NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline

Diabetes (type 1 and type 2) in children and young people: diagnosis and management

Draft for consultation, January 2023

This guideline will update NICE guideline NG18 (published August 2015).

Who is it for?

- Healthcare professionals caring for people with diabetes
- Commissioners and providers
- Children and young people with type 1 or type 2 diabetes, and their families and carers

What does it include?

- the new recommendations
- recommendations for research
- rationale and impact sections that explain why the committee made the 2023 recommendations and how they might affect practice
- the guideline context.

Information about how the guideline was developed is on the guideline's webpage. This includes the evidence reviews, the scope, details of the committee and any declarations of interest.

New and updated recommendations

We have reviewed the evidence on pharmacological agents for improving glycaemic control in children and young people with type 2 diabetes. You are invited to comment on the new recommendations. These are marked as [**2023**].

Sections of the guideline that have had no changes at all have been temporarily removed for this consultation and will be re-instated when the final guideline is published. See the current version of the guideline.

See update information for a full explanation of what is being updated.

Full details of the evidence and the committee's discussion on the 2023 recommendations are in the evidence reviews. Evidence for the 2015 recommendations is in the full version of the 2015 guideline.

Contents

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.3 Type 2 diabetes in children and young people

Education and information

1.3.1 Offer children and young people with type 2 diabetes and their families or carers a continuing programme of education from diagnosis. Include the following core topics:

- the importance of controlling blood glucose levels, including achieving and maintaining blood glucose and HbA1c targets
- how and when to take capillary blood glucose measurements (self-monitoring)
- how diet, increasing physical activity and reducing body weight can improve and reverse type 2 diabetes
- how diet, physical activity, body weight and intercurrent illness affects blood glucose levels
- how metformin can help, and possible adverse effects
- the complications of type 2 diabetes and how to prevent them.

(2015, updated 2023)

1.3.2 Give children and young people with type 2 diabetes who are taking insulin, information and education about:

- insulin therapy (including its aims and how it works)
- insulin delivery (including rotating injection sites within the same body region)
- dosage adjustment
- the risk of hypoglycaemia
- the importance of monitoring their capillary blood glucose levels. **(2023)**

At diagnosis

1.3.21 Offer children and young people with type 2 diabetes:

- advice and support on dietary management (see recommendations 1.3.13 to 1.3.20)
- standard-release metformin monotherapy and
- equipment for capillary blood glucose monitoring (2015, updated 2023)

1.3.22 In addition, as per recommendation 1.3.21, offer children and young people with type 2 diabetes:insulin if their HbA1c level is 69 mmol/mol (8.5%) or more

- multiple daily injections of basal-bolus insulin if they have ketosis. **(2023)**

Monitoring blood glucose levels and reviewing treatment

1.3.23 Measure HbA1c levels and review in conjunction with blood glucose data from capillary blood glucose monitoring at least every 3 months, as needed, in children and young people with type 2 diabetes. **(2015, updated 2023)**

1.3.24 Adjust the frequency of capillary blood glucose monitoring based on the person's treatment and ensure they have enough test strips to do it. **(2023)**

When to reduce insulin use

1.3.25 For children and young people with type 2 diabetes who have been on insulin therapy from diagnosis, gradually reduce insulin therapy if they have achieved:

- an HbA1c level of 48 mmol/mol (6.5%) or less **or**
- a plasma glucose level of 4 to 7 mmol/litre, on 3 or more days a week, when fasting or before meals **or**
- a plasma glucose level of 5 to 9 mmol/litre, on 3 or more days a week, after meals.

See also recommendations 1.2.17 to 1.2.31 on insulin therapy. **(2023)**

Adding liraglutide or dulaglutide to metformin

1.3.26 At 4 weeks and at subsequent reviews, offer liraglutide or dulaglutide as appropriate, in addition to metformin, to children and young people aged 10 or over with type 2 diabetes, rather than insulin, if they have:

- an HbA1c level of more than 48 mmol/mol (6.5%) **or**
- a plasma glucose level of more than 7 mmol/litre, on 3 or more days a week, when fasting or before meals **or**
- a plasma glucose level of more than 9 mmol/litre, on 3 or more days a week, after meals.

