	The following groups will be considered separately if data are available: • None specified The following factors will be considered for subgroup analysis if heterogeneity is present: • frequency of CGM • Type of CGM method/monitor (real-time and retrospective)
Intervention	Intermittent real-time CGM
Comparison	Continuous real-time CGM – comparison group must be on similar insulin regimen as the treatment group
Outcomes	• HbA1c (continuous) • Hypoglycaemia - preferably severe hypoglycaemia if reported (dichotomous or continuous outcome, depending how it is reported) • Quality of life – measured by any measure stated in the paper (continuous) • Adverse events – (dichotomous) • Adherence (dichotomous)
Importance of outcomes	Critical outcomes • HbA1c • Hypoglycaemia
Study design	RCTs, observational (retrospective and prospective cohort studies) • Unit of randomisation: individual patient
Population size and directness	• No restrictions on sample size • Exclude studies <1 week duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used, ○ the population contains ≥70% of type 1 diabetes patients, ○ if ≥50% of people are aged >18 years the study will be included.
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists • Where possible, the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given)

	○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.4 Insulin therapy

C.1.4.1 Rapid-acting insulin

Review question	In adults with type 1 diabetes, which are the most effective rapid-acting insulins for meal times: analogues versus human (intermediate NPH), for optimal diabetic control?
Objectives	The aim of this review is to determine which is the most effective rapid-acting insulin for use at meal-times for diabetic control in adults with type 1 diabetes.
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • None specified The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • different doses of insulin
Intervention	Rapid-acting insulin: analogues, human (intermediate NPH) • Rapid human • Aspart • Lispro • Glulisine Note: only UK licensed interventions and doses will be considered
Comparison	Each other Note: only UK licensed interventions and doses will be considered
Outcomes	• HbA1c (continuous) • Hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Severe hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Nocturnal hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Quality of life – measured by DQoL or any measure used in the studies retrieved (continuous) • Patient satisfaction (dichotomous or continuous outcome, depending how it is reported) • Adverse events – Cancer (dichotomous) • Injection site issues (dichotomous or continuous outcome, depending how it is reported) • Weight gain/loss (continuous) • DKA (dichotomous or continuous outcome, depending how it is reported)

Importance of outcomes	Critical outcomes • HbA1c • Hypoglycaemia
Study design	RCTs • Unit of randomisation: individual patient
Population size and directness	• No restrictions on sample size • Studies with a follow-up time of <4 weeks will be excluded. • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used, ○ the population contains ≥70% of type 1 diabetes patients, ○ if ≥50% of people are aged >18 years the study will be included.
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists and the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.4.2 Long-acting insulin

Component	Description
Review question	In adults with type 1 diabetes, what are the most effective long-acting insulins (detemir versus degludec versus glargine versus NPH) for optimal diabetic control?
Objectives	The aim of this review is to determine which is the most effective long-acting insulin in adults with type 1 diabetes.
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • None specified upfront The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • Clinically relevant regiment (for example, once or twice/day) Baseline HbA1c (if there are vast differences between studies in baseline HbA1c levels) • Different doses/regimens (clinically relevant regimens) • Elderly/older people/frailty (if there are vast differences between studies in ages) • Baseline weight (may not be possible to do this, because some studies give BMI and

	some give weight in kg) • Baseline hypoglycaemia (if this is known and there are vast differences)
Intervention	Long-acting insulins: • detemir • degludec • glargine • NPH/other intermediate Note: only UK licensed interventions and doses will be considered
Comparison	Each other (all of the above) Note: only UK licensed interventions and doses will be considered
Outcomes	Outcomes • HbA1c (continuous) • Hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Severe hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Nocturnal hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Quality of life – measured by DQoL or any measure used in the studies retrieved (continuous) • Adverse events – Cancer (dichotomous) • Injection site issues • Weight gain/loss • DKA
Importance of outcomes	Critical outcomes • HbA1c • Hypoglycaemia
Study design	RCTs • Unit of randomisation: individual patient
Population size and directness	• No restrictions on sample size (unless have >10 papers for any type of insulin, then sample sizes N<100 will be excluded within that category) • Studies with a follow-up time <4 weeks will be excluded. • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will NOT be considered, unless data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. • Studies only comparing different dosages of the same drug will not be included (for example, NPH 100 mg versus NPH 200 mg)
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists • Where possible, the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate. Nocturnal hypoglycaemia will not be meta-analysed. But the data just reported in the evidence tables. This is because this outcome has not been prioritised for the NMA, and does not appear in the HE model.

	• Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes • A network meta-analysis will be conducted for each of the critical outcomes (HbA1cand severe hypoglycaemia).
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.4.3 Mixed insulin

Component	Description
Review question	In adults with type 1 diabetes, what are the most effective mixed for optimal diabetic control?
Objectives	The aim of this review is to determine which is the most effective mixed insulin in adults with type 1 diabetes.
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • None specified The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • Baseline HbA1c (if there are vast differences between studies in baseline HbA1clevels) • Different doses or regimens (clinically relevant regimens) • Elderly/older people/frailty (if there are vast differences between studies in ages) • Baseline weight (may not be possible to do this, because some studies give BMI and some give weight in kg) • Baseline hypoglycaemia (if this is known and there are vast differences)
Intervention	Mixed insulins: • Degludec-aspart – (IDegAsp) NPH-aspart (NovoMix 30)- analogue mix • NPH-lispro (Humalog Mix 25 and Humalog Mix 50)- analogue mixes • NPH-human (Humulin M3, Insuman Combo 25 and Insuman Combo 50) • BD premix – the below repeat the above mixes that are available
Comparison	• Each other (all of the above) • Long- and short-acting insulin (basal-bolus) regimen
Outcomes	• HbA1c (continuous) • Hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Severe hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Nocturnal hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Quality of life – measured by DQoL or any measure used in the studies retrieved (continuous) • Adverse events – Cancer (dichotomous)

	• Injection site issues (dichotomous) • Weight gain/loss (continuous) • DKA (dichotomous or continuous outcome, depending how it is reported)
Importance of outcomes	Critical outcomes • HbA1c • Hypoglycaemia
Study design	RCTs • Unit of randomisation: individual patient
Population size and directness	• No restrictions on sample size (unless have >10 papers for each type of drug, then sample sizes N<100 will be excluded within that category) • Studies with a follow-up time <4 weeks will be excluded. • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. ○ the population contains ≥70% of type 1 diabetes patients ○ if ≥50% of people are aged >18 years the study will be included • Studies only comparing different dosages of the same drug will not be included (for example, NPH 100 mg versus NPH 200 mg)
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists • Where possible, the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes • A network meta-analysis will be conducted for each of the critical outcomes (HbA1c and severe hypoglycaemia).
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.4.4 Adjuncts

Component	Description
Review question	In adults with type 1 diabetes, is metformin (with or without insulin), or GLP1-agonists (with or without insulin) as effective as insulin alone for optimal diabetic control?
Objectives	The aim of this review is to determine whether insulin in combination with another pharmacological agent (that is, Metformin or GLP-1 agonists) is as effective as insulin alone for diabetic control in adults with type 1 diabetes. Also to determine the extra benefits such as decreased insulin doses (<costs) and decrease in weight.
Population	Adults with type 1 diabetes

	• Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • Patients with BMI >30 • Combination therapy • Monotherapy The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • different doses of insulin, metformin or GLP1-agonist • different frequencies of administration

Intervention	• Metformin
	• Metformin + insulin
	• GLP-1 agonists
	  ○ exenatide
	  ○ pramlintide
	  ○ liraglutide
	• GLP1 + insulin
	
	Note: only UK licensed interventions and doses will be considered

Comparison	Insulin Note: only UK licensed interventions and doses will be considered
Outcomes	• HbA1c (continuous) • Hypoglycaemia - preferably severe hypoglycaemia if reported (dichotomous or continuous outcome, depending how it is reported) • Severe hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Nocturnal hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Quality of life – (continuous) • Adverse events – (dichotomous) • Weight loss/change – (dichotomous) • Dose of insulin – (dichotomous)
Importance of outcomes	Critical outcomes • HbA1c • Hypoglycaemia • Weight loss/change
Study design	RCTs • Unit of randomisation: individual patient

Population size and directness	• No restrictions on sample size
	• Studies with a follow-up time <4 weeks will be excluded.
	• Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if:
	  ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used,
	  ○ the population contains ≥70% of type 1 diabetes patients,
	  ○ if ≥50% of people are aged >18 years the study will be included.

Setting	• All settings (as per Scope)

Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists and the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.4.5 Long-acting: once versus twice daily basal insulin administration

Component	Description
Review question	In adults with type 1 diabetes, is once daily basal insulin more effective than twice daily basal insulin for optimal diabetic control?
Objectives	The aim of this review is to determine the most effective administration regimen for basal/long-acting insulin: once daily versus twice daily for diabetic control in adults with type 1 diabetes.
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • Age (if available) • Duration of diabetes (<15 years and >15 years) • Control (that is, HbA1c <8% and >8%) The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • different drugs • different doses
Intervention	Basal/long-acting insulin given once/day: detemir, degludec, degludec/aspart, glargine, NPH Note: only UK licensed interventions and doses will be considered
Comparison	Basal/long-acting insulin given twice/day: detemir, degludec, degludec/aspart, glargine, NPH Note: the same LA insulin must be used in the comparison arm as for the intervention arm. Note: only UK licensed interventions and doses will be considered
Outcomes	• HbA1c (continuous) • Hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Severe hypoglycaemia (dichotomous or continuous outcome, depending how it is reported)

	• Nocturnal hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Quality of life – measured by whatever is used in the study (continuous) • Adverse events – (dichotomous)
Importance of outcomes	Critical outcomes • HbA1c • Hypoglycaemia
Study design	RCTs • Unit of randomisation: individual patient
Population size and directness	• No restrictions on sample size • Studies with a follow-up time <4 weeks will be excluded. • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will NOT be considered, unless data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used.
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists • Where possible the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used to assess imprecision: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.5 Insulin delivery

C.1.5.1 Needle length

Component	Description
Review question	In adults with type 1 diabetes, what is the optimum needle length for insulin delivery?
Objectives	The aim of this review is to determine the most effective needle length for administering insulin in adults with type 1 diabetes. Issues of adherence?
Population	Adults with type 1 diabetes • Adult is defined as aged ≥ 18 years
Subgroups	The following groups will be considered separately if data are available: • None specified The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • different types of needle

	• different frequencies of insulin delivery • different sites of delivery • different insulin given
Intervention	Insulin – delivered by needle Note: only UK licensed interventions and doses will be considered
Comparison	As for intervention, but different length of needle Note: only UK licensed interventions and doses will be considered
Outcomes	Outcomes • Pain (continuous) • Discomfort (continuous) • Patient satisfaction (continuous) • HbA1c (continuous) • Quality of life – measured by sale reported in the study (continuous) • Adverse events (dichotomous) • Adherence (dichotomous)
Importance of outcomes	Critical outcomes • HbA1c
Study design	RCTs, observational (retrospective and prospective cohort studies) • Unit of randomisation: individual patient • Studies will be excluded if they are non-comparative studies
Population size and directness	• No restrictions on sample size • No restrictions on treatment duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. ○ the population contains ≥70% of type 1 diabetes patients ○ if ≥50% of people are aged >18 years the study will be included • However, if very little evidence is found meeting the above population criteria, studies with mixed diabetes (type 1 diabetes and type 2 diabetes) populations will be considered, regardless of the % of type 1 diabetes patients. • Studies will be excluded if they compare insulin pens with vial and syringe. Delivery of insulin must be by the same type of insulin 'device' in order to show the effect of the needle length only, rather than the device.
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists • Where possible, the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes

Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.5.2 Site and rotation

Component	Description
Review question	In adults with type 1 diabetes, what is the optimum injection site and rotation for insulin delivery?
Objectives	The aim of this review is to determine which is the most effective delivery site and rotation for administering insulin in adults with type 1 diabetes. Issues of adherence?
Population	Adults with type 1 diabetes • Adult is defined as aged ≥ 18 years
Subgroups	The following groups will be considered separately if data are available: • Pregnancy • Exercise • Nocturnal hypoglycaemia The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • different types/lengths of needle • different frequencies of insulin delivery • different doses
Intervention	Insulin – delivered by needle Note: only UK licensed interventions and doses will be considered
Comparison	As for intervention, but different site of delivery Note: only UK licensed interventions and doses will be considered
Outcomes	Outcomes • HbA1c (continuous) • Hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Severe hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Nocturnal hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Quality of life – measured by whatever is used in the study (continuous) • Adverse events – (dichotomous) • Adherence (dichotomous)
Importance of outcomes	Critical outcomes • HbA1c • Hypoglycaemia
Study design	RCTs, observational (retrospective and prospective cohort studies) • Unit of randomisation: individual patient
Population size and directness	• No restrictions on sample size • No restrictions on treatment duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes)

	populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. ○ the population contains ≥70% of type 1 diabetes patients ○ if ≥50% of people are aged >18 years the study will be included
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists • Where possible, the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.6 Pancreas transplant and islet cell transplantation

Component	Description
Review question	Which adults with type 1 diabetes are most suitable to be considered for a pancreas transplant, or pancreatic islet cell transplantation?
Objectives	The aim of this review is to determine the referral criteria indicating that an adult with type 1 diabetes should be considered for pancreas transplant or pancreatic islet cell transplantation.
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years • Type 1 diabetes is defined (WHO definition and NICE 2004 GL)
Subgroups	The following groups will be considered separately if data are available: • Islet cell transplantation - alone and with kidney transplant • Pancreas transplantation - alone (not in combination with kidney)
Intervention	• Pancreas transplantation • Islet cell transplantation
Comparison	• Any comparison • No comparison
Outcomes	• The referral criteria themselves • HbA1c • Severe hypoglycaemia • Longevity of the transplant/organ survival (c-peptide and insulin independence) • Insulin dependence at 1 year and 5 years

	• Mortality - in-hospital/procedural • Mortality – long-term • Quality of life – any measure used in the paper
Importance of outcomes	Critical outcomes • Mortality • Severe hypoglycaemia • Longevity of transplant • Insulin dependence/independence
Study design/review strategy	**Strategy for this review is:** • Use available clinical data for obtaining clinical outcomes. This will be sourced from: ○ Publications of the UK consortia data (National transplant programmes); to see whether patients do well after a transplant which is based on the current UK referral criteria. ○ NICE IPG 257 guidance on transplantation. • Report what referral criteria are currently used in the UK. This will be sourced from: ○ NHS England service specifications document ○ NICE IPG 257 guidance for any information given on referral criteria. • International criteria : CITR (data can be found on their website and any relevant publications)
Population size and directness	• Information on transplantation before 2003 will be excluded (as not current/relevant technology for the procedures). • Studies with outcomes at <5 years will be excluded unless there is not much other data. • No restrictions on sample size • No restrictions on treatment duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. ○ the population contains ≥70% of type 1 diabetes patients ○ if ≥50% of people are aged >18 years the study will be included
Setting	• All settings (as per Scope)
Search Strategy	See study design/review strategy section above
Review Strategy	Synthesis of data • Narrative summary of the data will be given, as there will be no RCT or trial data for this review.
Notes	If no/insufficient evidence is found we will move to GDG consensus

C.1.7 Hypoglycaemia

C.1.7.1 Identification and quantification of impaired awareness of hypoglycaemia

Component	Description
Review question	In adults with type 1 diabetes, how is impaired awareness of hypoglycaemia best identified and quantified?
Objectives	The aim of this review is to look at how effective are scoring systems in predicting impaired awareness of hypoglycaemia and increased risk of severe hypoglycaemia. Also how frequently should we be monitoring for it, and using which tool. What is the

	quickest and most reliable tool?
Population	• Adults with type 1 diabetes ○ Adult is defined as aged ≥18 years
Subgroups	None identified.
Prognostic variable?	• Impaired awareness of hypoglycaemia according to known validated scoring systems: ○ Gold score ○ Clarke score ○ Ryan score (Hypoglycaemia burden score) ○ Pedersen-Bjergaard score
Comparison	• Other scoring systems • No scoring system
Outcomes	• Ability to identify impaired awareness of hypoglycaemia • Ability to predict severe hypoglycaemia (incidence of severe hypoglycaemia) • Ability to predict driving or work related accidents (incidence of accidents)
Importance of outcomes	Critical outcomes • Ability to predict severe hypoglycaemia
Study design	All study types
Population size and directness	• No restrictions on sample size • No restrictions on study duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data have been reported for the subgroup of type 1 diabetes patients, in which case these subgroup data will be used. ○ the population contains ≥70% of type 1 diabetes patients ○ if ≥50% of people are aged >18 years the study will be included
Setting	• All settings (as per Scope)
Search Strategy	• See appendix F
Review Strategy	• Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists and the quality of the evidence will be assessed by GRADE for each outcome.
Notes	• If no/insufficient RCT evidence is found we will (in order of preference): ○ Consider evidence from non-randomised, non-comparative and observational studies ○ Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) ○ Move to GDG consensus

C.1.7.2 Recovering hypoglycaemia awareness

Review question	**In adults with type 1 diabetes and impaired awareness of hypoglycaemia, what is the most effective strategy for recovering hypoglycaemia awareness?**
Objectives	The aim of this review is to look at what are the most effective methods to increase awareness of hypoglycaemia in people with type 1 diabetes and impaired awareness of hypoglycaemia.
Population	Adults with type 1 diabetes and with impaired awareness of hypoglycaemia • Adult is defined as aged ≥18 years

Subgroups	The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present, in the following order: • Age (>60 years) • Disease duration (>15 years) • Differing insulin regimens – those on MDI, bd. or PUMP • Duration of unawareness (>6 months) • People with previous hypoglycaemia unawareness versus those without • HbA1c (>7.5%)
Intervention	• Adjusting treatment/adjusting insulin regime/less intensive glycaemic control • Pancreas/islet cell transplant • Hypoglycaemia avoidance • Adjusting monitoring of blood glucose for example CGM • Education interventions • Psychological interventions • Treatments that bring back the warning signs of hypoglycaemia? (no specific treatments have been suggested yet) Only intervention durations of ≥1 month will be considered
Comparison	• Any • None
Outcomes	• HbA1c (continuous) • Autonomic symptoms/symptom scores during hypoglycaemia clamp study • Hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Severe hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Nocturnal hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Hospital admissions (dichotomous or continuous, depending how it is reported) • Hypoglycaemia unawareness or awareness (dichotomous or continuous, depending how it is reported) • Quality of life – measured by DQoL, DSQoL, PAID, HADS, fear of hypoglycaemia, anxiety, depression, cognitive function (continuous) • Road traffic accidents and work related accidents
Importance of outcomes	Critical outcomes • HbA1c • Severe hypoglycaemia • Hypoglycaemia unawareness or awareness • Quality of life
Study design	• RCTs: unit of randomisation: individual patient, cluster randomised trials • Observational studies
Population size and directness	• No restrictions on sample size • Studies with a follow-up time <4 weeks will be excluded. • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes)

	populations will only be considered, if: ○ data have been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. ○ the population contains ≥70% of type 1 diabetes patients ○ if ≥50% of people are aged >18 years the study will be included
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists and the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.8 Ketone monitoring

C.1.8.1 Ketone self-monitoring

Component	Description
Review questions	In adults with type 1 diabetes (including atypical ketosis-prone diabetes), does patient self-monitoring of blood (and urine) ketones reduce the incidence of DKA and hospital admissions?
Objectives	The aim of this review is to determine whether ketone monitoring is an effective method to help prevent DKA occurring in adults with type 1 diabetes.
Population	Adults with type 1 diabetes • Adult is defined as aged ≥ 18 years
Subgroups	The following groups will be considered separately if data are available: • Atypical ketosis-prone diabetes The following factors will be considered for subgroup analysis if heterogeneity is present: • Frequency of monitoring • Frequency of DKA • Whether patients had formal education in insulin monitoring • Recurrent DKA or Intermittent DKA • Whether DKA had a clear precipitating factor (for example, heart attack)
Intervention and comparisons	• Blood ketone versus urine ketone measurements • Any or no comparison
Outcomes	• Hospital admissions – for DKA if specified (dichotomous)

	• Duration of admission/length of hospital stay (continuous) • DKA (dichotomous) • HbA1c (continuous) • Hypoglycaemia - preferably severe hypoglycaemia if reported (dichotomous or continuous outcome, depending how it is reported) • Quality of life – measured by PAID, anxiety (continuous) • Severity of acidosis at admission - duration of acidosis and degree of acidosis (continuous or dichotomous if split into categories)
Importance of outcomes	Critical outcomes • Hospital admissions
Study design	All study types
Population size and directness	• No restrictions on sample size • No restrictions on duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will not be considered unless ≥75% are type 1 diabetes, or data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. • However, if there are very few studies found (n<5) then we will consider the following indirect populations: ○ mixed type 1 diabetes and type 2 diabetes populations, (as DKA usually occurs most frequently in type 1 diabetes patients so studies are most likely to have a higher % of type 1 diabetes) ○ mixed aged diabetes populations (adults, young people and children)
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists • Where possible, the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider indirect populations (as stated above) • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.8.2 Ketone monitoring in-hospital

Component	Description
Review questions	In adults with type 1 diabetes does in-patient monitoring of blood ketones by the healthcare professional reduce the length of hospital stay, exposure to IV insulin and the development of in-hospital complications: • in patients with suspected DKA? • in patients admitted with DKA and/or those that get it in hospital.

Objectives	The aim of this review is to determine whether ketone monitoring is an effective method to help prevent DKA occurring in adults with type 1 diabetes, and in those already with DKA does it reduce the length of hospital stay and the development of other adverse events.
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • None specified The following factors will be considered for subgroup analysis if heterogeneity is present: • Frequency of monitoring • Hospital admissions • Ketone measurement: finger strip or lab measurement • Severity of type 1 diabetes and DKA (mild, moderate or severe)
Intervention	• Blood Ketone monitoring Note: only UK licensed interventions and doses will be considered
Comparison	• Urine ketone • No monitoring Note: only UK licensed interventions and doses will be considered
Outcomes	Outcomes • Length of hospital stay (continuous) • In-hospital complications of the admission – for example cerebral oedema, mortality, serious electrolyte imbalance (dichotomous) • Exposure to IV insulin (dichotomous) • How often admission occurs (continuous) • HbA1c (continuous) • Hypoglycaemia - preferably severe hypoglycaemia if reported (dichotomous or continuous outcome, depending how it is reported) • Quality of life - (continuous)
Importance of outcomes	Critical outcomes • Mortality
Study design	All study types

Population size and directness	• No restrictions on sample size
	• No restrictions on duration
	• Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will not be considered unless ≥75% are type 1 diabetes, or data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used.
	• However, if there are very few studies found (n<5) then we will consider indirect populations:
	  ○ mixed type 1 diabetes and type 2 diabetes populations, (as DKA usually occurs most frequently in type 1 diabetes patients so studies are most likely to have a higher % of type 1 diabetes)
	  ○ mixed aged diabetes populations (adults, young people and children)

Setting	• All settings (as per Scope)
Search Strategy	See appendix F

Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists • Where possible, the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider indirect populations (as stated above) • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.9 Arterial risk control

C.1.9.1 Aspirin

Component	Description
Review question	In adults with type 1 diabetes, is aspirin an effective anti-platelet agent for the primary prevention of CV events?
Objectives	The aim of this review is to determine whether aspirin is an effective agent for preventing CV events in terms of clinical and cost-effectiveness as well as safety for use in adults with type 1 diabetes.
Population	Adults with type 1 diabetes • Adult is defined as aged ≥ 18 years
Subgroups	The following groups will be considered separately if data are available: • none specified The following factors will be considered for subgroup analysis if heterogeneity is present: • aspirin dose • hypertension • micro albuminuria • statin use • PPI use (for adverse event outcomes) • smoking (versus non-smoking)
Intervention	Aspirin Note: only UK licensed interventions and doses will be considered
Comparison	• Placebo • Usual care/no treatment • Low dose versus high dose Note: only UK licensed interventions and doses will be considered
Outcomes	Outcomes

	• Mortality – all cause (dichotomous/time-to event) • Mortality – CV (dichotomous/time-to event) • MI – all cause (dichotomous/time-to event) • MI – fatal (dichotomous/time-to event) • MI – non-fatal (dichotomous/time-to event) • Stroke – all cause (dichotomous/time-to event) • Stroke – fatal (dichotomous/time-to event) • Stroke – non-fatal (dichotomous/time-to event) • Quality of life – measured by SF-36, DQoL, DSQoL (continuous) • Adverse events – bleeding or GI complications (dichotomous) • HbA1c (continuous) • Hypoglycaemia - preferably severe hypoglycaemia if reported (dichotomous or continuous outcome, depending how it is reported)
Importance of outcomes	Critical outcomes • Mortality • MI • Stroke
Study design	RCTs, observational studies • Unit of randomisation: individual patient
Population size and directness	• No restrictions on sample size • Studies with a follow-up time <4 weeks will be excluded. • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will not be considered, unless data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. • Studies only comparing different dosages of aspirin will not be included
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists and the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.10 Inpatient management

C.1.10.1 IV insulin (devices and regimens)

Review question	**In adults with** type 1 diabetes **who have been admitted to hospital (elective and emergency), what is the most effective intravenous insulin dose-adjustment devices and regimens for optimal diabetic control?**

Objectives	The aim of this review is to determine whether IV insulin should be used for treating inpatients with type 1 diabetes, and if so what is the best regimen.
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • Emergency (non-diabetic) • Elective (when nil by mouth) • Surgery • indication groups: DKA or other acute illness, surgical patients, enteral feeding The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • Dose
Intervention	• IV insulin Note: only UK licensed interventions and doses will be considered
Comparison	• Subcutaneous insulin • Each other (different regimens) • Each other (different devices) • No comparison Note: only UK licensed interventions and doses will be considered
Outcomes	• Achieving target BG levels (dichotomous or continuous outcome, depending how it is reported) • Hypoglycaemia - preferably severe hypoglycaemia if reported (dichotomous or continuous outcome, depending how it is reported) • Time spent out of target glucose, that is, hypoglycaemia/hyperglycaemia (dichotomous or continuous outcome, depending how it is reported) • Duration of IV treatment (continuous) • In-patient stay (continuous) • In-patient mortality (dichotomous) • Infection rate /wound healing (dichotomous or continuous outcome, depending how it is reported) • Quality of life – measured by SF-36, DQoL, DSQoL (continuous)
Importance of outcomes	Critical outcomes • Achieving target BG levels • Mortality • Hypoglycaemia
Study design	RCTs, observational studies • Unit of randomisation: individual patient
Population size and directness	• Exclude studies in ACS populations • No restrictions on sample size • No restrictions on study duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. ○ the population contains ≥70% of type 1 diabetes patients ○ if ≥50% of people are aged >18 years the study will be included
Setting	• All settings (as per Scope)

Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists and the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.11 Complications

C.1.11.1 Gastroparesis

Component	Description
Review question	In adults with type 1 diabetes, what is the most effective treatment for Gastroparesis?
Objectives	The aim of this review is to determine which is the most effective treatment for Gastroparesis?
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • young poorly controlled females The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • different doses • different interventions and comparisons • use of PPI
Intervention	• Prokinetic agents/gastroprokinetic agents (for example, erythromycin) • 5-Hydoxytryptamine antagonists (for example, ondansetron) • Anti-emetics • Botulinum toxin • Electrical stimulation interventions • Intensive insulin treatment/glucose control • Dietary changes • Enteral feeding • Acupuncture • Aldose reductase inhibitors (including epalrestat) • Histamine-2 receptor antagonists • Centrally acting antidepressants • Surgical interventions (including gastrectomy)

	Note: only UK licensed interventions and doses will be considered
Comparison	• Placebo • Standard care • Each other (within class and between-class comparisons) • Continuous agent versus other agents • Rotation of medications Note: only UK licensed interventions and doses will be considered
Outcomes	• Hospital admissions (dichotomous) • Severe hypoglycaemia (dichotomous or continuous outcome, depending how it is reported) • Vomiting (dichotomous or continuous outcome, depending how it is reported) • Weight loss (continuous) • Quality of Life - SF-36 (continuous) • HbA1c (continuous) • Symptom control (as defined by the study; dichotomous or continuous outcome, depending how it is reported)
Importance of outcomes	Critical outcomes • Hospital admissions • Severe hypoglycaemia • Vomiting
Study design	RCTs Unit of randomisation: individual patient
Population size and directness	• No restrictions on sample size • Studies with a treatment duration of ≤1 day will be excluded • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will be considered if: ○ ≥50% of people are aged >18 years the study will be included ○ studies will be included if any percentage of type 1 diabetes is in a mixed diabetes population (because gastroparesis treatment is not dependent upon/affected by the type of diabetes). • Studies only comparing different dosages or regimens of the same intervention will be excluded • Studies looking at cisapride will be excluded as this is no longer used in the UK. • Studies looking at constipation or gastric emptying (in diabetics who do not have gastroparesis) will be excluded
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	• To find data published in 2003 and before, we will look for studies in the old guideline and search reference lists of systematic reviews which have included these dates. - Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists and the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for

	continuous outcomes
Notes	If no/insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies (prospective studies only) • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.11.2 Acute painful neuropathy

Review question	In adults with type 1 diabetes, what is the most effective treatment for acute painful neuropathy?
Objectives	The aim of this review is to determine which is the most effective treatment for acute painful neuropathy.
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • Newly diagnosed (up to 3 months) The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • Different doses
Intervention	• Analgesia, for example, Duloxetine, tramadol • Anti-epileptics, a-depressants - tricyclic antidepressants (SNRIs and duloxetine), anti-convulsants (gabapentin, pregabalin), pump therapy • Lidocaine/lignocaine (anaesthetics); capsaicin. • Using pump Note: only UK licensed interventions and doses will be considered
Comparison	• Anything • None Note: only UK licensed interventions and doses will be considered
Outcomes	• Pain scores (continuous) • Retinopathy – incidence (dichotomous) • Low-level (micro) albuminuria - incidence (dichotomous) • Resolution of symptoms (continuous) • Improvement in pain scores (dichotomous)
Importance of outcomes	Critical outcomes • Pain scores • Time to resolution of symptoms (continuous)
Study design	All study types
Population size and directness	• No restrictions on sample size • No restrictions on treatment duration • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. ○ the population contains ≥70% of type 1 diabetes patients ○ if ≥50% of people are aged >18 years the study will be included

Review question	In adults with type 1 diabetes, what is the most effective treatment for acute painful neuropathy?
Setting	• All settings (as per Scope)
Search Strategy	See Appendix F
Review Strategy	Appraisal of methodological quality The methodological quality of each study will be assessed using NICE checklists and the quality of the evidence will be assessed by GRADE for each outcome. Synthesis of data • Meta-analysis will be conducted where appropriate • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If insufficient RCT evidence is found we will (in order of preference): • Consider evidence from non-randomised, non-comparative and observational studies • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.1.11.3 Thyroid disease monitoring

Component	Description
Review question	How should adults with type 1 diabetes be monitored for thyroid disease, and how frequently
Objectives	The aim of this review is to determine whether and how often thyroid disease should be monitored for, as this is an association of type 1 diabetes
Population	Adults with type 1 diabetes • Adult is defined as aged ≥18 years
Subgroups	The following groups will be considered separately if data are available: • different monitoring strategies • different Abs – positive versus not positive The following factors will be considered for subgroup analysis (in the critical outcomes only) if heterogeneity is present: • Annual versus 5 yearly for hypo- and hyperthyroidism (positive peroxidase Abs) • Did the test (in the paper) specify which method was used • gender (male/female) • family history (yes/no)
Intervention	Thyroid disease monitoring: • Thyroid function tests • Autoantibodies/antibodies (for example, peroxidase)
Comparison	• As for the intervention but at a different frequency • Standard care/no monitoring • No comparison (non-comparative studies)
Outcomes	• Detection of thyroid disease – thyroid tests, for example, TSH, T4 (mainly prevalence) • Incidence of thyroid disease (mainly prevalence) • Frequency of treatment
Importance of	Critical outcomes

outcomes	• All of the above
Study design	• RCTs, observational studies, prognostic studies
Population size and directness	• No restrictions on sample size (unless >10 studies, then sample sizes of N<100 will be excluded) • No restriction on study duration • Not pregnancy • Studies with indirect, or mixed diabetes (type 1 diabetes and type 2 diabetes) populations will only be considered, if: ○ data has been reported for the subgroup of type 1 diabetes patients, in which case this subgroup data will be used. ○ the population contains ≥70% of type 1 diabetes patients ○ if ≥50% of people are aged >18 years the study will be included
Setting	• All settings (as per Scope)
Search Strategy	See appendix F
Review Strategy	Appraisal of methodological quality • The methodological quality of each study will be assessed using NICE checklists • Where possible, the quality of the evidence will be assessed by GRADE for each outcome. • Taking into consideration the advice on prognostic reviews in the NICE guidelines manual, meta-analysis or GRADE will not be undertaken for prognostic studies Synthesis of data • Meta-analysis will be conducted where appropriate • Data will be synthesised in a narrative review where meta-analysis is not possible • Outcomes will be grouped into the following categories based on time-points: ○ ≤6 months (or the one nearest to 6 months if multiple time-points are given) ○ >6 months (or the longest one if multiple time-points are given) • Default MIDs will be used: 0.75 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes
Notes	If no/insufficient RCT, observational or prognostic evidence is found, we will (in order of preference): • Consider unpublished or partially published studies (including abstracts – and contact the authors for more information) • Move to GDG consensus

C.2 Health economic review

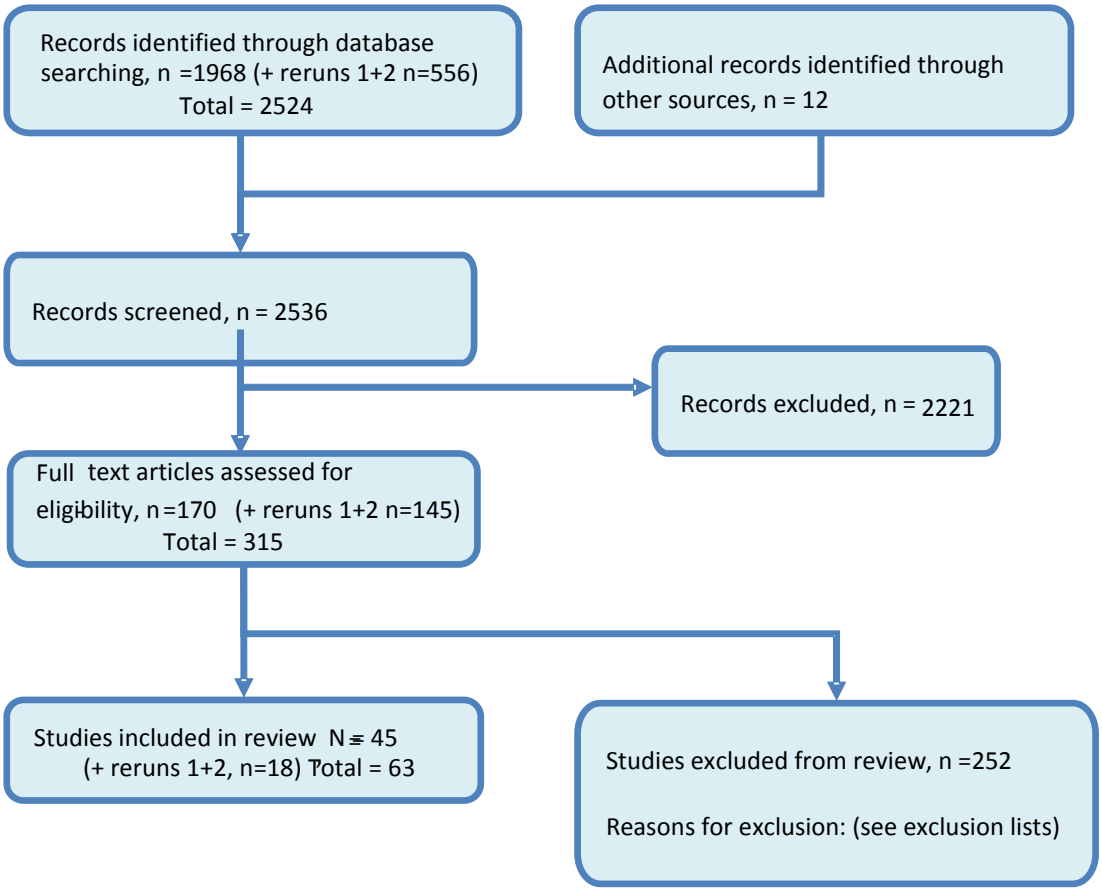
Review question	All questions – health economic evidence
Objectives	To identify economic evaluations relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the individual review protocol above. • Studies must be of a relevant economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be an abstract only, a letter, editorial or commentary, or a review of economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English. • Studies must not be published before 1999.

Search strategy	An economic study search will be undertaken using population-specific terms and an economic study filter – see Appendix F.
Review strategy	Each study fulfilling the criteria above will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in Appendix G of the NICE guidelines manual (2012).[1] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. An economic evidence table will be completed and it will be included in the economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then an economic evidence table will not be completed and it will not be included in the economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will 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 is to include studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the GDG if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation as excluded economic studies in Appendix K. The health economist will be guided by the following hierarchies. **Setting:** • UK NHS • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden) • OECD countries with predominantly private health insurance systems (for example, USA, Switzerland) • non-OECD settings (always 'Not applicable'). **Economic study type:** • cost–utility analysis • other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis) • comparative cost analysis • non-comparative cost analyses including cost-of-illness studies (always 'Not applicable'). **Year of analysis:** • The more recent the study, the more applicable it is. **Quality and relevance of effectiveness data used in the economic analysis:** • The more closely the effectiveness data used in the economic analysis matches with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix D: Clinical article selection

D.1 Diagnosis

Figure 1: Flow chart of clinical article selection for the review of distinguishing between different types of diabetes



D.2 Education programmes and self-care

Figure 2: Flow chart of clinical article selection for the review of Structured education programmes

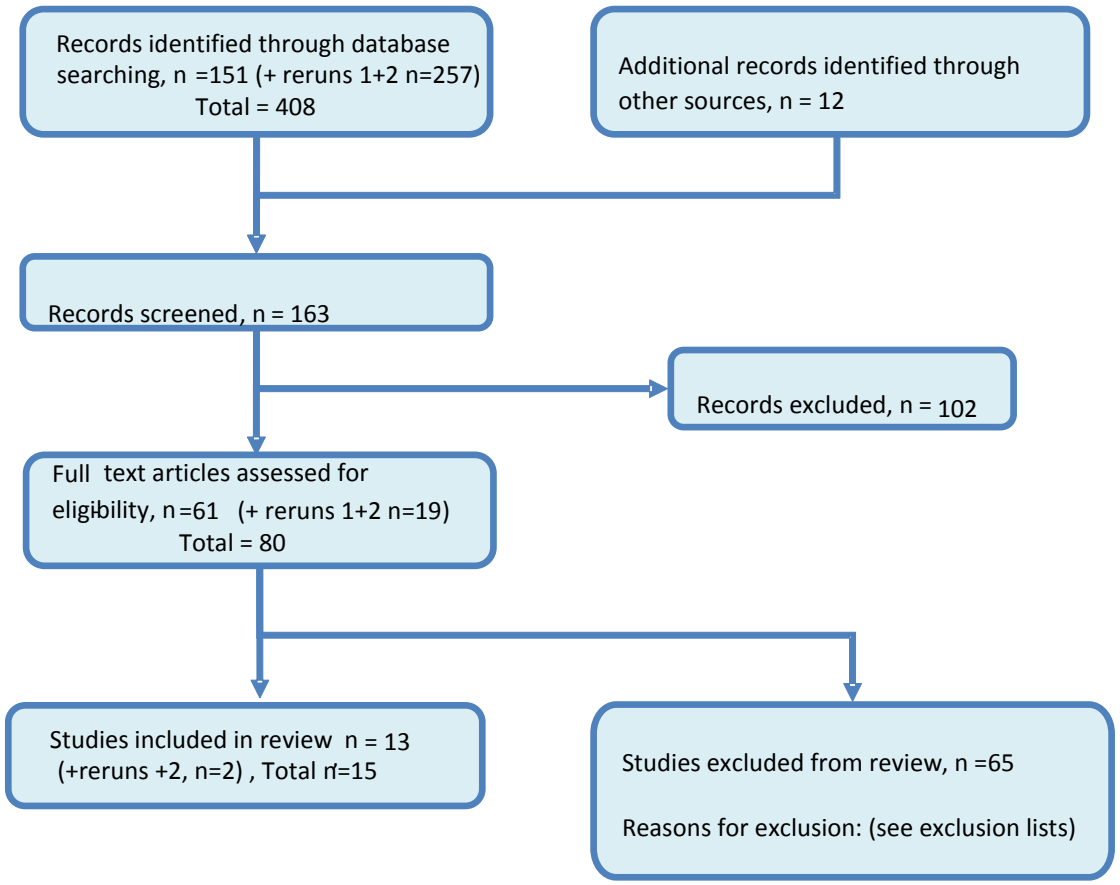


Figure 3: Flow chart of clinical article selection for the review of Carb counting