In January 2023, this was an off-label use of dulaglutide. See NICE's information on prescribing medicines. **(2023)**

1.3.27 If a child or young person aged 10 or over with type 2 diabetes is already on insulin therapy but is unable to be weaned off, as per recommendation 1.3.25, offer them liraglutide or dulaglutide before increasing their insulin dose. See also recommendation 1.3.13 on dietary management.

In January 2023, this was an off-label use of dulaglutide. See NICE's information on prescribing medicines. **(2023)**

1.3.28 For children and young people aged 10 or over with type 2 diabetes who are on liraglutide or dulaglutide, maintain the lowest dose that enables them to achieve the target ranges specified in recommendation 1.3.25. **(2023)**

Metformin and insulin therapy

1.3.29 Offer insulin to children and young people with type 2 diabetes in whom an HbA1c level of 48 mmol/mol (6.5%) or less cannot be achieved using metformin and a GLP-1 agonist. **(2023)**

Changing treatments and updating healthcare plans

1.3.30 Change treatment in line with

- recommendation 1.5.4 (2015) on service provision
- the NICE guideline on shared decision making (recommendations 1.2 to 1.4). **(2023)**

1.3.31 Ensure that the paediatric diabetes team updates the child's or young person's school healthcare plan annually, and if their treatment changes. **(2023)**

For a short explanation of why the committee made these recommendations see the rationale and impact section on pharmacological agents for improving glycaemic control in children and young people with type 2 diabetes .

Full details of the of the evidence and the committee's discussion are in evidence review A: pharmacological agents for improving glycaemic control in children and young people with type 2 Diabetes

Recommendations for research

The guideline committee has made the following recommendations for research.

Key recommendations for research

1. Weekly treatment with pharmacological agents for improving glycaemic control

In children and young people with type 2 diabetes, what is the effectiveness of weekly treatment with pharmacological agents for improving glycaemic control compared to daily treatment? **(2023)**

For a short explanation of why the committee made this recommendation and how it might affect practice, see the rationale section on pharmacological agents for improving glycaemic control in children and young people with type 2 diabetes .

Full details of the evidence and the committee's discussion are in evidence review A: pharmacological agents for improving glycaemic control in children and young people with type 2 Diabetes.

2. Effectiveness of pharmacological agents used to improve glycaemic control in adults with type 2 diabetes

In children and young people with type 2 diabetes, what is the effectiveness of pharmacological agents used to improve glycaemic control in adults with type 2 diabetes? **(2023)**

For a short explanation of why the committee made this recommendation and how it might affect practice, see the rationale section on pharmacological agents for improving glycaemic control in children and young people with type 2 diabetes.

Full details of the evidence and the committee's discussion are in evidence review A: pharmacological agents for improving glycaemic control in children and young people with type 2 Diabetes

Rationale and impact

These sections briefly explain why the committee made the updated recommendations and how they might affect practice.

Pharmacological agents for improving glycaemic control in children and young people with type 2 diabetes

Recommendations 1.3.1, 1.3.2, 1.3.21 to 1.3.30.

Why the committee made the recommendations

Education and information

The committee agreed, using their knowledge and experience, that children and young people with type 2 diabetes who are on insulin – whether from diagnosis or subsequently – should be given information and education about insulin therapy (including what it is for, how it works, where to inject it, dosage adjustment, the risk of hypoglycaemia, and the importance of self-monitoring of blood glucose levels) because it is vitally important for them to understand it and be aware of the signs and symptoms of hypoglycaemia.