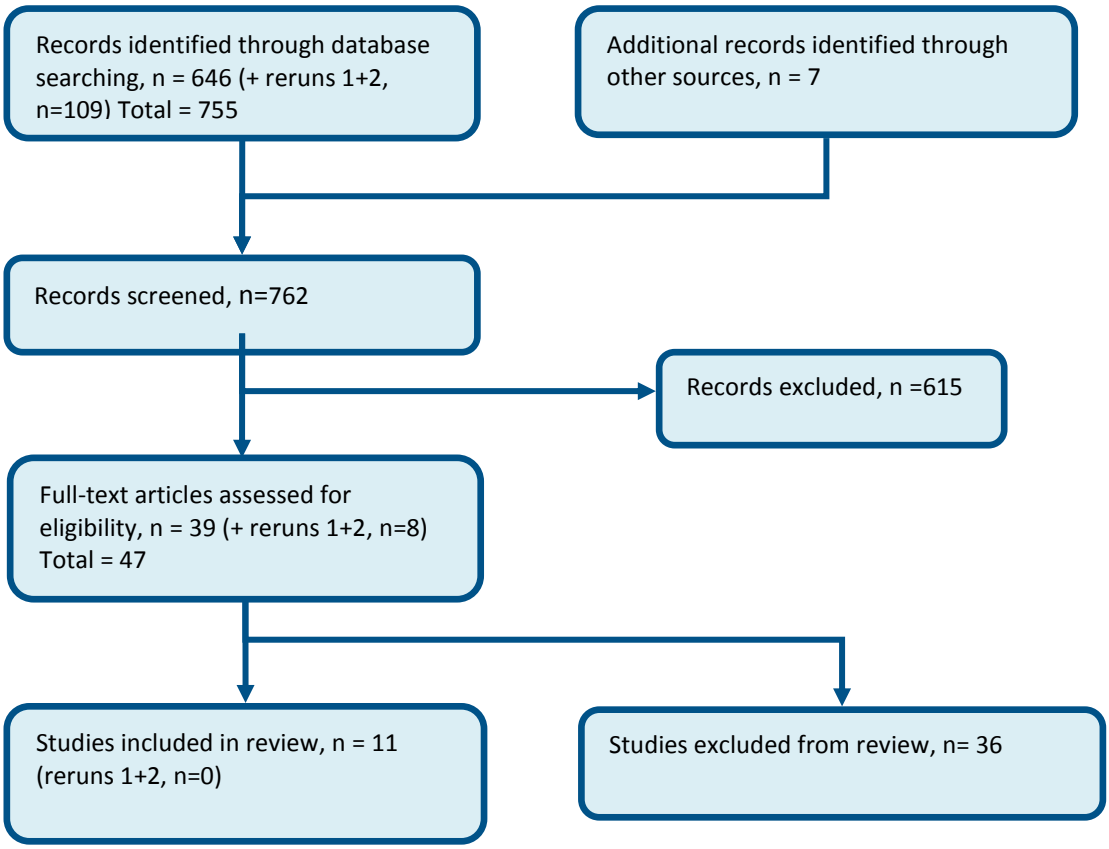
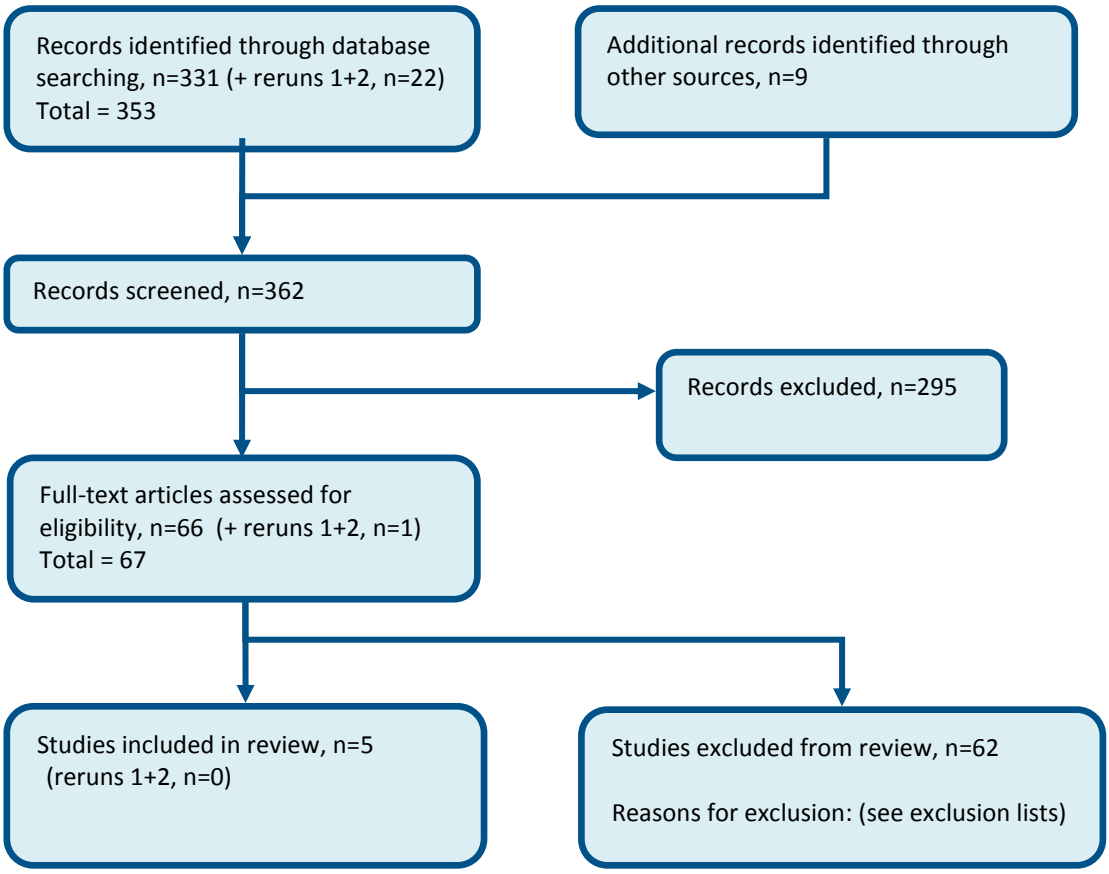


Figure 4: Flow chart of clinical article selection for the review of Glycaemic index diet



D.3 Blood glucose monitoring

Figure 5: Flow chart of clinical article selection for the review of HbA1c

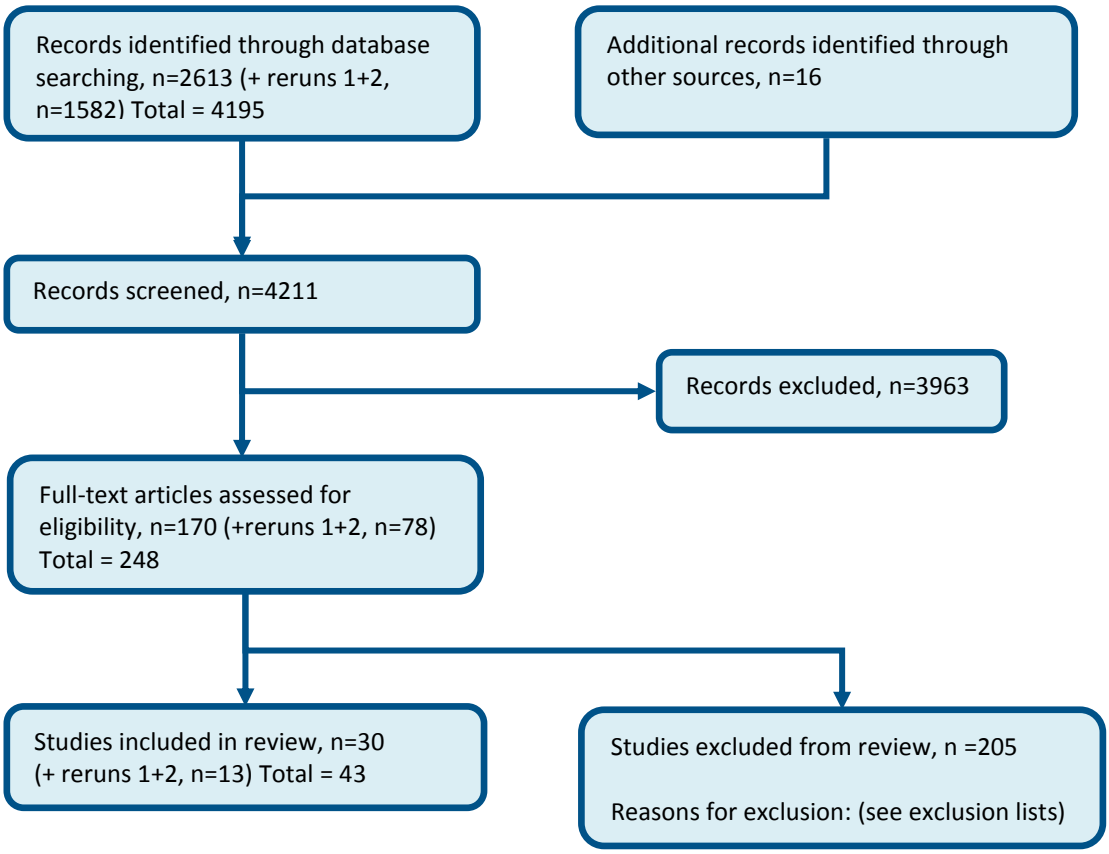


Figure 6: Flow chart of clinical article selection for the review of SMBG targets, timing and frequency

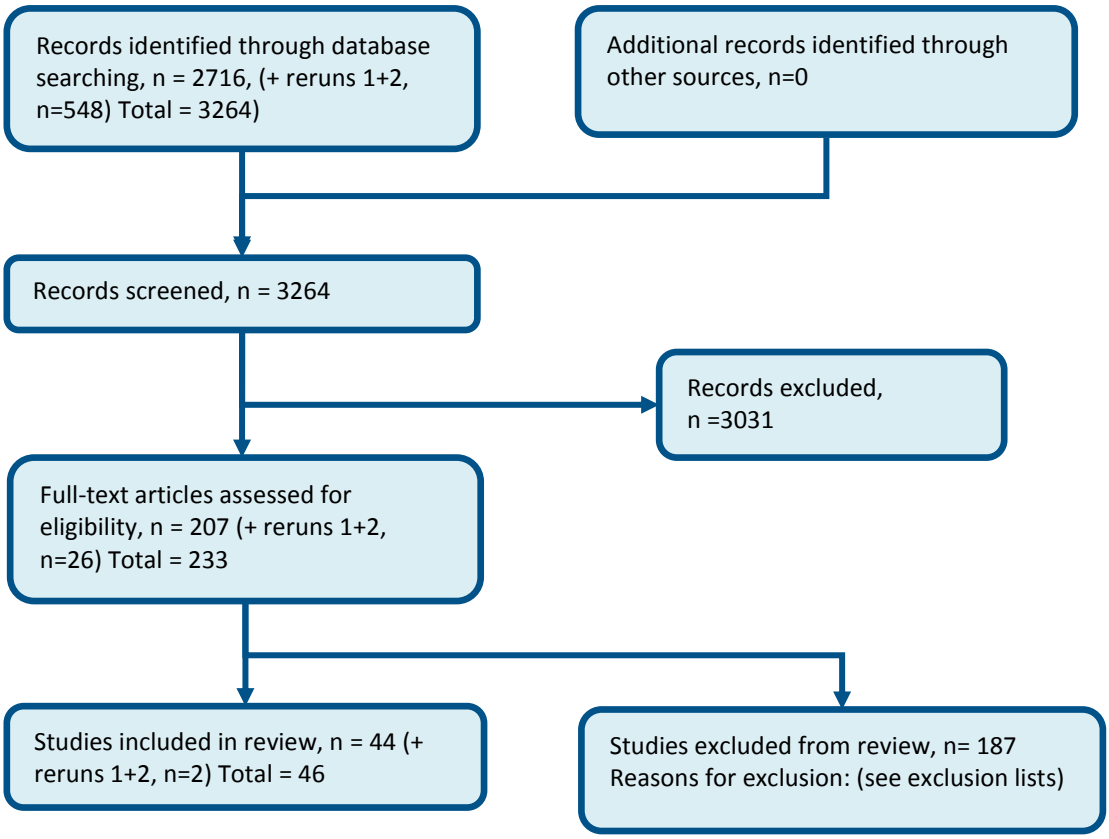


Figure 7: Flow chart of clinical article selection for the review of SMBG technologies

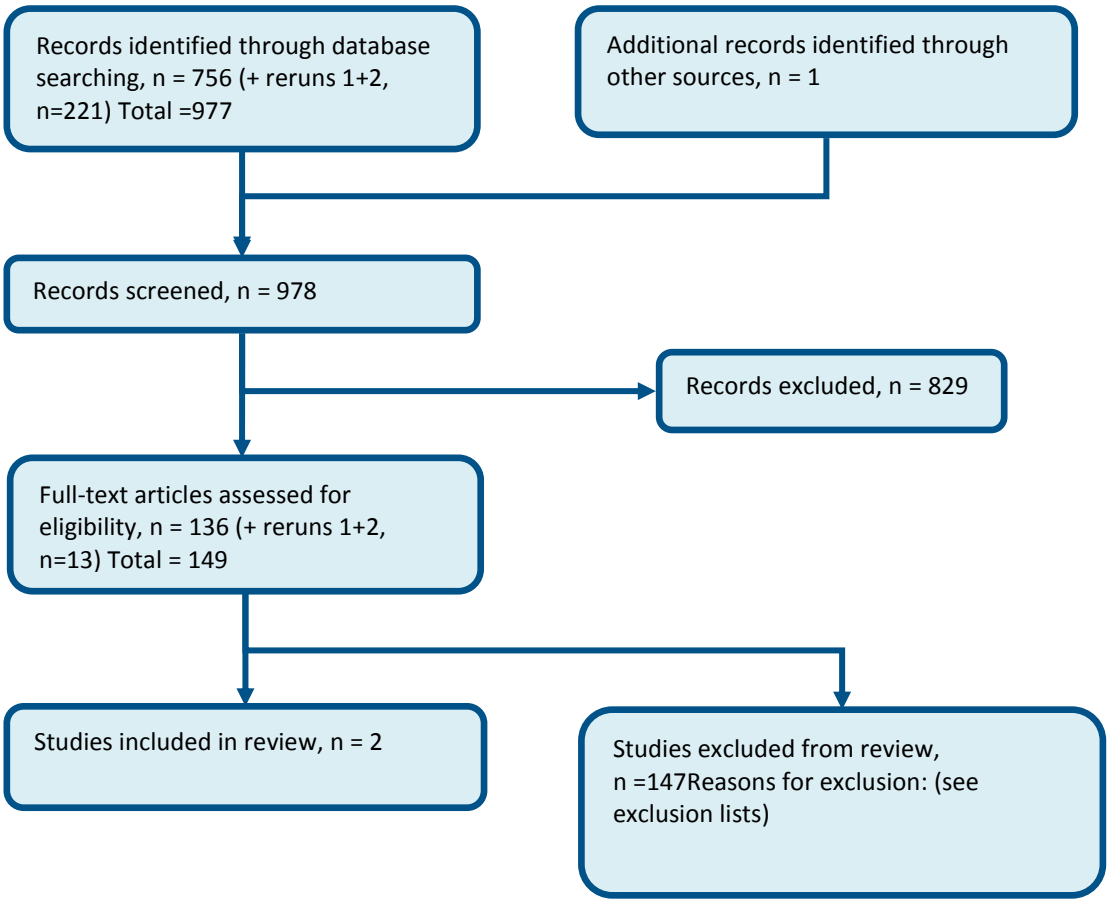
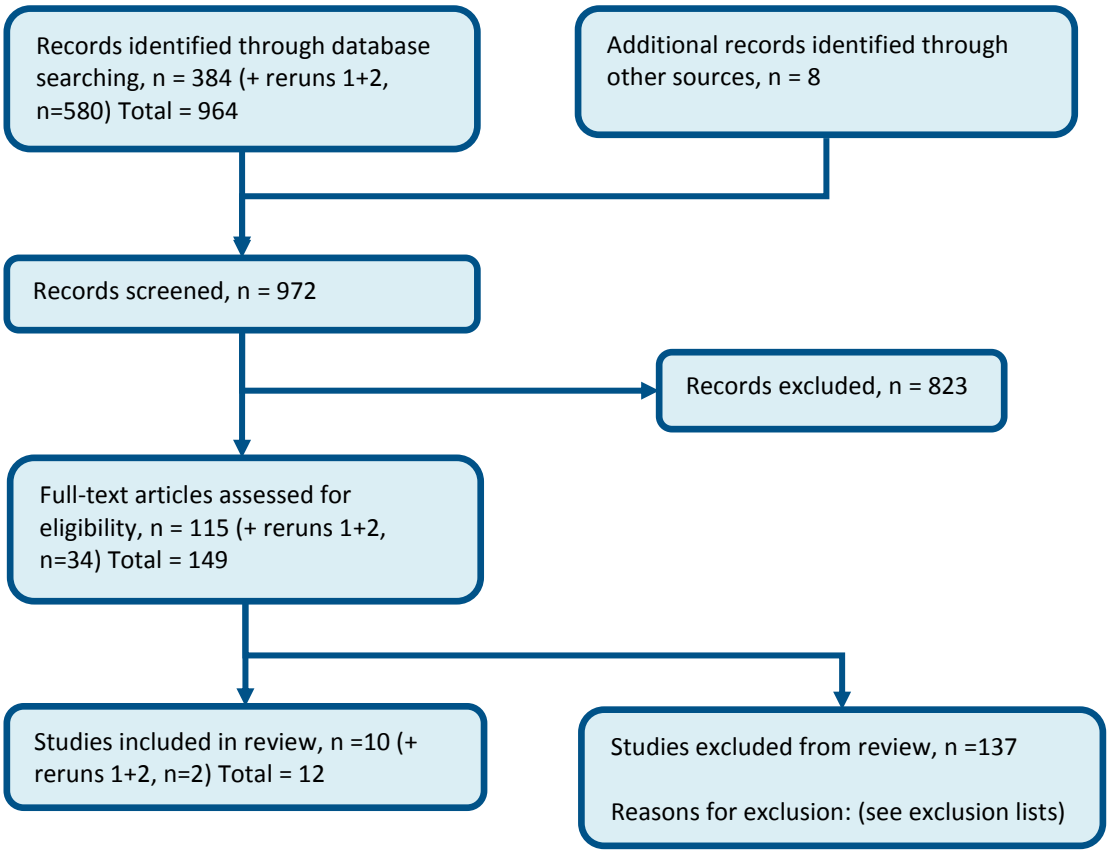


Figure 8: Flow chart of clinical article selection for the review of SMBG versus CGM



D.3.1 Insulin therapy

Figure 9: Flow chart of clinical article selection for the review of Rapid-acting insulin

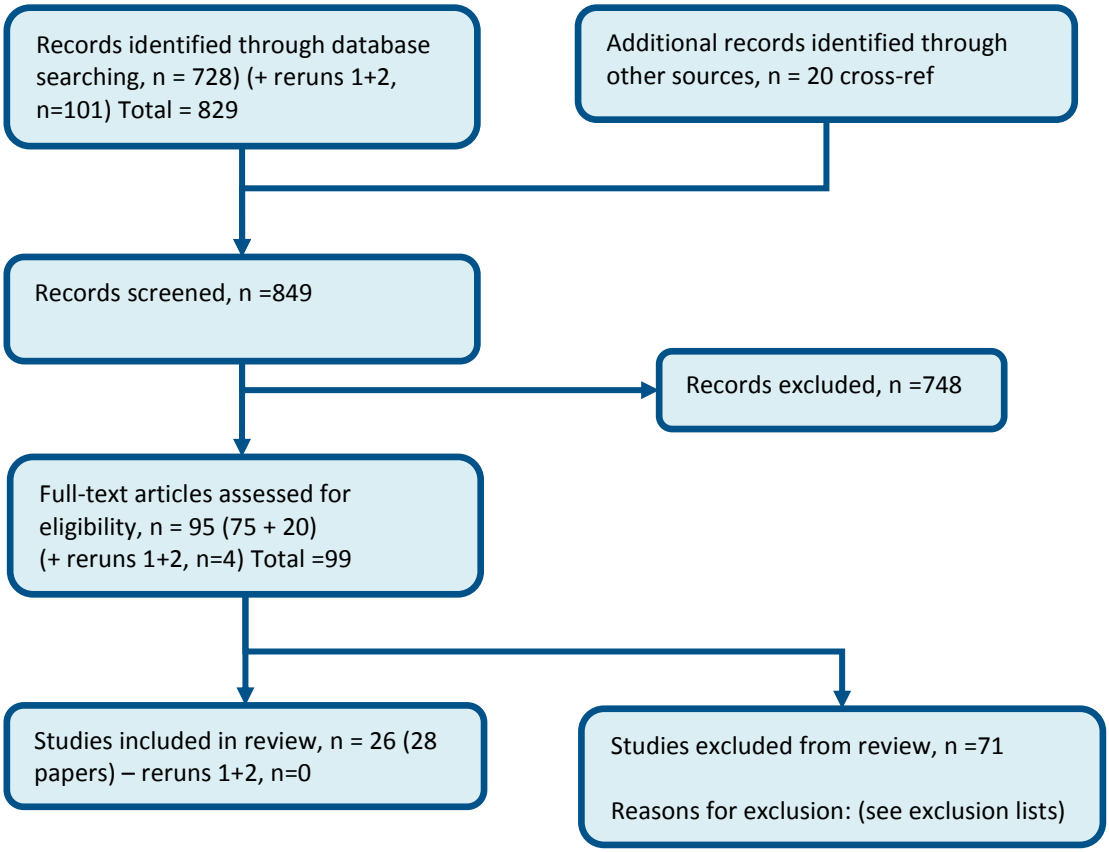


Figure 10: Flow chart of clinical article selection for the review of Long-acting insulin

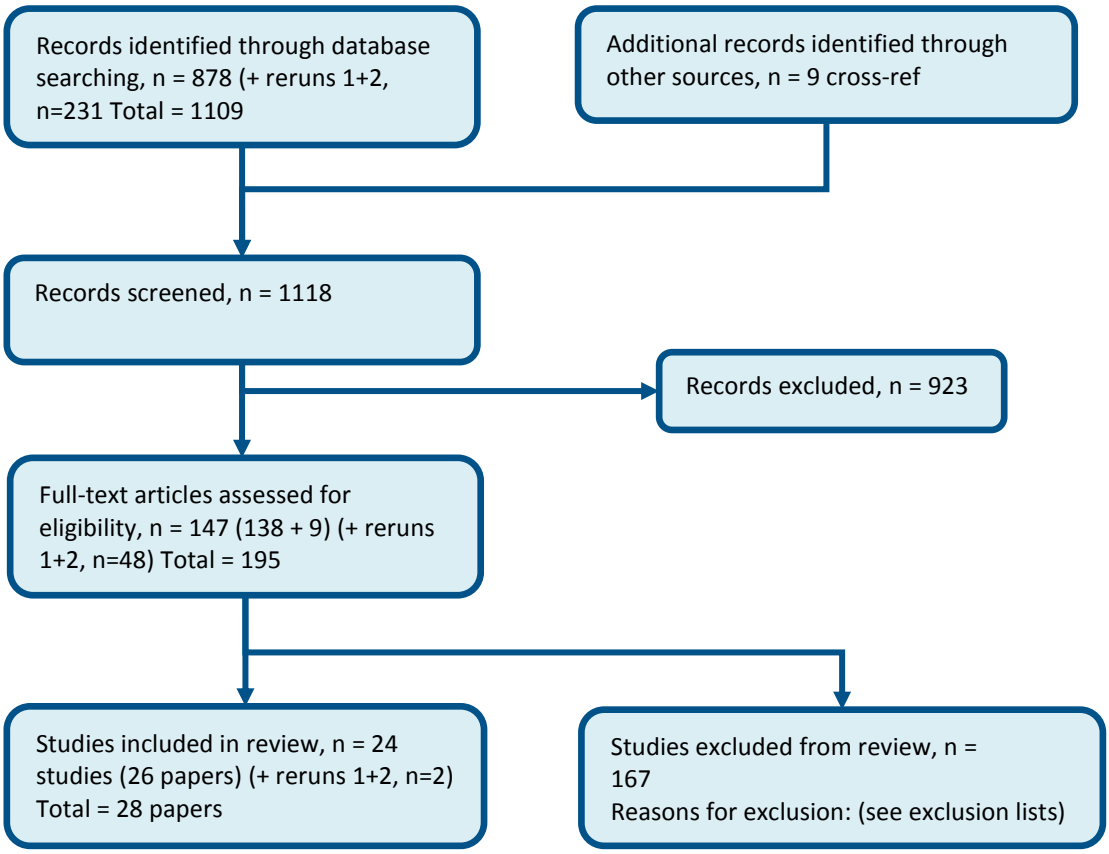


Figure 11: Flow chart of clinical article selection for the review of Mixed insulin

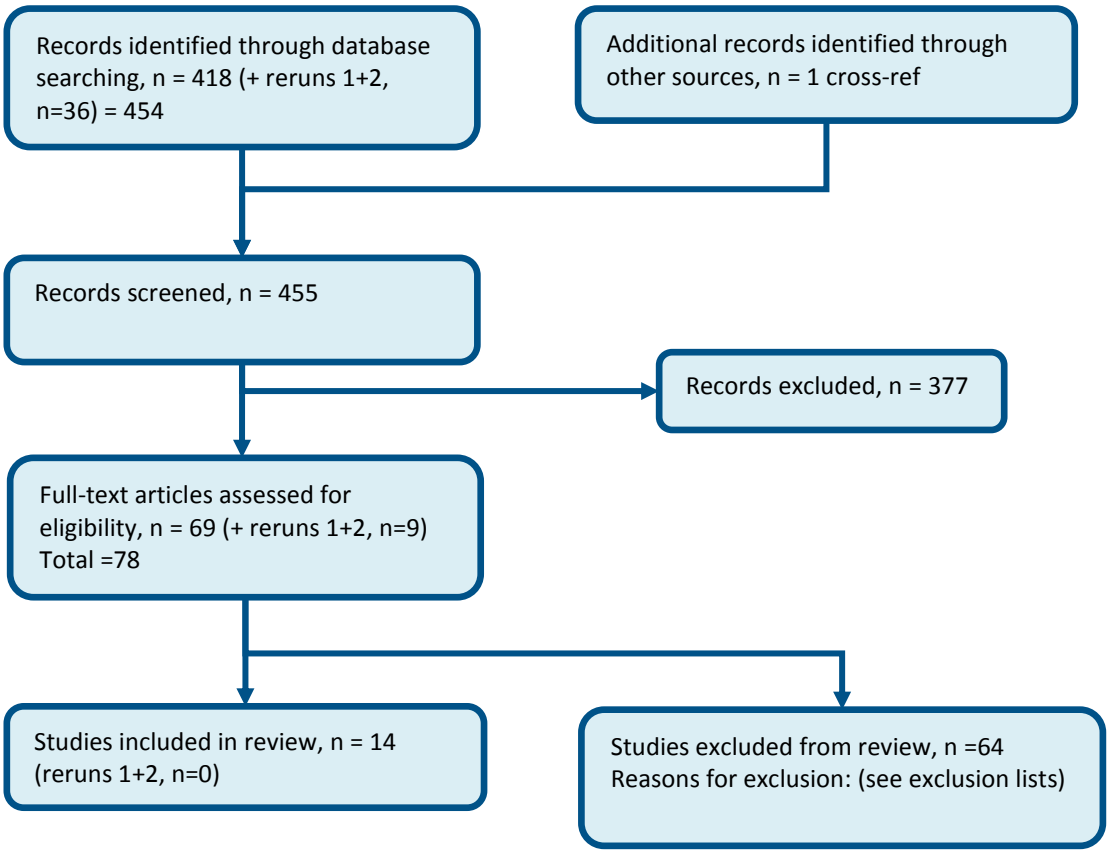


Figure 12: Flow chart of clinical article selection for the review of Metformin

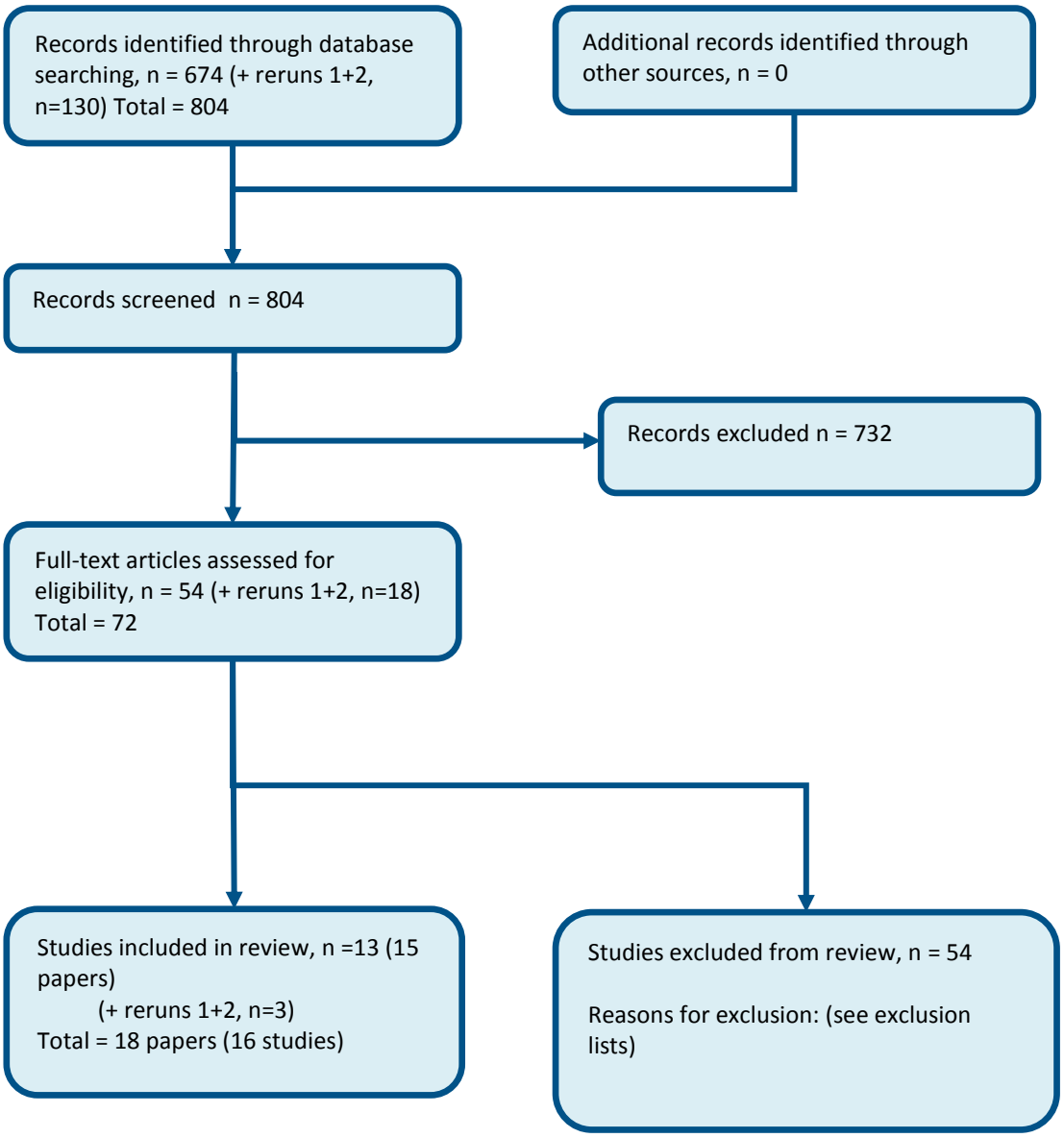


Figure 13: Flow chart of clinical article selection for the review of Once versus twice daily basal insulin

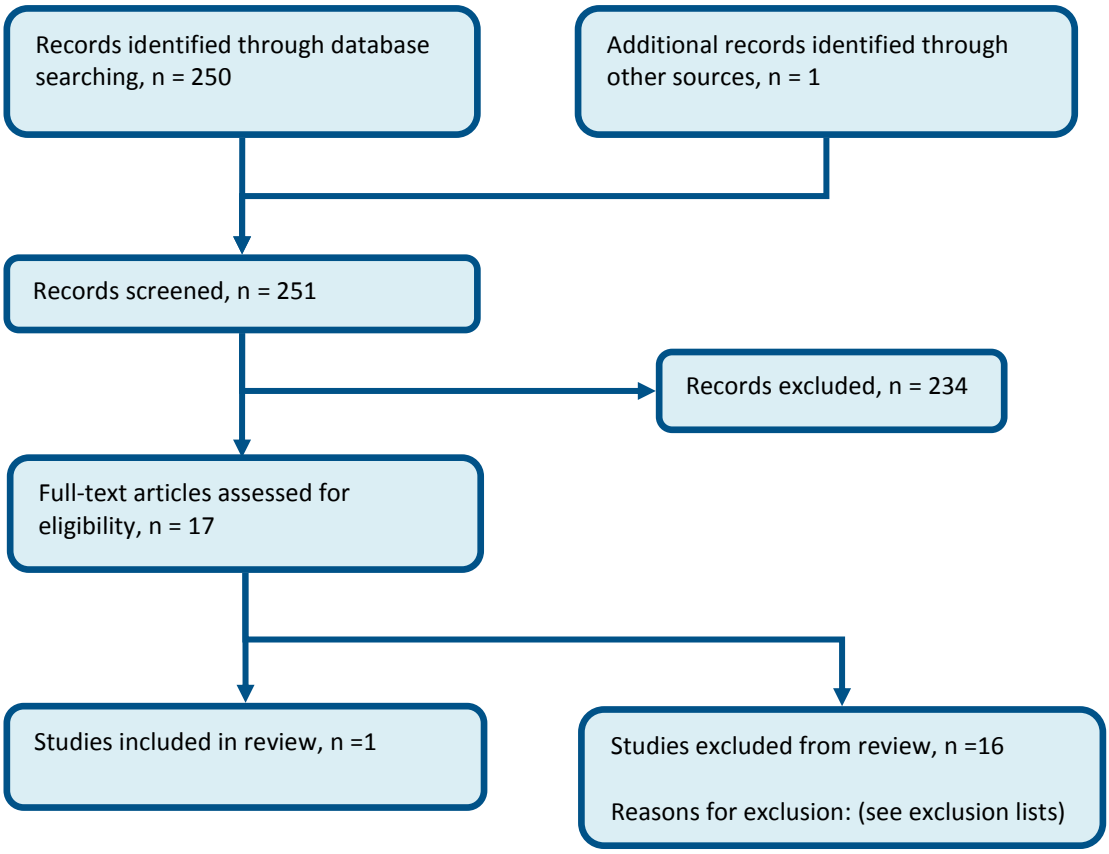


Figure 14: Flow chart of clinical article selection for the review of Insulin delivery (needle length, site and rotation)

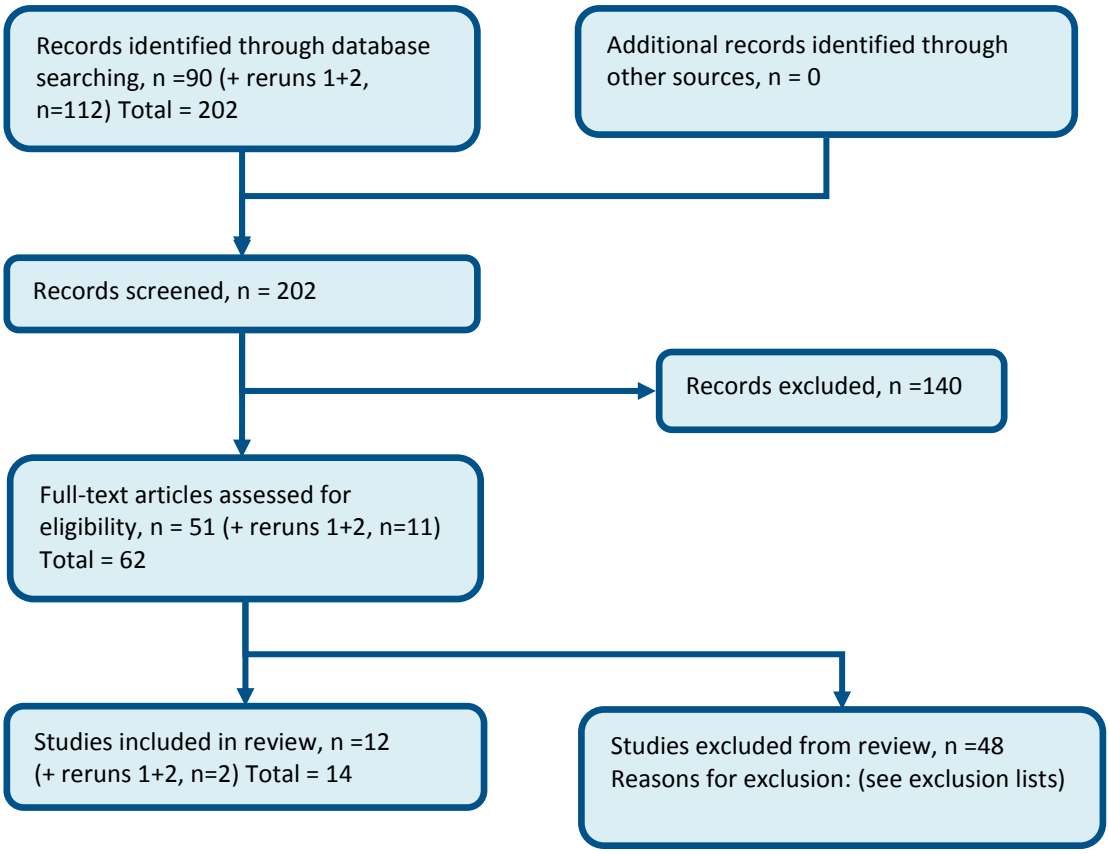
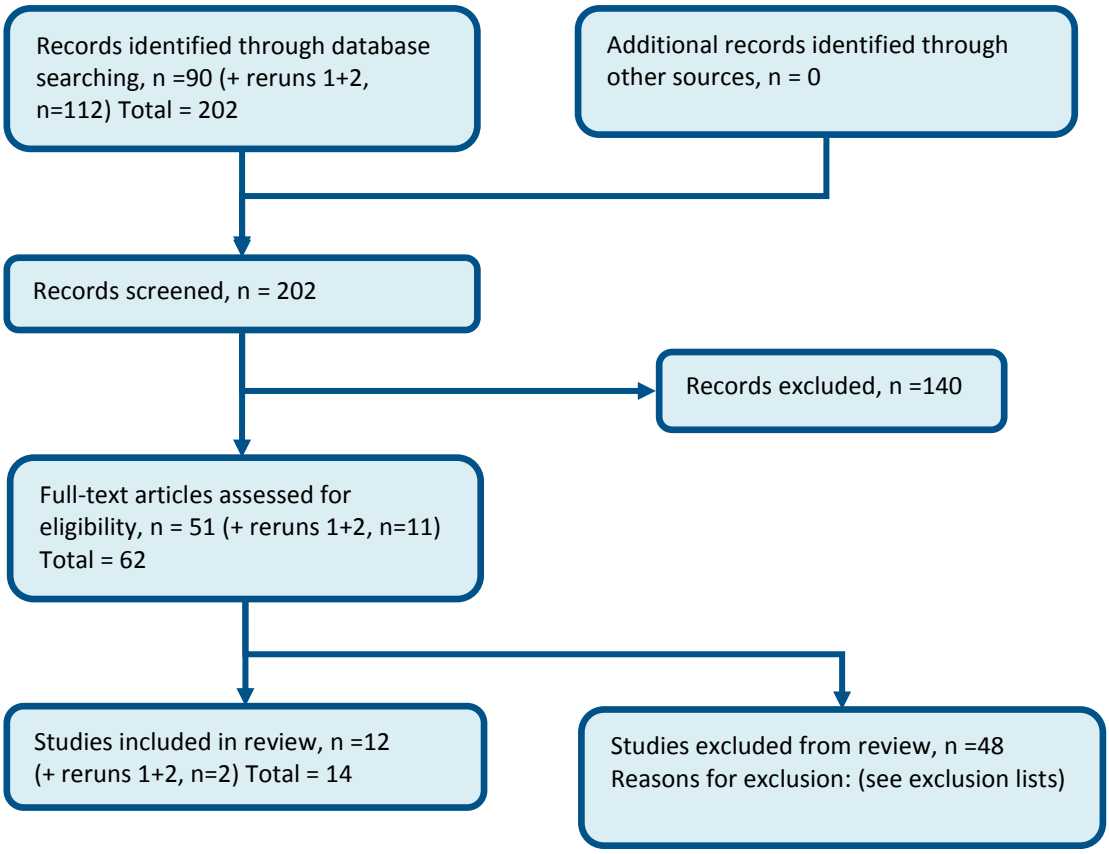


Figure 15: Flow chart of clinical article selection for the review of Insulin delivery (needle length, site and rotation)



D.4 Hypoglycaemia

Figure 16: Flow chart of clinical article selection for the review of the Identification of hypoglycaemia awareness

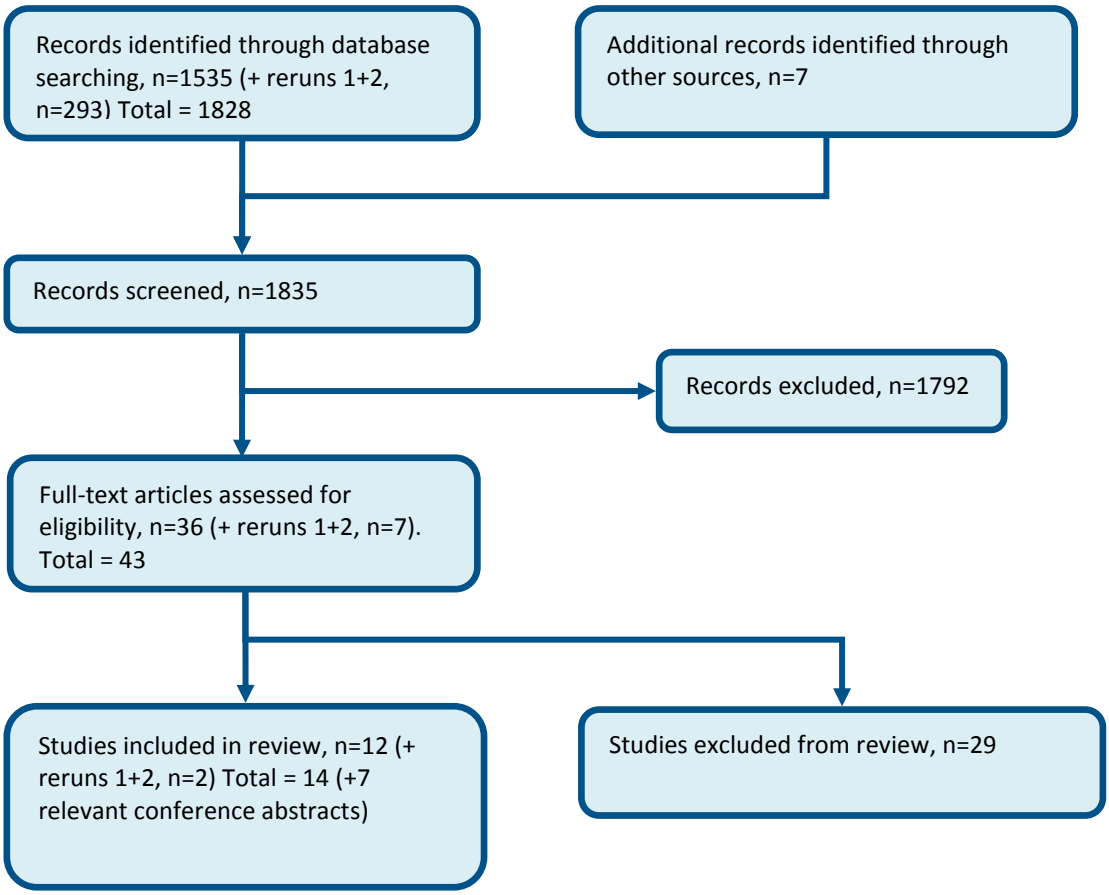
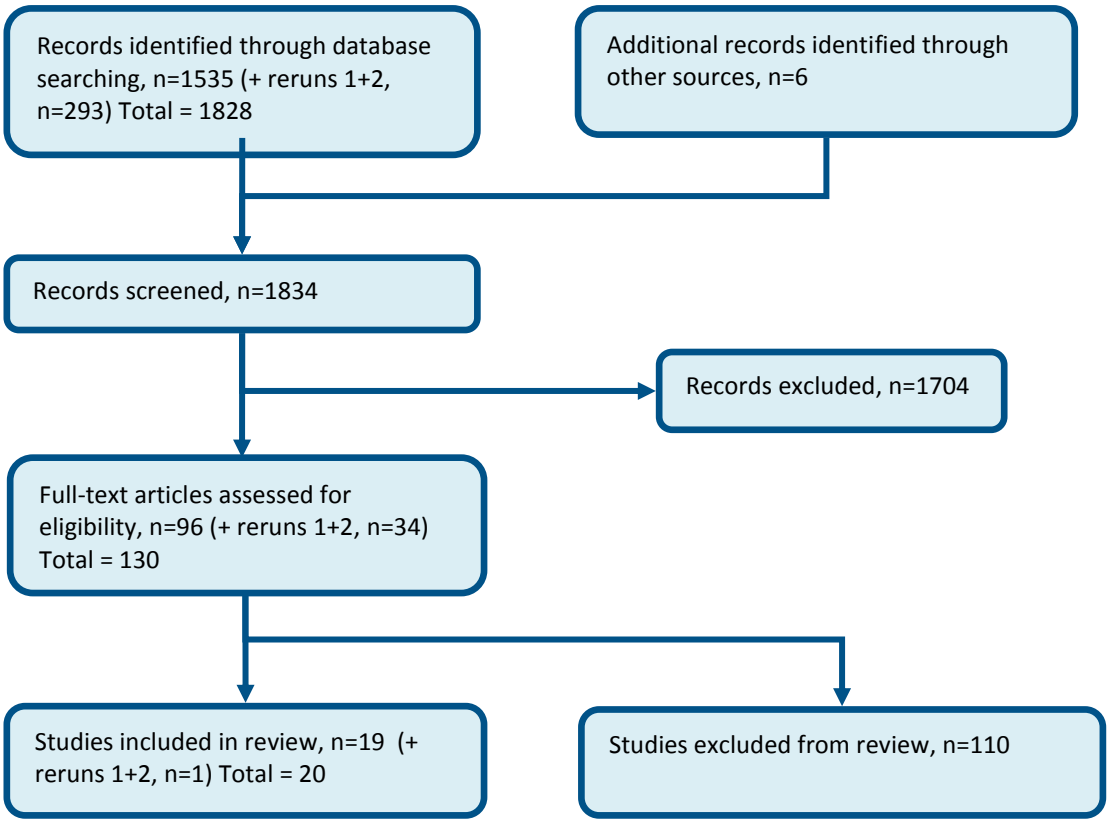
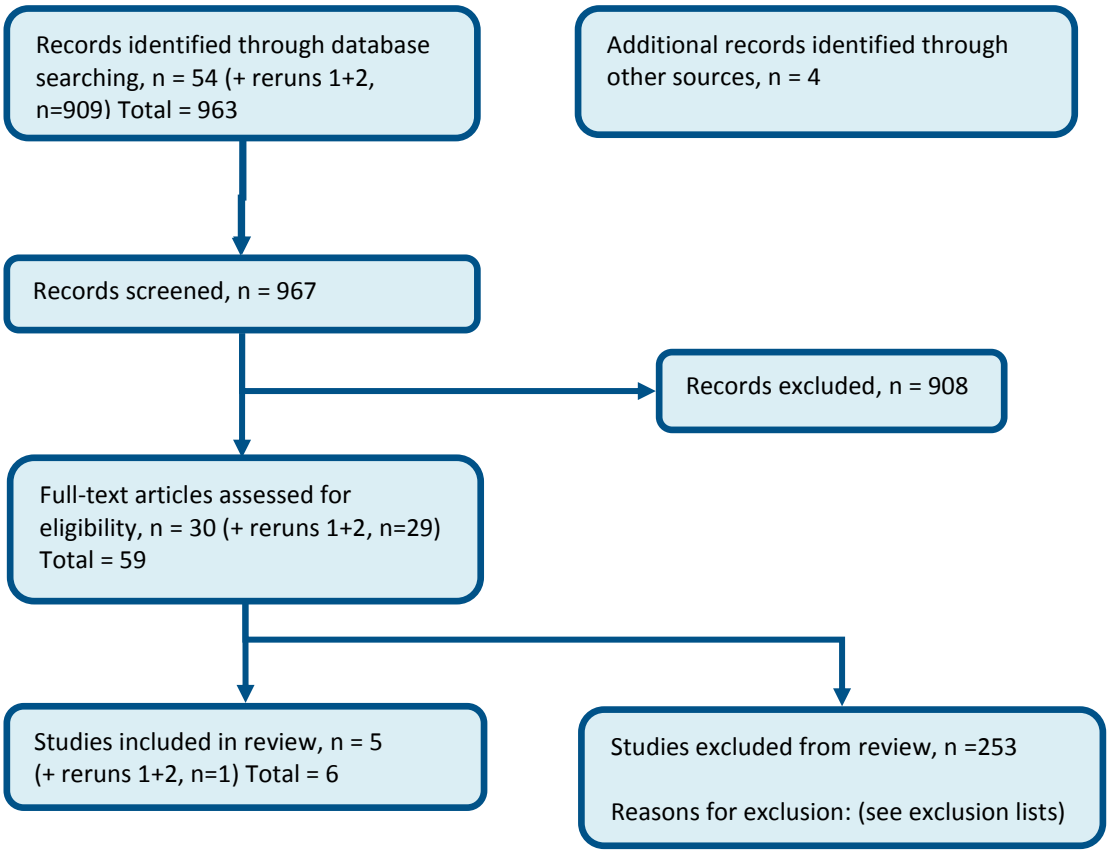