At diagnosis

Compared to children with type 1 diabetes, type 2 diabetes is the most aggressive type of diabetes for children and young people and is associated with the most complications at diagnosis. As a result, the committee agreed that for children and young people with type 2 diabetes, it is important to:

- achieve glycaemic control as early as possible in the treatment pathway – that is, achieve an HbA1c level of 48 mmol/mol (6.5%) or lower as early as possible in the treatment pathway – to avoid later complications (such as cardiovascular, kidney and liver disease) and
- avoid staying on the same treatment for too long without reassessing its effectiveness if that treatment does not allow the person to maintain glycaemic control.

The committee agreed that metformin should be offered at diagnosis, alongside advice and support on dietary management (see recommendations 1.3.13 to 1.3.20 and equipment for capillary blood glucose monitoring.

The committee agreed, using their knowledge and experience, that clinicians lack guidance on when to initiate insulin therapy and that two additional recommendations were needed for children and young people with type 2 diabetes and:

- an HbA1c level of 69 mmol/mol (8.5%) or higher; or
- ketosis.

In the first case, the committee agreed that a high HbA1c level at diagnosis merited the addition of insulin therapy to metformin to quickly reduce blood glucose levels to improve symptoms of hyperglycaemia and reduce the risk of developing both diabetic ketoacidosis, and in the long term, hyperglycaemia-related complications. The committee agreed that the choice of insulin therapy (for example, short-, long-, or intermediate- acting) should be left to the relevant healthcare professional to allow flexibility of treatment.

In the second case, the committee agreed that even though a child or young person may appear at diagnosis to have the symptoms of type 2 diabetes, the presence of ketosis – a metabolic state in which the body uses fat and ketones for energy rather than glucose - indicates a current insulin deficiency and an increased risk of developing diabetic ketoacidosis (see recommendations 1.4.1 to 1.4.63 [add hyperlink]). As such, it is clinically uncertain at this point in the diagnostic pathway whether they have type 2 diabetes or type 1 diabetes. The committee therefore recommended a multiple daily injection basal-bolus insulin regimen to:

- determine which type of diabetes the child or young person has (for example, if the insulin deficiency resolves after this insulin regimen, then type 2 diabetes can be confirmed), and

- ensure (as a matter of safety) that diabetic ketoacidosis does not develop.

In this context, the committee noted that in such cases a substantial proportion of these people may have their diagnosis adjusted as it becomes clear whether the insulin deficiency is temporary and not symptomatic of type 1 diabetes.

Monitoring blood glucose levels and reviewing treatment

The committee recommended, using their knowledge and experience, that children and young people with type 2 diabetes should be offered capillary blood glucose monitoring to allow them to monitor their own glucose levels (sometimes referred to as 'self-monitoring of blood glucose' [SMBG]) and plan their activities (e.g. when to eat) accordingly. They noted that some blood test meters allow people to upload their blood glucose profile data to a PC or share it online. This data can then be shared on a regular basis with the relevant healthcare professionals to enable them to make treatment recommendations in a timely manner. Furthermore, they agreed that the frequency of monitoring should be appropriate to the treatment because some (e.g. insulin) will require more frequent monitoring than others (e.g. metformin). As such, enough test strips should be prescribed to enable them to self-monitor as required by their treatment until the next review.

When to reduce insulin use and risk of hypoglycaemia

The committee recognised that insulin use substantively increases the risk of hypoglycaemia and weight gain and that it should be gradually reduced and stopped when glycaemic control is achieved. They agreed 3 criteria for when to reduce insulin use, based on those recommended for type 1 diabetes (see recommendation 1.2.55 [hyperlink to be added]).

The committee recognised that the choice of how frequently glucose levels could exceed the target ranges was somewhat arbitrary although they were keen to avoid basing decisions on single events and agreed that having high

glucose levels more often than not (e.g. four days a week) would certainly indicate that they need reducing.

Note on BMI

The committee also discussed whether BMI should be a criterion for starting pharmacological treatment – as it is for adults – but decided that this was not needed because a small proportion of children and young people with type 2 diabetes are not overweight and specifying such a criterion would exclude this group from treatment.