Figure 17: Flow chart of clinical article selection for the review of Strategies to recover hypoglycaemia awareness



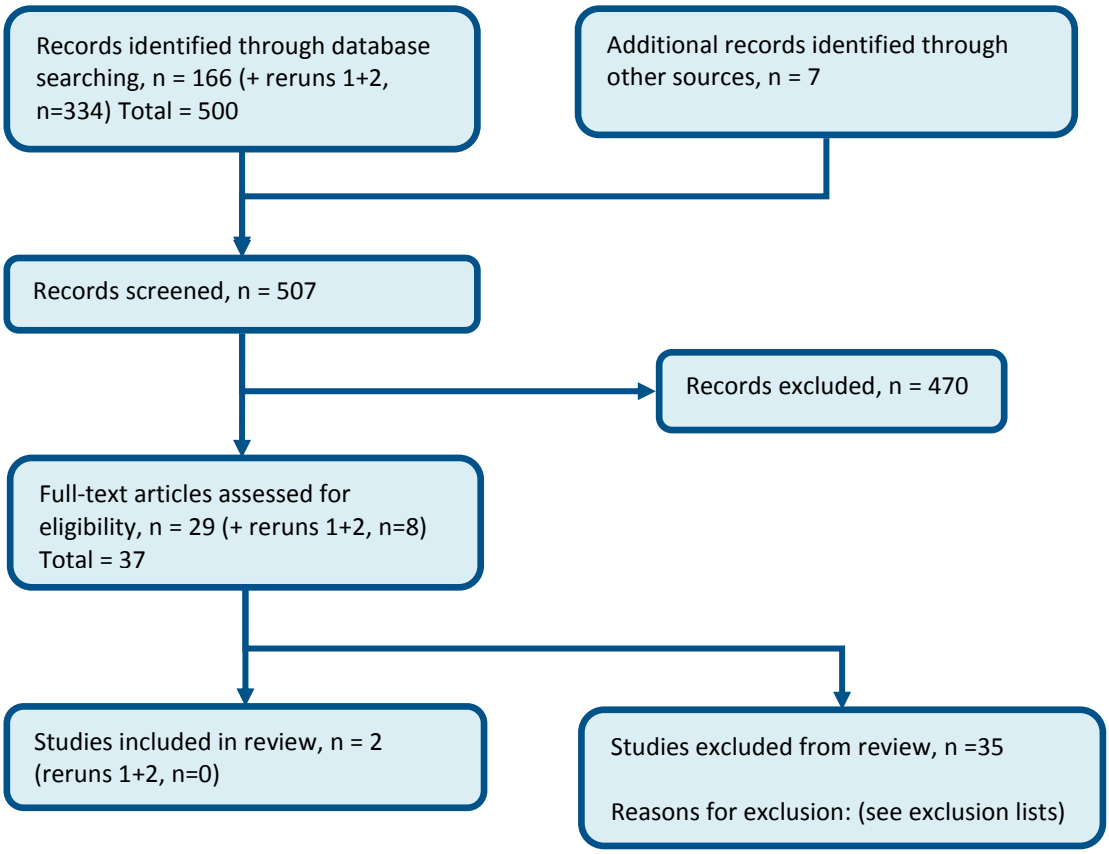
D.5 Ketone monitoring

Figure 18: Flow chart of clinical article selection for the review of Ketone self-monitoring and in-hospital self-monitoring



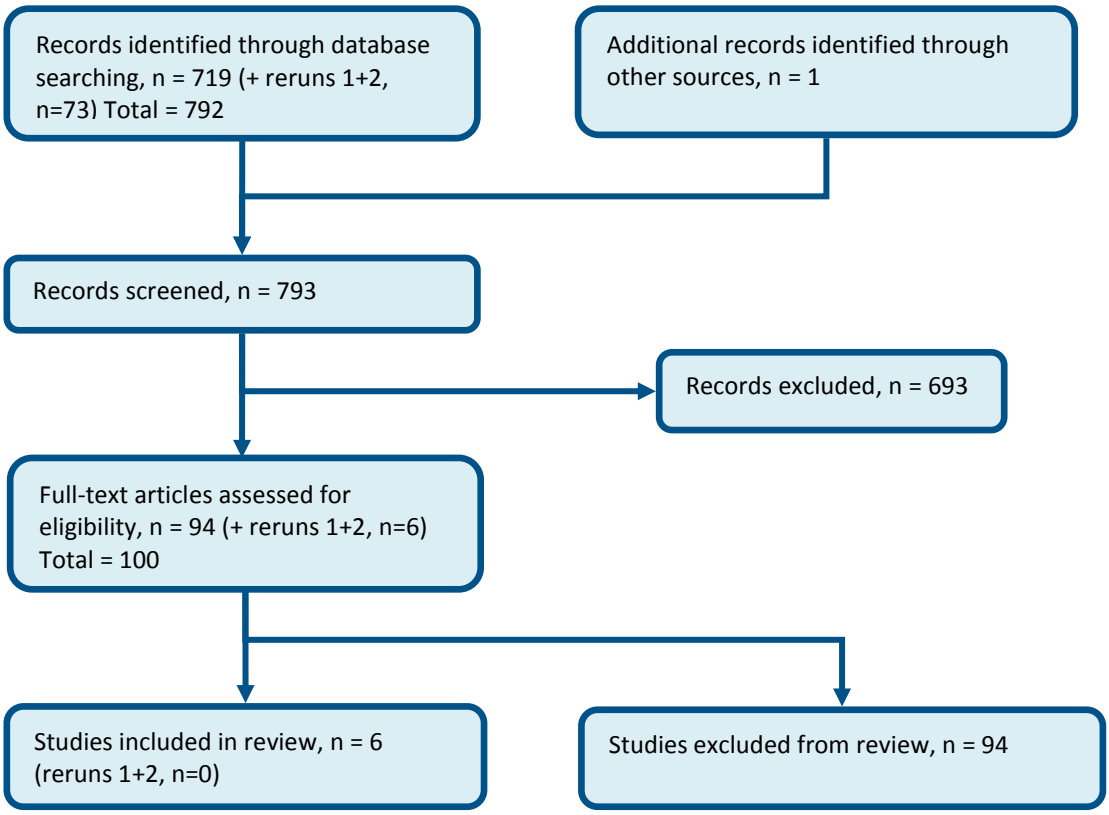
D.6 Arterial risk control

Figure 19: Flow chart of clinical article selection for the review of Aspirin



D.7 Inpatient management

Figure 20: Flow chart of clinical article selection for the review of IV insulin



D.8 Complications

Figure 21: Flow chart of clinical article selection for the review of Gastroparesis

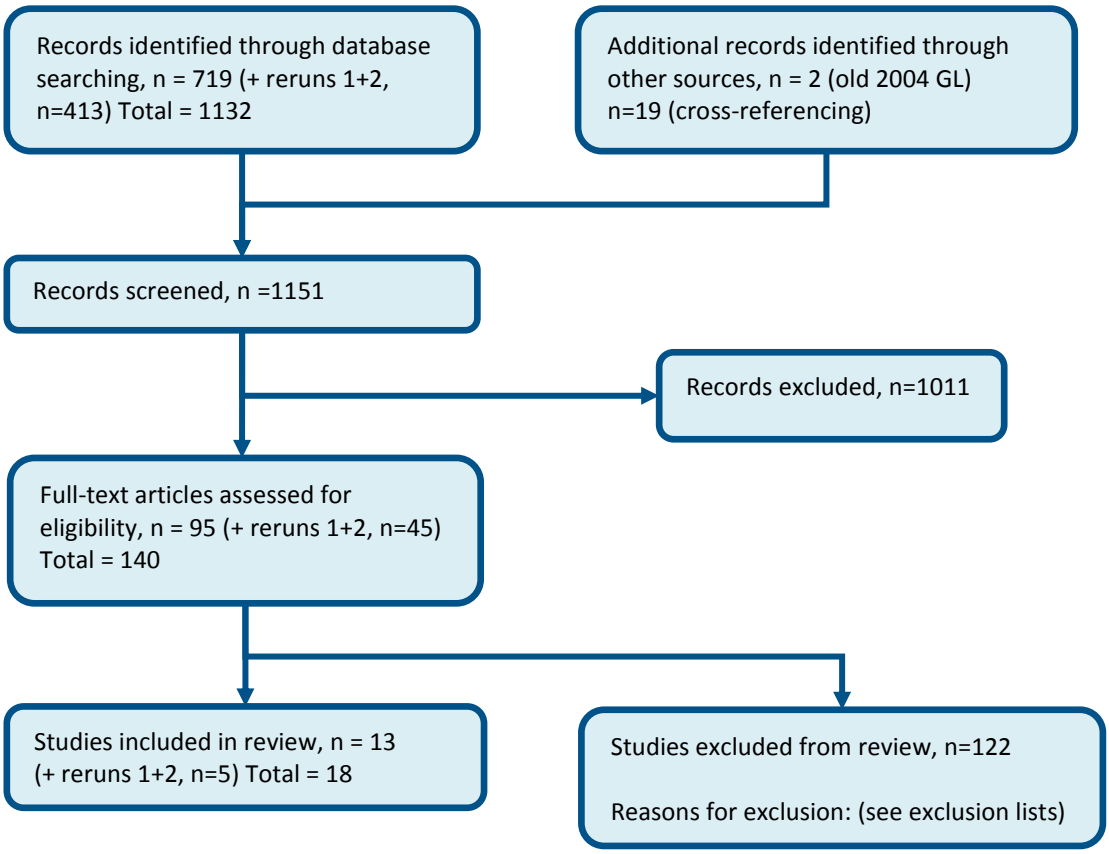


Figure 22: Flow chart of clinical article selection for the review of Acute painful neuropathy

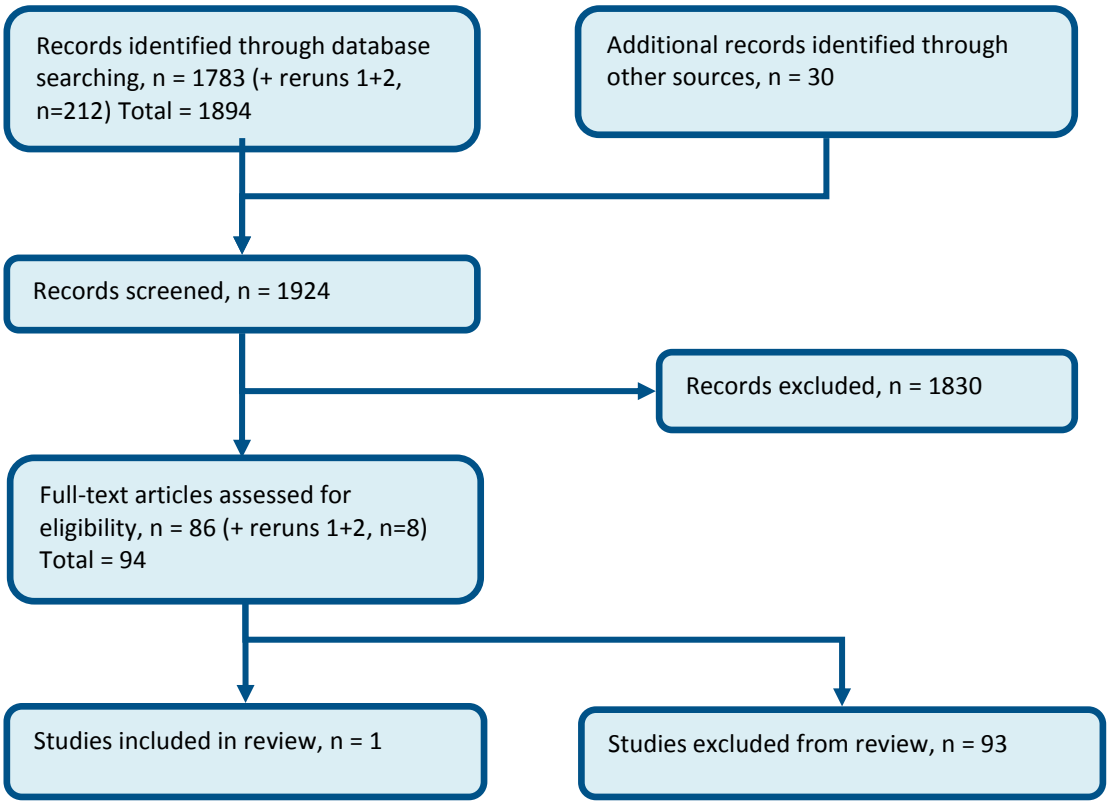
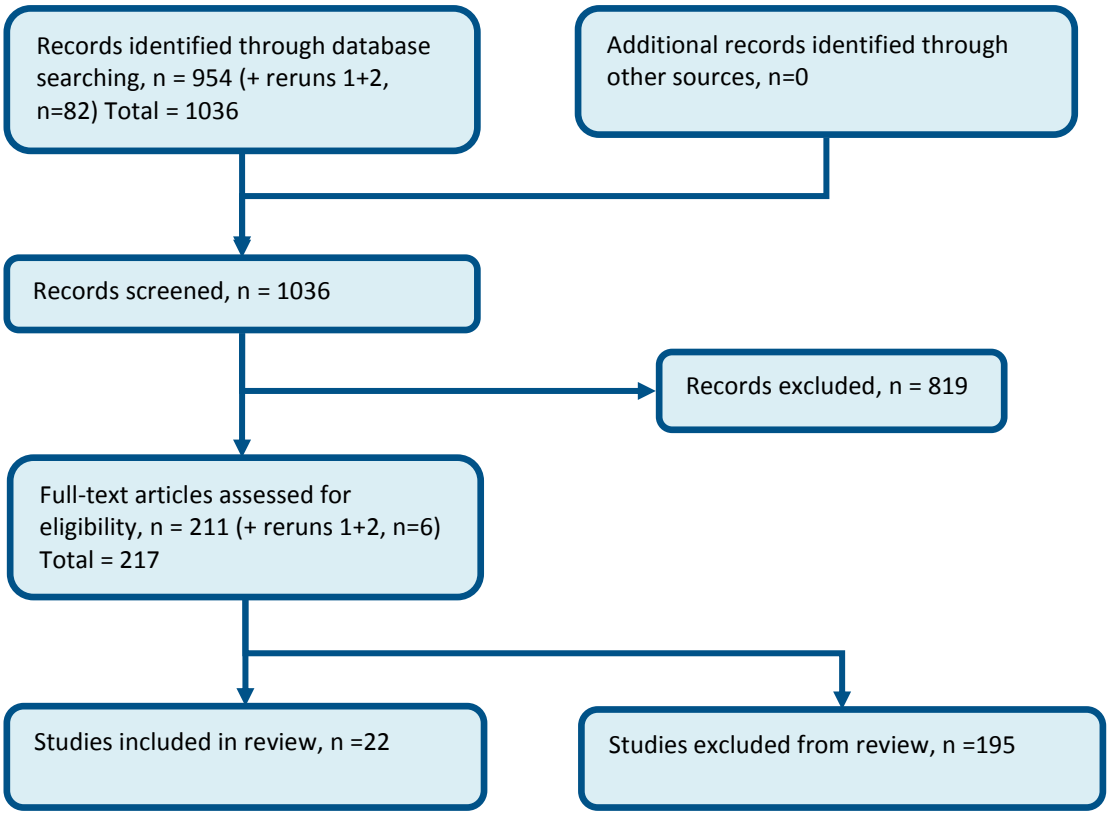
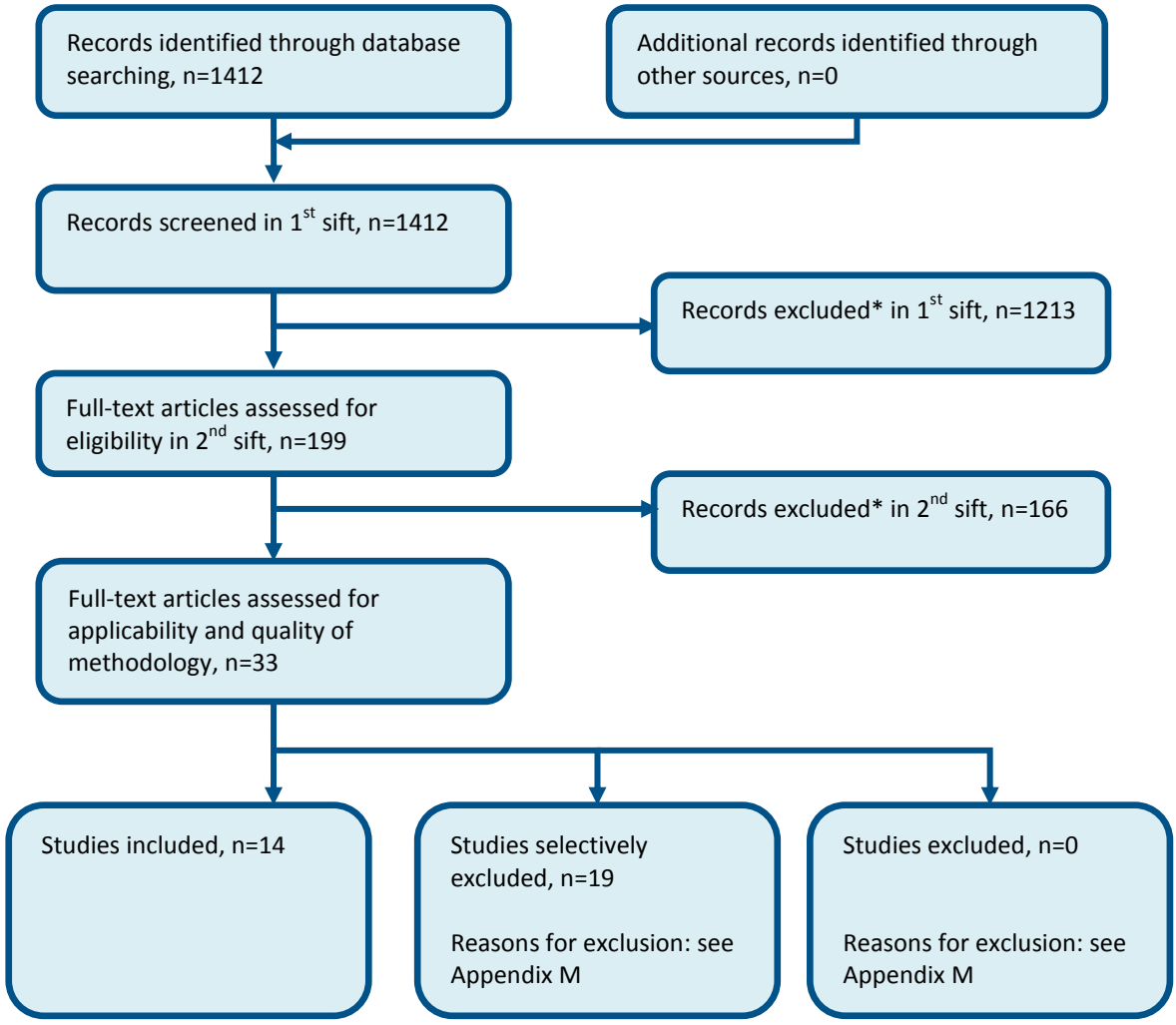


Figure 23: Flow chart of clinical article selection for the review of Thyroid disease - frequency of monitoring



Appendix E: Economic article selection

Figure 24: Flow chart of clinical article selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

Appendix F: Literature search strategies

Contents

Introduction

Search strategies used for the Type 1 Diabetes guideline update were run in accordance with the NICE Guidelines Manual 2012[1]. All searches were run up to 28 August 2014 unless otherwise stated. Any studies added to the databases after this date were not included unless specifically stated in the text. Where possible searches were limited to retrieve material published in English.