Assessment and review

The 2015 version of this guideline recommended that the HbA1c levels of children and young people with type 2 diabetes be measured every 3 months. In practice, this assessment is conducted as a routine outpatient appointment and may occur more often if needed. The committee agreed that this recommendation should be amended to reflect current practice to

- allow for more frequent appointments, and
- require blood glucose data (of at least the past 2 weeks) from capillary blood glucose monitoring.

More appointments may be needed to allow for follow up because some children and young people with type 2 diabetes may need closer observation (for example, they may have a high HbA1c level, or they may not self-monitor blood glucose levels or adhere to treatment). Blood glucose data, which can be downloaded from children's or young people's blood test meters, in addition to HbA1c levels, should also be reviewed at these appointments because they are both needed to determine how and whether treatment should be changed. Blood glucose data is needed because HbA1c is the average blood glucose level over the past 2 to 3 months and reliance solely on this measure would potentially delay timely intervention.

Adding liraglutide or dulaglutide to metformin

First visit after diagnosis

The committee indicated that it is standard practice to see newly-diagnosed children and young people with type 2 diabetes before the first clinical visit 3-months after diagnosis to measure HbA1c levels and review blood glucose data because they will often need more support than those who have already stabilised their glucose levels. This is particularly important for those children and young people with type 2 diabetes who present at diagnosis with either a high HbA1c level (more than 69 mmol/mol [8.5%]) or ketosis, because it provides clinicians with the opportunity to amend insulin treatment considering the results of the child or young person's capillary blood glucose monitoring. Furthermore, the committee indicated, using their knowledge and experience, that weaning off insulin can typically be achieved within 2 to 6 weeks. As such, the committee recommended that children and young people with type 2 diabetes should be seen 4 weeks after diagnosis.

Thresholds for adding liraglutide or dulaglutide to metformin

The committee chose three thresholds for when to initiate metformin therapy with liraglutide or dulaglutide at this point in the treatment pathway in children and young people with type 2 diabetes:

- an HbA1c threshold of 48 mmol/mol (6.5%); or
- a plasma glucose level of more than 7.0 mmol/litre, on 3 or more days a week, when fasting or before meals; or
- a plasma glucose level of more than 9.0 mmol/litre, on 3 or more days a week, after meals.

These thresholds reflect the chosen HbA1c threshold and upper limits of the blood glucose target ranges in recommendation 1.3.25. The committee agreed that, though their recommendation meant potentially combining a GLP-1 agonist with metformin earlier than it would be carried out for an adult, such an early intervention is justified by the relatively small number of

available treatments for the paediatric population and the risks associated with:

- not achieving an HbA1c level of 48 mmol/mol (6.5%) or lower, and
- developing complications related to diabetes.

The committee agreed that liraglutide or dulaglutide in combination with metformin should be considered in preference to insulin as treatment to improve glycaemic control in children and young people with type 2 diabetes who are aged 10 years and over, because of the risks of hypoglycaemia and weight gain associated with insulin use. The restriction to children and young people aged 10 years or over reflects the licencing conditions for liraglutide.

Similarly, for children and young people with type 2 diabetes who are already on insulin therapy but who are unable to educe and then stop insulin, the committee agreed to offer liraglutide or dulaglutide as appropriate to help achieve glycaemic control, before attempting to increase insulin dose because of the risk of hypoglycaemia and weight gain associated with the latter.

The committee also agreed that the lowest dose of liraglutide or dulaglutide needed to achieve glycaemic control should be maintained because higher doses can lead to side effects and poorer treatment adherence.

Evidence showed that liraglutide or dulaglutide in combination with metformin were effective at improving glycaemic control in children and young people with type 2 diabetes up to 26 weeks of use. There was also evidence to show this effect was maintained at 54 weeks for liraglutide although there was an increased risk of nausea and vomiting. Long term use of liraglutide was also associated with a small reduction in BMI z-score.

Dulaglutide is administered as a weekly injection, whereas liraglutide requires daily injections. The committee agreed to recommend both drugs despite the risk of nausea and vomiting with long-term use of liraglutide because some children and young people may prefer 1 treatment regime over the other.