For questions not covered in the original NICE guideline the dates searched for each database were as follows in Table 1. For questions in the original guideline that were updated, searches were undertaken from 2003 onwards – the date of the last searches conducted for the original guideline. Dates searched for each question are documented in the tables under each question in section F.3.

Table 1: Database date parameters

Database	Dates searched
Medline	1946 – 28 August 2014
Embase	1980 – August 2014 (week 34)
The Cochrane Library	Cochrane Reviews to 2014 Issue 7 of 12 CENTRAL to 2014 Issue 7 of 12 DARE, HTA and NHSEED to 2013 Issue 3 of 4

Clinical searches

Searches for **clinical reviews** were run in Medline (OVID), Embase (OVID) and the Cochrane Library (Wiley). Typically, searches were constructed in the following way:

- A PICO format was used for intervention searches. **Population** (P) terms were combined with **Intervention** (I) and sometimes **Comparison** (C) terms (as indicated in the tables under each individual question in F.3). An intervention can be a drug, a procedure or a diagnostic test. **Outcomes** (O) are rarely used in search strategies for interventions. Study type filters were added where appropriate (see F.1).
- A PEO format was used for **prognosis** searches where population (P) terms were combined with exposure (E) terms and sometimes outcomes (O).

In addition to the databases outlined above, searches for the structured education question (F.3.1) were run in PsycINFO (OVID).

Economic searches

Searches for **economic evidence** were run in Medline (Ovid), Embase (Ovid), the NHS Economic Evaluations Database (NHS EED), the Health Technology Assessment (HTA) database and the Health Economic Evaluation Database (HEED). NHS EED and HTA were searched via the Cochrane (Wiley) or Centre for Reviews and Dissemination (CRD) interfaces. For Medline and Embase an economic filter (see F.1.6) was added to the standard populations (see F.2). All other searches were conducted using only population terms.

F.1 Study filter search terms

F.1.1 Systematic review (SR) search terms

Medline search terms

1.	meta-analysis/
2.	meta-analysis as topic/
3.	(meta analy* or metanaly* or metaanaly*).ti,ab.

4.	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
5.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7.	(search* adj4 literature).ab.
8.	(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.
9.	cochrane.jw.
10.	or/1-9

Embase search terms

1.	systematic review/
2.	meta-analysis/
3.	(meta analy* or metanaly* or metaanaly*).ti,ab.
4.	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
5.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7.	(search* adj4 literature).ab.
8.	(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.
9.	((pool* or combined) adj2 (data or trials or studies or results)).ab.
10.	cochrane.jw.
11.	or/1-10

F.1.2 Randomised controlled trials (RCT) search terms

Medline search terms

1.	randomized controlled trial.pt.
2.	controlled clinical trial.pt.
3.	randomi#ed.ab.
4.	placebo.ab.
5.	randomly.ab.
6.	clinical trials as topic.sh.
7.	trial*.ti.
8.	or/1-7

Embase search terms

1.	random*.ti,ab.
2.	factorial*.ti,ab.
3.	(crossover* or cross over*).ti,ab.
4.	((doubl* or singl*) adj blind*).ti,ab.
5.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
6.	crossover procedure/
7.	single blind procedure/
8.	randomized controlled trial/
9.	double blind procedure/
10.	or/1-9

F.1.3 Observational studies (OBS) search terms

Medline search terms

1.	epidemiologic studies/
2.	exp case control studies/
3.	exp cohort studies/
4.	cross-sectional studies/
5.	case control.ti,ab.
6.	(cohort adj (study or studies or analys*)).ti,ab.
7.	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
8.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab.
9.	or/1-8

Embase search terms

1.	clinical study/
2.	exp case control study/
3.	family study/
4.	longitudinal study/
5.	retrospective study/
6.	prospective study/
7.	cross-sectional study/
8.	cohort analysis/
9.	follow-up/
10.	cohort*.ti,ab.
11.	9 and 10
12.	case control.ti,ab.
13.	(cohort adj (study or studies or analys*)).ti,ab.
14.	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
15.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab.
16.	or/1-8,11-15

F.1.4 Cohort studies search terms

Medline search terms

1.	exp cohort studies/
2.	cross-sectional studies/
3.	retrospective studies/
4.	((prospective or cross sectional or retrospective or follow up or longitudinal or comparative) and (study or studies or review or analys*)).ti,ab.
5.	comparative study.pt.
6.	(cohort* or participant*).ti,ab.
7.	or/1-6

Embase search terms

1.	comparative study/
2.	longitudinal study/
3.	prospective study/
4.	cross-sectional study/
5.	retrospective study/
6.	cohort analysis/
7.	((prospective or retrospective or cross sectional or follow up or longitudinal or comparative) and (study or studies or review or analys*)).ti,ab.
8.	(cohort* or participant*).ti,ab.
9.	or/1-8

Cochrane search terms

#1.	MeSH descriptor: [cohort studies] explode all trees
#2.	MeSH descriptor: [cross-sectional studies] this term only
#3.	((prospective or retrospective or “cross sectional” or “follow up” or longitudinal or comparative) and (study or studies or review or analys*)):ti,ab
#4.	comparative study:pt
#5.	(cohort* or participant*):ti,ab
#6.	#1 or #2 or #3 or #4 or #5

F.1.5 Prognostic (PROG) studies search terms

Medline search terms

1.	predict.ti.
2.	(validat* or rule*).ti,ab.
3.	(predict* and (outcome* or risk* or model*)).ti,ab.
4.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
5.	decision*.ti,ab. and logistic models/
6.	(decision* and (model* or clinical*)).ti,ab.
7.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
8.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or auc or calibration or indices or algorithm or multivariable).ti,ab.
9.	roc curve/
10.	or/1-9

Embase search terms

1.	predict.ti.
2.	(validat* or rule*).ti,ab.
3.	(predict* and (outcome* or risk* or model*)).ti,ab.
4.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
5.	decision*.ti,ab. and statistical model/
6.	(decision* and (model* or clinical*)).ti,ab.
7.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
8.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or auc or

	calibration or indices or algorithm or multivariable).ti,ab.
9.	receiver operating characteristic/
10.	or/1-9

F.1.6 Health economic (ECON) search terms

Medline search terms

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

Embase search terms

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

F.1.7 Quality of life (QoL) search terms

Medline search terms

1.	quality-adjusted life years/
2.	sickness impact profile/
3.	(quality adj2 (wellbeing or well being)).ti,ab.
4.	sickness impact profile.ti,ab.
5.	disability adjusted life.ti,ab.
6.	(qal* or qtime* or qwb* or daly*).ti,ab.
7.	(euroqol* or eq5d* or eq 5d*).ti,ab.
8.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
9.	(health utility* or utility score* or disutilit*).ti,ab.
10.	(hui or hui1 or hui2 or hui3).ti,ab.
11.	health* year* equivalent*.ti,ab.
12.	(hye or hyes).ti,ab.
13.	rosser.ti,ab.
14.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
15.	(sf36 or sf 36 or short form 36 or shortform 36 or shortform36).ti,ab.
16.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
17.	(sf12 or sf 12 or short form 12 or shortform 12 or shortform12).ti,ab.
18.	(sf8 or sf 8 or short form 8 or shortform 8 or shortform8).ti,ab.
19.	(sf6 or sf 6 or short form 6 or shortform 6 or shortform6).ti,ab.
20.	or/1-20

Embase search terms

1.	quality adjusted life year/
2.	"quality of life index"/
3.	short form 12/ or short form 20/ or short form 36/ or short form 8/
4.	sickness impact profile/
5.	(quality adj2 (wellbeing or well being)).ti,ab.
6.	sickness impact profile.ti,ab.
7.	disability adjusted life.ti,ab.
8.	(qal* or qtime* or qwb* or daly*).ti,ab.
9.	(euroqol* or eq5d* or eq 5d*).ti,ab.
10.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
11.	(health utility* or utility score* or disutilit*).ti,ab.
12.	(hui or hui1 or hui2 or hui3).ti,ab.
13.	health* year* equivalent*.ti,ab.
14.	(hye or hyes).ti,ab.
15.	rosser.ti,ab.
16.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
17.	(sf36 or sf 36 or short form 36 or shortform 36 or shortform36).ti,ab.
18.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
19.	(sf12 or sf 12 or short form 12 or shortform 12 or shortform12).ti,ab.

20.	(sf8 or sf 8 or short form 8 or shortform 8 or shortform8).ti,ab.
21.	(sf6 or sf 6 or short form 6 or shortform 6 or shortform6).ti,ab.
22.	or/1-21

F.2 Population search strategies

Medline search terms

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.ti,ab.
6.	(diabet* adj2 (brittle or labile)).ti,ab.
7.	(diabet* adj2 (sudden 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.	(diabet* adj3 (type 2 or type ii)).ti.
13.	11 not 12
14.	or/1-10,13
15.	((children or adolescen* or school* or infant* or teenage* or paediatric* or pediatric*) not (adult* or onset)).ti.
16.	(pregnan* or gestation*).ti.
17.	14 not (15 or 16)
18.	letter/
19.	editorial/
20.	news/
21.	exp historical article/
22.	anecdotes as topic/
23.	comment/
24.	case report/
25.	(letter or comment*).ti.
26.	or/18-25
27.	26 not (randomized controlled trial/ or random*.ti,ab.)
28.	animals/ not humans/
29.	exp animals, laboratory/
30.	exp animal experimentation/
31.	exp models, animal/
32.	exp rodentia/
33.	(rat or rats or mouse or mice).ti.
34.	or/27-33
35.	17 not 34

Embase 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.ti,ab.
7.	(diabet* adj2 (brittle or labile)).ti,ab.
8.	(diabet* adj2 (sudden 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.	(diabet* adj3 (type 2 or type ii)).ti.
14.	12 not 13
15.	or/1-11,14
16.	((children or adolescen* or school* or infant* or teenage* or paediatric* or pediatric*) not (adult* or onset)).ti.
17.	(pregnan* or gestation*).ti.
18.	15 not (16 or 17)
19.	letter.pt. or letter/
20.	note.pt.
21.	editorial.pt.
22.	case report/ or case study/
23.	(letter or comment*).ti.
24.	or/19-23
25.	24 not (randomized controlled trial/ or random*.ti,ab.)
26.	animal/ not human/
27.	nonhuman/
28.	exp animal experiment/
29.	exp experimental animal/
30.	animal model/
31.	exp rodent/
32.	(rat or rats or mouse or mice).ti.
33.	or/25-32
34.	18 not 33

Cochrane 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.	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #10)
#12.	"diabetes mellitus":ti
#13.	(diabet* near/3 ("type 2" or "type ii")):ti
#14.	(#12 and not #13)
#15.	(#11 or #14)
#16.	((children or adolescen* or school* or infant* or teenage* or paediatric* or pediatric*) not (adult* or onset)):ti
#17.	(#15 and not #16)
#18.	(pregnan* or gestation*):ti
#19.	(#17 and not #18)

PsycINFO search terms

1.	((diabet* or dm) adj4 (type 1 or type1 or type i or type one)).ti,ab.
2.	(diabet* adj2 (autoimmun* or auto immun*)).ti,ab.
3.	lada.ti,ab.
4.	(diabet* adj2 (brittle or labile)).ti,ab.
5.	(diabet* adj2 (sudden onset or juvenile or childhood)).ti,ab.
6.	(diabet* adj3 (keto* or acido* or gastropare*)).ti,ab.
7.	(dm1 or iddm or t1d* or dka).ti,ab.
8.	((diabet* adj2 (insulin depend* or insulin deficien*)) not non insulin depend*).ti,ab.
9.	diabetes mellitus.ti.
10.	(diabet* adj3 (type 2 or type ii)).ti.
11.	9 not 10
12.	or/1-8,11
13.	((children or adolescen* or school* or infant* or teenage* or paediatric* or pediatric*) not (adult* or onset)).ti.
14.	12 not 13

F.3 Searches for specific questions

F.3.1 Differential diagnosis

For the following question a broad diabetes population was used, hence the searches for this question are reproduced in full below.

1. In adults and young people with diabetes, what is the best marker (c-peptides plus or minus antibodies) to distinguish between type 1 diabetes, type 2 diabetes and other forms of diabetes?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 or type 2 diabetes	Markers	The following filters were used in Medline and Embase only: RCTs or SRs or cohort studies [Medline and Embase only]	2003 - 28 August 2014 [see Table 1]

Medline search terms

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.	c-peptide/
34.	*autoantibodies/
35.	glutamate decarboxylase/
36.	insulinoma/
37.	glucose-6-phosphatase/
38.	c peptide*.ti,ab.
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/33-42
44.	32 and 43
45.	(diagnos* or screen* or test*).ti,ab,hw.
46.	exp "sensitivity and specificity"/

47.	roc curve/
48.	area under curve/
49.	proportional hazards models/
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/46-55
56.	44 and 55

Embase 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 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.	c peptide/
33.	glutamate decarboxylase 65 antibody/

34.	insulinoma/
35.	*autoantibody/
36.	glucose 6 phosphatase/
37.	((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod*or autoantibod*)).ti,ab.
38.	zinc transporter 8.ti,ab.
39.	(islet adj5 (phosphatase or catalytic)).ti,ab.
40.	(igrp* or ica* or ia-2* or ia2* or znt8* or gad*).ti,ab.
41.	or/32-40
42.	31 and 41
43.	(diagnos* or screen* or test*).ti,ab,hw.
44.	exp "sensitivity and specificity"/
45.	receiver operating characteristic/
46.	area under the curve/
47.	proportional hazards model/
48.	(roc or auc or (area and curve)).ti,ab.
49.	(sensitivity or specificity).ti,ab.
50.	gold standard.ab.
51.	(predictive value* or ppv or npv).ti,ab.
52.	likelihood ratio*.ti,ab.
53.	or/45-54
54.	42 and 53

Cochrane 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.	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.	#37 and #26

F.3.2 Structured education programmes

2. In adults with type 1 diabetes, what is the most effective structured education programme?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	Structured education programme	The following filters were used in Medline and Embase only: RCT, SR	2003 – 28 August 2014 [see Table 1]

Medline search terms

1.	self care/
2.	patient education as topic/
3.	(self adj (manage* or care or regulat* or monitor*)).ti.
4.	(educat* or learn* or teach* or train* or program* or dafne).ti.
5.	((train* or teach* or educat* or psycho*) and (model* or program* or structured or intervention* or support or diet* or eat*)).ab.
6.	or/1-5

Embase search terms

1.	patient education/
2.	self care/
3.	education program/
4.	eating/
5.	education/
6.	learning/
7.	diabetes education/
8.	(self adj (manage* or care or regulat* or monitor*)).ti.
9.	(educat* or learn* or teach* or train* or program* or dafne).ti.

10.	((train* or teach* or educat* or psycho*) and (model* or program* or structured or intervention* or support or diet* or eat*)).ab.
11.	or/1-10

PsycINFO search terms

1.	health education/
2.	client education/
3.	self management/
4.	educational programs/
5.	individual education programs/
6.	(self adj (manage* or care or regulat* or monitor*)).ti.
7.	(educat* or learn* or teach* or train* or program* or dafne).ti.
8.	((train* or teach* or educat* or psycho*) and (model* or program* or structured or intervention* or support or diet* or eat*)).ab.
9.	or/1-8

Cochrane search terms

#1.	MeSH descriptor patient education as topic, this term only
#2.	MeSH descriptor self care, this term only
#3.	(self next (manage* or care or regulat* or monitor*)):ti
#4.	(educat* or learn* or teach* or train* or program* or dafne):ti
#5.	((train* or teach* or educat* or psycho*) and (model* or program* or structured or intervention* or support or diet* or eat*)):ab
#6.	(#1 or #2 or #3 or #4 or #5)

F.3.3 Carbohydrates

3. In adults with type 1 diabetes, what is the clinical and cost-effectiveness of carbohydrate counting/restriction for optimal diabetic control?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	Carbohydrates	The following filters were used in Medline and Embase only: RCTs or SRs or cohort studies [Medline and Embase only]	All available dates [see Table 1]

Medline search terms

1.	(carb or carbs or carbohydrate*).ti,ab,hw.

Embase search terms

1.	(carb or carbs or carbohydrate*).ti,ab,hw.

Cochrane search terms

#1.	(carb or carbs or carbohydrate*):ti,ab,kw

F.3.4 Diet

4. In adults with type 1 diabetes, what is the clinical and cost-effectiveness of a diet based on the glycaemic index for optimal diabetic control?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	High glycaemic index diet	The following filters were used in Medline and Embase only: RCTs or SRs.	All available dates [see Table 1]

Medline search terms

1.	glycemic index/
2.	exp dietary carbohydrates/
3.	(glyc?emic index or gi).ti,ab.
4.	((carbohydrate? or cho) adj3 (count* or quant* or exchang* or diet* or intake)).ti,ab.
5.	chox.ti,ab.
6.	or/1-6

Embase search terms

1.	glycemic index/
2.	exp dietary carbohydrates/
3.	(glyc?emic index or gi).ti,ab.
4.	((carbohydrate? or cho) adj3 (count* or quant* or exchang* or diet* or intake)).ti,ab.
5.	chox.ti,ab.
6.	or/1-6

Cochrane search terms

#1.	MeSH descriptor: [Glycemic Index] this term only
#2.	MeSH descriptor: [Dietary Carbohydrates] explode all trees
#3.	(glyc?emic index or GI):ti,ab,kw
#4.	((carbohydrate? or CHO) near/3 (count* or quant* or exchang* or diet* or intake)):ti,ab,kw
#5.	chox:ti,ab
#6.	{or #1-#5}

F.3.5 HbA1c

The same search strategy was used for the following two questions.

5. In adults with type 1 diabetes, what is the optimum target HbA1c level that should be achieved to reduce the risk of complications?
6. In adults with type 1 diabetes, what is optimum frequency of HbA1c monitoring for effective diabetic control?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	HbA1c	The following filters were used in Medline and Embase only: RCTs or SRs or observational studies or prognostic studies [Medline and Embase only]	All available dates [see Table 1]

Medline search terms

1.	*hemoglobin a, glycosylated/

2.	time factors/
3.	1 and 2
4.	((HbA1c or hba or ghb or hbaic or a1c or hba1) adj3 (target* or profile* or goal* or timing or time* or frequency or frequent* or regularity or regular* or rate or control* or optimal or optimum or level or levels or concentration* or lower* or rais* or change* or higher or association* or recorded or decreas* or model* or control)).ti,ab.
5.	((glycosylated or glycated or glycoslated) adj3 (haemoglobin or hemoglobin) adj3 (target* or profile* or goal* or timing or time* or frequency or frequent* or regularity or regular* or rate or control* or optimal or optimum or level or levels or concentration* or lower* or rais* or change* or higher or association* or recorded or decreas* or model* or control)).ti,ab.
6.	or/4-5
7.	(HbA1c or hba or ghb or hbaic or a1c or hba1).ti,ab.
8.	((glycosylated or glycated or glycoslated) adj3 (haemoglobin or hemoglobin)).ti,ab.
9.	or/7-8
10.	((timing or time* or frequency or frequent* or regularity or regular* or rate) adj3 (monitor* or test* or check*)).ti,ab.
11.	9 and 10
12.	3 or 6 or 11

Embase search terms

1.	*glycosylated hemoglobin/
2.	time/
3.	1 and 2
4.	((HbA1c or hba or ghb or hbaic or a1c or hba1) adj3 (target* or profile* or goal* or timing or time* or frequency or frequent* or regularity or regular* or rate or control* or optimal or optimum or level or levels or concentration* or lower* or rais* or change* or higher or association* or recorded or decreas* or model* or control)).ti,ab.
5.	((glycosylated or glycated or glycoslated) adj3 (haemoglobin or hemoglobin) adj3 (target* or profile* or goal* or timing or time* or frequency or frequent* or regularity or regular* or rate or control* or optimal or optimum or level or levels or concentration* or lower* or rais* or change* or higher or association* or recorded or decreas* or model* or control)).ti,ab.
6.	or/4-5
7.	(HbA1c or hba or ghb or hbaic or a1c or hba1).ti,ab.
8.	((glycosylated or glycated or glycoslated) adj3 (haemoglobin or hemoglobin)).ti,ab.
9.	or/7-8
10.	((timing or time* or frequency or frequent* or regularity or regular* or rate) adj3 (monitor* or test* or check*)).ti,ab.
11.	9 and 10
12.	3 or 6 or 11

Cochrane search terms

#1.	MeSH descriptor: [hemoglobin a, glycosylated] this term only
#2.	MeSH descriptor: [time factors] this term only
#3.	#1 and #2
#4.	((HbA1c or hba or ghb or hbaic or a1c or hba1) near/3 (target* or profile* or goal* or timing or time* or frequency or frequent* or regularity or regular* or rate or control* or optimal or optimum or level or levels or concentration* or lower* or rais* or change* or higher or association* or recorded or decreas* or model* or control)):ti,ab,kw
#5.	((glycosylated or glycated or glycoslated) near/3 (haemoglobin or hemoglobin) near/3 (target* or profile* or goal* or timing or time* or frequency or frequent* or regularity or regular* or

	rate or control* or optimal or optimum or level or levels or concentration* or lower* or rais* or change* or higher or association* or recorded or decreas* or model* or control)):ti,ab,kw
#6.	{or #4-#5}
#7.	(HbA1c or hba or ghb or hbaic or a1c or hba1):ti,ab,kw
#8.	((glycosylated or glycated or glycoslated) near/3 (haemoglobin or hemoglobin)):ti,ab,kw
#9.	{or #7-#8}
#10.	((timing or time* or frequency or frequent* or regularity or regular* or rate) near/3 (monitor* or test* or check*)):ti,ab,kw
#11.	#9 and #10
#12.	#3 or #6 or #11

F.3.6 Self-monitoring of blood glucose (SMBG)

The same search strategy was used for the following two questions.

7. In adults with type 1 diabetes, what is optimum timing and frequency to self-monitor blood glucose for effective diabetic control?
8. In adults with type 1 diabetes, what is the optimum glucose target/profile for self-monitoring of blood glucose for effective diabetic control?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	Self-monitoring of blood glucose	None	All available dates [see Table 1]

Medline search terms

1.	blood glucose/ or (blood adj glucose*).ti,ab. or (blood adj sugar*).ti,ab.
2.	self monitor*.ti,ab.
3.	1 and 2
4.	blood glucose self-monitoring/
5.	((home or self) adj6 (blood or glucose) adj6 (monitor* or test*)).ti,ab.
6.	(hmbg* or smbg*).ti,ab.
7.	((glyc?emic or glucose) adj2 (target* or profile*)).ti,ab.
8.	or/4-7
9.	3 or 8

Embase search terms

1.	*glucose blood level/ or (blood adj glucose*).ti,ab. or (blood adj sugar*).ti,ab.
2.	self monitor*.ti,ab.
3.	1 or 2
4.	*blood glucose monitoring/
5.	((home or self) adj6 (blood or glucose) adj6 (monitor* or test*)).ti,ab.
6.	(smbg* or hmbg*).ti,ab.
7.	((glyc?emic or glucose) adj4 (target* or profile*)).ti,ab.
8.	or/4-7
9.	3 or 8

Cochrane search terms

#1.	MeSH descriptor: [blood glucose] this term only
#2.	(blood near/1 glucose*):ti,ab,kw

#3.	(blood near/1 sugar*):ti,ab,kw
#4.	{or #1-#3}
#5.	self monitor*:ti,ab,kw
#6.	#4 and #5
#7.	MeSH descriptor: [blood glucose self-monitoring] this term only
#8.	((home or self) near/6 (blood or glucose) near/6 (monitor* or test*)):ti,ab,kw
#9.	(smbg* or hmbg*):ti,ab,kw
#10.	((glycaemic or glycemic or glucose) near/4 (target* or profile*)):ti,ab,kw
#11.	{or #7-#10}
#12.	#6 or #11

F.3.7 Glucose monitoring

The same search strategy was used for the following three questions.

9. In adults with type 1 diabetes, is retrospective continuous glucose monitoring more effective than care without continuous glucose monitoring (with SMBG) for improving diabetic control?
10. In adults with type 1 diabetes, is real-time continuous glucose monitoring more effective than SMBG continuous glucose monitoring for optimum diabetic control?
11. In adults with type 1 diabetes, is continuous real-time monitoring more effective than intermittent real-time monitoring for optimum diabetic control?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	Glucose monitoring	The following filters were used in Medline and Embase only: RCTs or SRs or cohort studies [Medline and Embase only]	2003 - 28 August 2014 [see Table 1]

Medline search terms

1.	blood glucose self-monitoring/
2.	((glucose or continuous or real time or intermittent or retrospective) and monitor*).ti.
3.	((glucose or continuous or real time or intermittent or retrospective) adj5 (monitor* or measure*)).ab.
4.	(cgm* or bgm* or smbg*).ti,ab.
5.	*hemoglobin a, glycosylated/ and monitor*.ti,ab.
6.	or/1-5

Embase search terms

1.	blood glucose monitoring/
2.	blood glucose meter/
3.	((glucose or continuous or real time or intermittent or retrospective) and monitor*).ti.
4.	((glucose or continuous or real time or intermittent or retrospective) adj5 (monitor* or measure*)).ab.
5.	(cgm* or bgm* or smbg*).ti,ab.
6.	*glycosylated hemoglobin/ and monitor*.ti,ab.
7.	or/1-6

Cochrane search terms

#1.	MeSH descriptor: [blood glucose self-monitoring] explode all trees
#2.	((glucose or continuous or "real time" or intermittent or retrospective) and monitor*):ti
#3.	((glucose or continuous or “real time” or intermittent or retrospective) near/5 (monitor* or measure*)):ab
#4.	(cgm* or bgm* or smbg*):ti,ab
#5.	#1 or #2 or #3 or #4

F.3.8 Technologies

12. In adults with type 1 diabetes, what are the benefits of technologies (bolus calculators and downloads) for self-monitoring of blood glucose?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	Technologies	None	All available dates [see Table 1]

Medline search terms

1.	blood glucose self-monitoring/
2.	((blood or glucose or glycemic or sugar) adj6 (manage* or monitor* or test* or target* or control*)).ti,ab.
3.	(home or self).ti,ab.
4.	2 and 3
5.	(hmbg* or smbg* or finger prick*).ti,ab.
6.	or/1,4-5
7.	((new* or recent* or edge or latest or state or mobile or emerg* or innovat*) adj3 technolog*).ti,ab.
8.	application*.ti,ab.
9.	(in check or dafne online or on track or tracker or easy diabetes or ration wizard or calorie counter or diabetes self-management or diabetes diary or diabetes manager or diabetes planner or diabetes log* or glucose companion or diabetes companion or diabetes pilot or diabetes management system or diabetes recorder or bg monitor or my diabetes).ti,ab.
10.	or/7-9
11.	6 and 10
12.	patient-centered care/mt
13.	(smart phone* or smartphone* or iphone* or android or app or apps or mobile phone* or cell phone*).ti,ab.
14.	download*.ti,ab.
15.	cellular phone/
16.	((bolus or insulin dose) adj3 (calculator* or wizard*)).ti,ab.
17.	(carbs adj2 cals).ti,ab.
18.	(glucose buddy or insulin dose calculator pro or ibgstar or mysugr or tactiohealth or diamedic or rapidcalc or diappbetes or diabetes gps or healthsome g for glucose or bant or betabetes or ontrack or glucool diabetes or sidiary or dialog or ifora or glucatrends or d sharp or diabetical or glucowave or track3).ti,ab.
19.	or/12-18
20.	11 or 19

Embase search terms

1.	*blood glucose monitoring/

2.	((blood or glucose or glycemic or sugar) adj6 (manage* or monitor* or test* or target* or control*)).ti,ab.
3.	(home or self).ti,ab.
4.	2 and 3
5.	(hmbg* or smbg* or finger prick*).ti,ab.
6.	or/1,4-5
7.	((new* or recent* or edge or latest or state or mobile or emerg* or innovat*) adj3 technolog*).ti,ab.
8.	application*.ti,ab.
9.	(in check or dafne online or on track or tracker or easy diabetes or ration wizard or calorie counter or diabetes self-management or diabetes diary or diabetes manager or diabetes planner or diabetes log* or glucose companion or diabetes companion or diabetes pilot or diabetes management system or diabetes recorder or bg monitor or my diabetes).ti,ab.
10.	or/7-9
11.	6 and 10
12.	(smart phone* or smartphone* or iphone* or android or app or apps or mobile phone* or cell phone*).ti,ab.
13.	download*.ti,ab.
14.	mobile phone/
15.	((bolus or insulin dose) adj3 (calculator* or wizard*)).ti,ab.
16.	(glucose buddy or insulin dose calculator pro or ibgstar or mysugr or tactiohealth or diamedic or rapidcalc or diappbetes or diabetes gps or healthsome g for glucose or bant or betabetes or ontrack or glucool diabetes or sidiary or dialog or ifora or glucatrends or d sharp or diabetical or glucowave or track3).ti,ab.
17.	(carbs adj2 cals).ti,ab.
18.	or/12-17
19.	11 or 18

Cochrane search terms

#1.	MeSH descriptor: [blood glucose self-monitoring] this term only
#2.	((blood or glucose or glycemic or sugar) near/6 (manage* or monitor* or test* or target* or control*)):ti,ab,kw
#3.	(home or self):ti,ab,kw
#4.	#2 and #3
#5.	(hmbg* or smbg* or finger prick*):ti,ab,kw
#6.	#1 or #4 or #5
#7.	((new* or recent* or edge or latest or state or mobile or emerg* or innovat*) near/3 technolog*):ti,ab,kw
#8.	application*:ti,ab,kw
#9.	(in check or dafne online or on track or tracker or easy diabetes or ration wizard or calorie counter or diabetes self-management or diabetes diary or diabetes manager or diabetes planner or diabetes log* or glucose companion or diabetes companion or diabetes pilot or diabetes management system or diabetes recorder or bg monitor or my diabetes):ti,ab,kw
#10.	{or #7-#9}
#11.	#6 and #10
#12.	(smart phone* or smartphone* or iphone* or android or app or apps or mobile phone* or cell phone*):ti,ab,kw
#13.	download*:ti,ab,kw
#14.	MeSH descriptor: [cellular phone] this term only

#15.	((bolus or insulin dose) near/3 (calculator* or wizard*)):ti,ab,kw
#16.	(carbs near/2 cals):ti,ab,kw
#17.	(glucose buddy or insulin dose calculator pro or ibgstar or mysugr or tactiohealth or diamedic or rapidcalc or diappbetes or diabetes gps or healthsome g for glucose or bant or betabetes or ontrack or glucool diabetes or sidiary or dialog or ifora or glucatrends or d sharp or diabetical or glucowave or track3):ti,ab,kw
#18.	{or #12-#17}
#19.	#11 or #18

F.3.9 Long-acting/basal insulin

The same search strategy was used for the following two questions.

13. In adults with type 1 diabetes, what are the most effective long-acting insulins (detemir versus degludec versus glargine versus NPH) for optimal diabetic control?
14. In adults with type 1 diabetes, is once daily basal insulin more effective than twice daily basal insulin for optimal diabetic control?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	Long-acting insulins	The following filters were used in Medline and Embase only: RCTs and SRs [Medline and Embase only]	2003 - 28 August 2014 [see Table 1]

Medline search terms

1.	insulin, isophane/
2.	insulin, long-acting/
3.	(detemir* or degludec* or glargine*).ti,ab.
4.	(tresiba* or lantus* or optisulin* or levemir*).ti,ab.
5.	((isofan* or isophan* or nph or protaphan* or lente) and insulin*).ti,ab.
6.	(lente adj2 (hypurin* or insulin*)).ti,ab.
7.	(protamin* and (zinc or neutral or hagedorn)).ti,ab.
8.	(insuman adj5 basal).ti,ab.
9.	(humulin* adj (i or n or r)).ti,ab.
10.	(actraphan* or berlinsulin* or insulatard* or monotard* or mixtard * or novolin* or iletin* or umuline* or orgasuline*).ti,ab.
11.	or/1-10

Embase search terms

1.	long acting insulin/
2.	insulin degludec/
3.	insulin glargine/
4.	insulin detemir/
5.	isophane insulin/
6.	(detemir* or degludec* or glargine*).ti,ab.
7.	(tresiba* or lantus* or optisulin* or levemir*).ti,ab.
8.	((isofan* or isophan* or nph or protaphan* or lente) and insulin*).ti,ab.
9.	(lente adj2 (hypurin* or insulin*)).ti,ab.

10.	(protamin* and (zinc or neutral or hagedorn)).ti,ab.
11.	(insuman* adj5 basal).ti,ab.
12.	(humulin* adj (i or n or r)).ti,ab.
13.	(actraphan* or berlinsulin* or insulatard* or monotard* or mixtard * or novolin* or iletin* or umuline* or orgasuline*).ti,ab.
14.	or/1-13

Cochrane search terms

#1.	MeSH descriptor: [insulin, long-acting] explode all trees
#2.	(detemir* or degludec* or glargine*):ti,ab
#3.	(tresiba* or lantus* or detemir* or optisulin* or levemir*):ti,ab
#4.	((isofan* or isophan* or nph or protaphan* or lente) and insulin*):ti,ab
#5.	(lente near/2 (hypurin or insulin or insulins)):ti,ab
#6.	(protamin* and (zinc or neutral or hagedorn)):ti,ab
#7.	(insuman near/5 basal):ti,ab
#8.	("humulin i" or "humulin n" or "humulin r"):ti,ab
#9.	(actraphan* or berlinsulin* or insulatard* or monotard* or mixtard * or novolin* or iletin* or umuline* or orgasuline*):ti,ab
#10.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9

F.3.10 Rapid-acting insulins

15. In adults with type 1 diabetes, which are the most effective rapid-acting insulins for meal times: analogues versus human (intermediate NPH), for optimal diabetic control?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	Rapid-acting insulins	The following filters were used in Medline and Embase only: RCTs or SRs or cohort studies [Medline and Embase only]	2003 - 28 August 2014 [see Table 1]

Medline search terms

1.	postprandial period/
2.	(prandial* or postprandial* or preprandial*).ti,ab.
3.	(meal* or premeal or postmeal).ti,ab.
4.	(lunch* or dinner* or breakfast*).ti,ab.
5.	or/1-4
6.	exp insulin,short-acting/
7.	(insulin* and (short or rapid)).ti,ab.
8.	(insulin* and (fast adj3 act*)).ti,ab.
9.	(aspart or glulisine or lispro).ti,ab.
10.	((porcine or bovine or animal or human) adj3 insulin*).ti,ab.
11.	(nph or neutral protamine hagedorn).ti,ab.
12.	or/6-11
13.	5 and 12

Embase search terms

1.	postprandial state/
2.	(prandial* or postprandial* or preprandial*).ti,ab.
3.	(meal* or premeal or postmeal).ti,ab.
4.	(lunch* or dinner* or breakfast*).ti,ab.
5.	or/1-4
6.	short acting insulin/
7.	insulin aspart/
8.	insulin glulisine/
9.	insulin lispro/
10.	(insulin* and (short or rapid)).ti,ab.
11.	(insulin* and (fast adj3 act*)).ti,ab.
12.	(aspart or glulisine or lispro).ti,ab.
13.	((porcine or bovine or animal or human) adj3 insulin*).ti,ab.
14.	(nph or neutral protamine hagedorn).ti,ab.
15.	or/6-14
16.	5 and 15

Cochrane search terms

#1.	MeSH descriptor: [postprandial period] this term only
#2.	(prandial* or postprandial* or preprandial*):ti,ab
#3.	(meal* or premeal or postmeal):ti,ab
#4.	(lunch* or dinner* or breakfast*):ti,ab
#5.	#1 or #2 or #3 or #4
#6.	MeSH descriptor: [insulin, short-acting] explode all trees
#7.	(insulin* and (short or rapid)):ti,ab
#8.	(insulin* and (fast near/3 act*)):ti,ab
#9.	(aspart or glulisine or lispro):ti,ab
#10.	((porcine or bovine or animal or human) near/3 insulin*):ti,ab
#11.	(nph or “neutral protamine hagedorn”):ti,ab
#12.	#6 or #7 or #8 or #9 or #10 or #11
#13.	#5 and #12

F.3.11 Mixed insulins

16. In adults with type 1 diabetes, what are the most effective mixed insulins for optimal diabetic control?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	Mixed insulins	The following filters were used in Medline and Embase only: RCTs or SRs [Medline and Embase only]	All available dates [see Table 1]

Medline search terms

1.	biphasic insulins/
2.	((biphasic or mix* or premix*) adj4 insulin*).ti,ab.
3.	(novomix* or biasp* or iasp* or mixtard* or idegasp*).ti,ab.

4.	(degludec* adj3 aspart).ti,ab.
5.	(insuman* adj3 comb*).ti,ab.
6.	((humalog* or bd or lispro* or novolog* or aspart* or novolin* or humulin* or isophan* or nph* or neutral protamine hagedorn or glulisine or insuman*) adj4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")).ti,ab.
7.	(degludec* adj4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")).ti,ab.
8.	((tresiba* or optisulin*) adj4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")).ti,ab.
9.	((isofan* or protaphan* or lente) adj4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")).ti,ab.
10.	((isofan* or protaphan* or lente) adj4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")).ti,ab.
11.	((actraphan* or berlinsulin* or insulatard* or monotard* or iletin* or umuline* or orgasuline*) adj4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")).ti,ab.
12.	((hypurin or porcine) adj4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")).ti,ab.
13.	or/1-12

Embase search terms

1.	biphasic insulin/
2.	((biphasic or mix* or premix*) adj4 insulin*).ti,ab.
3.	(novomix* or biasp* or iasp* or mixtard* or idegasp*).ti,ab.
4.	(degludec* adj3 aspart).ti,ab.
5.	(insuman* adj3 comb*).ti,ab.
6.	((humalog* or bd or lispro* or novolog* or aspart* or novolin* or humulin* or isophan* or nph* or neutral protamine hagedorn or glulisine or insuman*) adj4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")).ti,ab.
7.	(degludec* adj4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")).ti,ab.
8.	((tresiba* or optisulin*) adj4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")).ti,ab.
9.	((isofan* or protaphan* or lente) adj4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")).ti,ab.
10.	(protamin* adj4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")).ti,ab.
11.	((actraphan* or berlinsulin* or insulatard* or monotard* or iletin* or umuline* or orgasuline*) adj4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")).ti,ab.
12.	((hypurin or porcine) adj4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")).ti,ab.
13.	or/1-12

Cochrane search terms

#1.	MeSH descriptor: [biphasic insulins] this term only
#2.	((biphasic or mix* or premix*) near/4 insulin*):ti,ab,kw
#3.	(novomix* or biasp* or iasp* or mixtard* or idegasp*):ti,ab,kw
#4.	((humalog* or lispro* or novolog* or aspart* or novolin* or humulin* or isophan* or nph* or neutral protamine hagedorn or glulisine or insuman*) near/4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")):ti,ab,kw
#5.	(degludec* near/3 aspart):ti,ab,kw
#6.	(insuman* near/3 comb*):ti,ab,kw
#7.	(degludec* near/4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")):ti,ab,kw

#8.	((tresiba* or optisulin*) near/4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")):ti,ab,kw
#9.	((isofan* or protaphan* or lente) near/4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")):ti,ab,kw
#10.	((isofan* or protaphan* or lente) near/4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")):ti,ab,kw
#11.	((actraphan* or berlinsulin* or insulatard* or monotard* or iletin* or umuline* or orgasuline*) near/4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")):ti,ab,kw
#12.	((hypurin or porcine) near/4 (mix* or premix* or biphasic or "25" or "30" or "50" or "70" or "75")):ti,ab,kw
#13.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12

F.3.12 Metformin and GLP-1 agonists

17. In adults with type 1 diabetes, are metformin (with or without insulin), or GLP1-agonists (with or without insulin) as effective as insulin alone for optimal diabetic control?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	Metformin or exenatide or liraglutide or pramlintide	The following filters were used in Medline and Embase only: RCTs or SRs [Medline and Embase only]	2003 - 28 August 2014 [see Table 1]

Medline search terms

1.	metformin/
2.	*glucagon-like peptide 1/
3.	(metformin* or exenatide* or exendin 4 or pramlintide* or liraglutide*).ti,ab.
4.	(byetta* or bydureon* or symlin* or victoza* or glucophage* or riomet* or fortamet* or glumetza* or bolamyn* or glucient* or metabet*).ti,ab.
5.	or/1-4

Embase search terms

1.	metformin/
2.	*glucagon like peptide 1/
3.	exendin 4/
4.	pramlintide/
5.	liraglutide/
6.	(metformin* or exenatide* or exendin 4 or pramlintide* or liraglutide*).ti,ab.
7.	(byetta* or bydureon* or symlin* or victoza* or glucophage* or riomet* or fortamet* or glumetza* or bolamyn* or glucient* or metabet*).ti,ab.
8.	or/1-7

Cochrane search terms

#1.	MeSH descriptor: [metformin] this term only
#2.	(metformin* or exenatide* or "exendin 4" or pramlintide* or liraglutide*):ti,ab
#3.	(byetta* or bydureon* or symlin* or victoza* or glucophage* or riomet* or fortamet* or glumetza* or bolamyn* or glucient* or metabet*):ti,ab
#4.	#1 or #2 or #3

F.3.13 Glucose injections

The same search strategy was used for the following two questions.

18.In adults with type 1 diabetes, what is the optimum needle length for insulin delivery?

19.In adults with type 1 diabetes, what is the optimum injection site and rotation for insulin delivery?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	Needles (length, site, rotation)	The following filters were used in Medline and Embase only: RCTs or SRs or cohort studies [Medline and Embase only]	2003 - 28 August 2014 [see Table 1]

Medline search terms

1.	needles/
2.	syringes/
3.	(needle* or syringe* or pen or pens or microneedle* or vial*).ti,ab.
4.	(inject* and (length or gauge* or width or technique* or site* or rotat*)).ti,ab.
5.	(autopen or clikstar or humapen or novopen or opticlik or optipen or flexpen or solostar or kwikpen or flextouch or miriopen).ti,ab.
6.	or/1-5

Embase search terms

1.	insulin pen/
2.	needle/
3.	syringe/
4.	(needle* or syringe* or pen or pens or microneedle* or vial*).ti,ab.
5.	(inject* and (length or gauge* or width or technique* or site* or rotat*)).ti,ab.
6.	(autopen or clikstar or humapen or novopen or opticlik or optipen or flexpen or solostar or kwikpen or flextouch or miriopen).ti,ab.
7.	or/1-6

Cochrane search terms

#1.	MeSH descriptor: [needles] this term only
#2.	MeSH descriptor: [syringes] this term only
#3.	(pen or pens or microneedle* or vial* or syringe* or needle*):ti,ab
#4.	(inject* and (length or gauge* or width or technique* or rotat* or site*)):ti,ab
#5.	(autopen or clikstar or humapen or novopen or opticlik or optipen or flexpen or solostar or kwikpen or flextouch or miriopen):ti,ab
#6.	#1 or #2 or #3 or #4 or #5

F.3.14 Pancreas transplantation

For the following question specific sources were used to obtain the data on referral criteria. These data sources are detailed in the review protocol in Appendix C.

20.Which adults with type 1 diabetes are most suitable to be considered for a pancreas transplant, or pancreatic islet cell transplantation?

F.3.15 Hypoglycaemic awareness

The same search strategy was used for the following two questions.

21. In adults with type 1 diabetes, how is impaired awareness of hypoglycaemia best identified and quantified?
22. In adults with type 1 diabetes and impaired awareness of hypoglycaemia, what is the most effective strategy for recovering hypoglycaemia awareness?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	Hypoglycaemic awareness	None	All available dates [see Table 1]

Medline search terms

1.	exp hypoglycemia/
2.	(hypoglycaem* or hypoglycem* or hypo glycem* or hypo glycaem*).ti,ab.
3.	(low adj3 blood adj3 (sugar or glucose)).ti,ab.
4.	((glycemic or glycaemic) adj control).ti,ab.
5.	or/1-4
6.	awareness/
7.	(aware* or unaware*).ti,ab.
8.	(symptom* adj3 (detect* or recogni*)).ti,ab.
9.	(gold or clarke or ryan or danish or pedersen or bjergaard).ti,ab.
10.	or/6-9
11.	5 and 10
12.	((glycaem* or glycem* or hypoglycem* or hypoglycaem*) adj2 (impair* or recogni* or aware* or unaware* or identif* or quantif* or problem* or autonomic or iatrogenic)).ti,ab.
13.	(iah or haaf).ti,ab.
14.	((hypo or beta or hypoglycaem* or hypoglycem*) adj3 (burden or compass or score* or scale* or method* or algorithm* or recurrent)).ti,ab.
15.	or/12-14
16.	11 or 15

Embase search terms

1.	exp hypoglycemia/
2.	(hypoglycaem* or hypoglycem* or hypo glycem* or hypo glycaem*).ti,ab.
3.	(low adj3 blood adj3 (sugar or glucose)).ti,ab.
4.	((glycemic or glycaemic) adj control).ti,ab.
5.	or/1-4
6.	awareness/
7.	(aware* or unaware*).ti,ab.
8.	(symptom* adj3 (detect* or recogni*)).ti,ab.
9.	(gold or clarke or ryan or danish or pedersen or bjergaard).ti,ab.
10.	or/6-9
11.	5 and 10
12.	((glycaem* or glycem* or hypoglycem* or hypoglycaem*) adj2 (impair* or recogni* or aware* or unaware* or identif* or quantif* or problem* or autonomic or iatrogenic)).ti,ab.
13.	(iah or haaf).ti,ab.

14.	((hypo or beta or hypoglycaem* or hypoglycem*) adj3 (burden or compass or score* or scale* or method* or algorithm* or recurrent)).ti,ab.
15.	or/12-14
16.	11 or 15

Cochrane search terms

#1.	MeSH descriptor: [hypoglycemia] explode all trees
#2.	(hypoglycaem* or hypoglycem* or hypo glycem* or hypo glycaem*):ti,ab
#3.	(low near/3 blood near/3 (sugar or glucose)):ti,ab
#4.	((glycemic or glycaemic) near/1 control):ti,ab
#5.	{or #1-#4}
#6.	MeSH descriptor: [awareness] this term only
#7.	(aware* or unaware*):ti,ab
#8.	(symptom* near/3 (detect* or recogni*)):ti,ab
#9.	(gold or clarke or ryan or danish or pedersen or bjergaard):ti,ab
#10.	{or #6-#9}
#11.	#5 and #10
#12.	((glycaem* or glycem* or hypoglycem* or hypoglycaem*) near/2 (impair* or recogni* or aware* or unaware* or identif* or quantif* or problem* or autonomic or iatrogenic)):ti,ab
#13.	(haaf or iah):ti,ab
#14.	((hypo or beta or hypoglycaem* or hypoglycem*) near/3 (burden or compass or score* or scale* or method* or algorithm* or recurrent)):ti,ab
#15.	{or #12-#14}
#16.	#11 or #15

F.3.16 Ketone monitoring

The same search strategy was used for the following two questions.

23. In adults with type 1 diabetes (including atypical ketosis-prone diabetes), does patient self-monitoring of blood (and urine) ketones reduce the incidence of diabetic ketoacidosis and hospital admissions?
24. In adults with type 1 diabetes does in-patient monitoring of blood ketones by the healthcare professional reduce the length of hospital stay, exposure to IV insulin and the development of in-hospital complications:
    a. in patients with suspected diabetic ketoacidosis?
    b. in patients admitted with diabetic ketoacidosis and/or those that get it in hospital.

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	Ketone monitoring	None	All available dates [see Table 1]

Medline search terms

1.	ketone bodies/
2.	3-hydroxybutyric acid/
3.	(hydroxybutyrate or hydroxybutyric).ti,ab.
4.	(ketone* or ketosis or ketogenesis).ti,ab.
5.	or/1-4

6.	monitoring, physiologic/
7.	blood glucose self-monitoring/
8.	point-of-care systems/
9.	predictive value of tests/
10.	"sensitivity and specificity"/
11.	exp reagent kits, diagnostic/
12.	(test* or monitor* or screen* or measure* or detect* or diagnos* or predict* or sensitivity or specificity).ti,ab.
13.	or/6-12
14.	5 and 13

Embase search terms

1.	3 hydroxybutyric acid/
2.	ketone/
3.	ketone body/
4.	ketogenesis/
5.	ketonuria/
6.	(hydroxybutyrate or hydroxybutyric).ti,ab.
7.	(ketone* or ketosis or ketogenesis).ti,ab.
8.	or/1-7
9.	patient monitoring/
10.	monitoring/
11.	blood glucose monitoring/
12.	diagnostic test accuracy study/
13.	diagnostic value/
14.	glucose blood level/
15.	predictive value/
16.	"sensitivity and specificity"/
17.	point of care testing/
18.	test strip/
19.	(test* or monitor* or screen* or measure* or detect* or diagnos* or predict* or sensitivity or specificity).ti,ab.
20.	or/9-19
21.	8 and 20

Cochrane search terms

#1.	MeSH descriptor ketone bodies, this term only
#2.	MeSH descriptor ketosis, this term only
#3.	MeSH descriptor 3-hydroxybutyric acid, this term only
#4.	(hydroxybutyrate or hydroxybutyric):ti,ab
#5.	(ketone* or ketosis or ketogenesis):ti,ab
#6.	(#1 or #2 or #3 or #4 or #5)
#7.	MeSH descriptor monitoring, physiologic, this term only
#8.	MeSH descriptor blood glucose self-monitoring, this term only
#9.	MeSH descriptor point-of-care systems, this term only
#10.	MeSH descriptor predictive value of tests, this term only

#11.	MeSH descriptor sensitivity and specificity, this term only
#12.	MeSH descriptor reagent kits, diagnostic explode all trees
#13.	(test* or monitor* or screen* or measure* or detect* or diagnos* or predict* or sensitivity or specificity):ti,ab
#14.	(#7 or #8 or #9 or #10 or #11 or #12 or #13)
#15.	(#6 and #14)

F.3.17 Aspirin for prevention of cardiovascular events

For the following question a broad diabetes population was used, hence the searches for this question are reproduced in full below.

25. In adults with type 1 diabetes, is aspirin an effective anti-platelet agent for the primary prevention of cardiovascular events?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Diabetes	Aspirin	The following filters were used in Medline and Embase only: RCTs or SRs [Medline and Embase only]	2003 - 28 August 2014 [see Table 1]

Medline search terms

1.	diabet*.ti,ab,hw.
2.	((children or adolescen* or school* or infant* or teenage* or paediatric* or pediatric*) not (adult* or onset)).ti.
3.	(pregnan* or gestation* or foot or feet or optic or eye* or retin* or ocular).ti.
4.	1 not (2 or 3)
5.	(acetylsalicylic acid or aspirin).ti,ab,hw.
6.	4 and 5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	anecdotes as topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	15 not (randomized controlled trial/ or random*.ti,ab.)
17.	animals/ not humans/
18.	exp animals, laboratory/
19.	exp animal experimentation/
20.	exp models, animal/
21.	exp rodentia/
22.	(rat or rats or mouse or mice).ti.
23.	or/16-22
24.	6 not 23

Embase search terms

1.	diabet*.ti,ab,hw.
2.	((children or adolescen* or school* or infant* or teenage* or paediatric* or pediatric*) not (adult* or onset)).ti.
3.	(pregnan* or gestation* or foot or feet or optic or eye* or retin* or ocular).ti.
4.	1 not (2 or 3)
5.	letter.pt. or letter/
6.	note.pt.
7.	editorial.pt.
8.	case report/ or case study/
9.	(letter or comment*).ti.
10.	or/5-9
11.	10 not (randomized controlled trial/ or random*.ti,ab.)
12.	animal/ not human/
13.	nonhuman/
14.	exp animal experiment/
15.	exp experimental animal/
16.	animal model/
17.	exp rodent/
18.	(rat or rats or mouse or mice).ti.
19.	or/11-18
20.	4 not 19
21.	aspirin.ti,ab,hw.
22.	*acetylsalicylic acid/
23.	20 and (21 or 22)

Cochrane search terms

#1.	MeSH descriptor diabetes mellitus explode all trees
#2.	diabet*:ti,ab
#3.	(#1 or #2)
#4.	((children or adolescen* or school* or infant* or teenage* or paediatric* or pediatric*) not (adult* or onset)):ti
#5.	(pregnan* or gestation* or foot or feet or optic or eye* or retin* or ocular):ti
#6.	(#3 and not (#4 or #5))
#7.	MeSH descriptor aspirin, this term only
#8.	("acetylsalicylic acid" or aspirin):ti,ab
#9.	(#6 and (#7 or #8))

F.3.18 IV insulin

26. In adults with type 1 diabetes who have been admitted to hospital (elective and emergency), what is the most effective intravenous insulin dose-adjustment devices and regimens for optimal diabetic control?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	IV insulin	The following filters were used in Medline	All available dates [see Table 1]

Population	Intervention	Study filter used	Date parameters
		and Embase only: RCTs or SRs or Observational studies [Medline and Embase only]	

Medline search terms

1.	exp insulins/
2.	exp administration, intravenous/
3.	1 and 2
4.	(ivit or vriii).ti,ab.
5.	((intravenous* or iv) adj6 insulin*).ti,ab.
6.	((infusion* adj6 insulin*) not subcutaneous).ti,ab.
7.	((actraphan* or aspart or berlinsulin* or biasp* or degludec* or detemir* or glargine* or glulisine or humalog* or humulin* or hypurin or iasp* or idegasp* or iletin* or insulatard* or insuman or isofan* or isophan* or lantus* or lente or levemir* or lispro or mixtard* or monotard* or novolin* or novolog* or novomix* or optisulin* or orgasuline* or protaphan* or protamin* or tresiba* or umuline*) adj6 (intravenous* or iv or infusion*)).ti,ab.
8.	or/4-7
9.	3 and 8

Embase search terms

1.	exp insulin derivative/
2.	intravenous drug administration/
3.	1 and 2
4.	exp insulin derivative/iv [intravenous drug administration]
5.	(ivit or vriii).ti,ab.
6.	((intravenous* or iv) adj6 insulin*).ti,ab.
7.	((infusion* adj6 insulin*) not subcutaneous).ti,ab.
8.	((actraphan* or aspart or berlinsulin* or biasp* or degludec* or detemir* or glargine* or glulisine or humalog* or humulin* or hypurin or iasp* or idegasp* or iletin* or insulatard* or insuman or isofan* or isophan* or lantus* or lente or levemir* or lispro or mixtard* or monotard* or novolin* or novolog* or novomix* or optisulin* or orgasuline* or protaphan* or protamin* or tresiba* or umuline*) adj6 (intravenous* or iv or infusion*)).ti,ab.
9.	or/4-8
10.	3 or 9

Cochrane search terms

#1.	MeSH descriptor: [insulins] explode all trees
#2.	MeSH descriptor: [administration, intravenous] explode all trees
#3.	#1 and #2
#4.	(ivit or vriii):ti,ab
#5.	((intravenous* or iv) near/6 insulin*):ti,ab
#6.	((infusion* near/6 insulin*) not subcutaneous):ti,ab
#7.	((actraphan* or aspart or berlinsulin* or biasp* or degludec* or detemir* or glargine* or glulisine or humalog* or humulin* or hypurin or iasp* or idegasp* or iletin* or insulatard* or insuman or isofan* or isophan* or lantus* or lente or levemir* or lispro or mixtard* or monotard* or novolin* or novolog* or novomix* or optisulin* or orgasuline* or protaphan* or protamin* or tresiba* or umuline*) near/6 (intravenous* or iv or infusion*)):ti,ab
#8.	{or #4-#7}
#9.	#3 or #8

F.3.19 Gastroparesis

For the following question a broad diabetes population was used, hence the searches for this question are reproduced in full below.

27.In adults with type 1 diabetes, what is the most effective treatment for gastroparesis?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Diabetes	Gastroparesis	The following filters were used in Medline and Embase only: RCTs, SRs and cohort studies [Medline and Embase only]	2003 - 28 August 2014 [see Table 1]

Medline search terms

1.	diabet*.ti,ab,hw.
2.	((children or adolescen* or school* or infant* or teenage* or paediatric* or pediatric*) not (adult* or onset)).ti.
3.	(pregnan* or gestation*).ti.
4.	1 not (2 or 3)
5.	letter/
6.	editorial/
7.	news/
8.	exp historical article/
9.	anecdotes as topic/
10.	comment/
11.	case report/
12.	(letter or comment*).ti.
13.	or/5-12
14.	13 not (randomized controlled trial/ or random*.ti,ab.)
15.	animals/ not humans/
16.	exp animals, laboratory/
17.	exp animal experimentation/
18.	exp models, animal/
19.	exp rodentia/
20.	(rat or rats or mouse or mice).ti.
21.	or/14-20
22.	4 not 21
23.	(gastropare* or gastropleg*).ti,ab,hw.
24.	exp gastrointestinal motility/
25.	((gastr* or stomach) adj3 (empty* or motility or dysmotility or transit or passage or aton* or pares* or paralys*)).ti,ab.
26.	or/23-25
27.	22 and 26

Embase search terms

1.	diabet*.ti,ab,hw.
2.	((children or adolescen* or school* or infant* or teenage* or paediatric* or pediatric*) not

	(adult* or onset)).ti.
3.	(pregnan* or gestation*).ti.
4.	1 not (2 or 3)
5.	letter.pt. or letter/
6.	note.pt.
7.	editorial.pt.
8.	case report/ or case study/
9.	(letter or comment*).ti.
10.	or/5-9
11.	10 not (randomized controlled trial/ or random*.ti,ab.)
12.	animal/ not human/
13.	nonhuman/
14.	exp animal experiment/
15.	exp experimental animal/
16.	animal model/
17.	exp rodent/
18.	(rat or rats or mouse or mice).ti.
19.	or/11-18
20.	4 not 19
21.	stomach emptying/
22.	stomach paresis/
23.	gastrointestinal motility/
24.	gastrointestinal transit/
25.	migrating myoelectric complex/
26.	peristalsis/
27.	(gastropare* or gastropleg*).ti,ab.
28.	((gastr* or stomach) adj3 (empty* or motility or dysmotility or transit or passage or aton* or pares* or paralys*)).ti,ab.
29.	or/21-28
30.	20 and 29

Cochrane search terms

#1.	MeSH descriptor diabetes mellitus explode all trees
#2.	diabet*:ti,ab
#3.	(#1 or #2)
#4.	((children or adolescen* or school* or infant* or teenage* or paediatric* or pediatric*) not (adult* or onset)):ti
#5.	(pregnan* or gestation*):ti
#6.	(#3 and not (#4 or #5))
#7.	MeSH descriptor gastrointestinal motility explode all trees
#8.	MeSH descriptor gastroparesis, this term only
#9.	(gastropare* or gastropleg*):ti,ab
#10.	((gastr* or stomach) near/3 (empty* or motility or dysmotility or transit or passage or aton* or pares* or paralys*)):ti,ab
#11.	(#6 and (#7 or #8 or #9 or #10))

F.3.20 Thyroid disease

28.How should adults with type 1 diabetes be monitored for thyroid disease, and how frequently?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Exposure	Study filter used	Date parameters
Type 1 diabetes	Thyroid disease	The following filters were used in Medline and Embase only: RCTs or SRs or cohort studies or prognostic [Medline and Embase only]	All available dates [see Table 1]

Medline search terms

1.	exp thyroid diseases/ not exp thyroid neoplasms/
2.	exp thyroid hormones/ or thyroid function tests/ or thyrotropin-releasing hormone/
3.	(thyroid* or hypothyroid* or hyperthyroid* or hyperthyrox* or myxedem* or myxoedem* or thyrotoxic*).ti,ab.
4.	(hashimoto* or ords or euthyroid* or grave* or nodular struma or plummer* or hashitoxicosis or goitre or goiter or thyroglossal duct*).ti,ab.
5.	(peroxidase or antithyroglobulin*).ti,ab.
6.	(protein-bound iodine or pbi).ti,ab.
7.	(thyroxine or thyrotropin or triiodothyronine or diiodothyronine or iodothyronine or dextrothyroxine or diiodotyrosine or monoiodotyrosine or iodotyrosine).ti,ab.
8.	or/1-7

Embase search terms

1.	exp thyroid disease/ not exp thyroid tumor/
2.	thyroid hormone/ or thyroid function test/ or protirelin/
3.	(thyroid* or hypothyroid* or hyperthyroid* or hyperthyrox* or myxedem* or myxoedem* or thyrotoxic*).ti,ab.
4.	(hashimoto* or ords or euthyroid* or grave* or nodular struma or plummer* or hashitoxicosis or goitre or goiter or thyroglossal duct*).ti,ab.
5.	(peroxidase or antithyroglobulin*).ti,ab.
6.	(protein-bound iodine or pbi).ti,ab.
7.	(thyroxine or thyrotropin or triiodothyronine or diiodothyronine or iodothyronine or dextrothyroxine or diiodotyrosine or monoiodotyrosine or iodotyrosine).ti,ab.
8.	or/1-7

Cochrane search terms

#1.	MeSH descriptor: [thyroid diseases] explode all trees
#2.	MeSH descriptor: [thyroid neoplasms] explode all trees
#3.	#1 not #2
#4.	MeSH descriptor: [thyroid hormones] explode all trees
#5.	MeSH descriptor: [thyroid function tests] this term only
#6.	MeSH descriptor: [thyrotropin-releasing hormone] this term only
#7.	(thyroid* or hypothyroid* or hyperthyroid* or hyperthyrox* or myxedem* or myxoedem* or thyrotoxic*):ti,ab
#8.	(hashimoto* or ords or euthyroid* or grave* or nodular struma or plummer* or hashitoxicosis or goitre or goiter or thyroglossal duct*):ti,ab
#9.	(peroxidase or antithyroglobulin*):ti,ab

#10.	(protein-bound iodine or pbi):ti,ab
#11.	(thyroxine or thyrotropin or triiodothyronine or diiodothyronine or iodothyronine or dextrothyroxine or diiodotyrosine or monoiodotyrosine or iodotyrosine):ti,ab
#12.	{or #4-#11}
#13.	#3 or #12

F.3.21 Neuropathy

29. In adults with type 1 diabetes, what is the most effective treatment for insulin-induced neuropathy?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention	Study filter used	Date parameters
Type 1 diabetes	Neuropathy	The following filters were used in Medline and Embase only: RCTs or SRs or observational studies [Medline and Embase only]	All available dates [see Table 1]

Medline search terms

1.	diabetic neuropathies/
2.	polyneuropathies/
3.	mononeuropathies/
4.	(neuropath* or polyneuropath* or mononeuropath* or neuriti* or polyneuriti* or mononeuriti*).ti,ab.
5.	third nerv*.ti,ab.
6.	((diabet* or insulin*) adj3 (amyotroph* or neuralgi*)).ti,ab.
7.	or/1-6

Embase search terms

1.	diabetic neuropathy/
2.	polyneuropathy/
3.	mononeuropathy/
4.	autonomic neuropathy/
5.	peripheral neuropathy/
6.	(neuropath* or polyneuropath* or mononeuropath* or neuriti* or polyneuriti* or mononeuriti*).ti,ab.
7.	third nerv*.ti,ab.
8.	((diabet* or insulin*) adj3 (amyotroph* or neuralgi*)).ti,ab.
9.	or/1-8

Cochrane search terms

#1.	MeSH descriptor: [diabetic neuropathies] this term only
#2.	MeSH descriptor: [polyneuropathies] this term only
#3.	MeSH descriptor: [mononeuropathies] this term only
#4.	(neuropath* or polyneuropath* or mononeuropath* or neuriti* or polyneuriti* or mononeuriti*):ti,ab
#5.	("third nerve"):ti,ab
#6.	((diabet* or insulin*) near/3 (amyotroph* or neuralgi*)):ti,ab
#7.	{or #1-#6}

F.4 Economic searches

F.4.1 Economic reviews

Economic searches were run in Medline and Embase by combining the standard population with the economic filter (F.1.6) and limiting by a date range of 2009 onwards. Economic searches were executed in the HEED and CRD (NHS EED and HTA) databases by running a population with a date limit of 2003 onwards. Search terms are given below.

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Study filter used	Date parameters
Type 1 diabetes	The following filters were used in Medline and Embase only: Economic [only Embase and Medline]	2009 – 28 August 2014 (Medline and Embase) 2003 - 28 August 2014 (NHS EED, HTA and HEED)

CRD (NHS EED, HTA) search terms

#1.	MeSH descriptor diabetes mellitus, type 1 explode all trees
#2.	MeSH descriptor diabetic ketoacidosis
#3.	(diabet*)
#4.	MeSH descriptor blood glucose
#5.	((blood near1 (glucose* or sugar)))
#6.	(((glucose or sugar or glycemic) near2 (control* or monitor* or level* or measur* or test*)))
#7.	#1 or #2 or #3 or #4 or #5 or #6

HEED search terms

1.	ax=diabet*
2.	ax=type 1
3.	ax=type i
4.	ax=insulin dependent
5.	ax=autoimmune
6.	ax=sudden onset
7.	ax=juvenile
8.	ax=childhood
9.	cs=1 and (2 or 3 or 4 or 5 or 6 or 7 or 8)

F.4.2 Quality of life reviews

Quality of life (QOL) searches were run in Medline and Embase by combining the standard population with the QOL filter (F.1.7) and limiting to a date range of 2003 onwards.

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Study filter used	Date parameters
Type 1 diabetes	The following filters were used in Medline and Embase only: QOL	2003 - 28 August 2014

References

1 National Institute for Health and Clinical Excellence. The guidelines manual. London: National Institute for Health and Clinical Excellence; 2012. Available from: http://publications.nice.org.uk/the-guidelines-manual-pmg6/