Choosing the appropriate GLP-1 agonist

The evidence for liraglutide, which is administered as a daily subcutaneous injection, combined with metformin was limited to 1 well-reported trial. All the participants were on metformin and the short- and long-term results compared to placebo indicated that it is effective at improving glycaemic control. However, long-term results suggested an increased risk of experiencing gastrointestinal side effects (nausea and vomiting).

By contrast, although the evidence for the effectiveness of dulaglutide, which is administered as a weekly subcutaneous injection, combined with metformin was also limited to 1 trial, which only reported short-term results, only 78% of participants were on metformin. There were also some concerns about how the trial was reported with few details provided about the randomisation process and allocation concealment. Nevertheless, the short-term results compared to placebo indicated that it is likely even more effective than liraglutide in improving glycaemic control.

The committee recognised that they did not have direct evidence comparing the effectiveness of weekly treatments compared to daily treatments with glucose-lowering agents for improving glycaemic control. So, they made a research recommendation to:

- address this gap
- assess whether weekly injections could help reduce stigma and treatment burden for children and young people with type 2 diabetes.

There are a lot of medicines that can be used to improve glycaemic control in adults with type 2 diabetes. In contrast, there are very few licenced, effective, and safe medicines to improve glycaemic control for children and young people with type 2 diabetes. The committee thus made a research recommendation for further clinical trials in children and young people of drugs used for adults.

Other licensed treatments

As of January 2023, there are 2 other pharmacological agents that are licensed for use in the UK in a paediatric population:

- exenatide (a GLP-1 agonist)
- dapagliflozin (a SGLT2 inhibitor).

Evidence for the short-term effectiveness of exenatide in combination with metformin suggests that it is generally less effective at improving glycaemic control, compared to placebo, than either liraglutide or dulaglutide.

Evidence for the short-term effectiveness of dapagliflozin did not show a difference with placebo on any critical or important outcome.

The committee agreed that the evidence was not sufficient for either of these licensed medicines to be recommended.

Metformin and insulin

The committee agreed, using their knowledge and experience, that insulin should be offered to children and young people with type 2 diabetes in whom an HbA1c level of 48 mmol/mol (6.5%) cannot be achieved through dietary management and metformin in combination with either liraglutide or dulaglutide, because their glucose levels remain dangerously high and insulin is the only remaining available treatment that will help directly reduce them.

Changing treatments and updating healthcare plans

The committee used their clinical knowledge and experience to produce recommendations on changing treatment and updating healthcare plans.

Finally, the committee agreed that the paediatric diabetes team should update the child or young person's healthcare plan annually (when they move up a school year) and when any changes to treatment are agreed to enable coordination of care with the child's or young person's school.

How the recommendations might affect practice

The recommendations on capillary blood glucose monitoring and an initial review 4 weeks after diagnosis reflect current practice in England and so will have no significant impact.

Although GLP-1 agonists are relatively expensive compared to other possible treatments, the prevalence of type 2 diabetes in the paediatric population is relatively low. Therefore recommending a GLP-1 agonist is unlikely to surpass NICE's £1 million threshold for significant resource impact. Similar considerations apply to using insulin at diagnosis where the prevalence of type 2 diabetes combined with a high HbA1c level or ketones is even lower.

Increased support from a paediatric diabetic nurse and consultant will be needed when the child or young person starts on a GLP-1 agonist. However, once the child or young person's glycaemic control is stabilised, this will no longer be required because repeat prescriptions can be made by the GP.

Return to recommendations

Context

Diabetes is a long-term condition that can have a major impact on the life of a child or young person, as well as their family or carers. In addition to insulin therapy, diabetes management should include education, support and access to psychological services, as detailed in this guideline. Preparations should also be made for the transition from paediatric to adult services, which have a somewhat different model of care and evidence base.

Type 1 diabetes is becoming more common in the UK, and since 2004 type 2 diabetes is also being diagnosed with increasing frequency. The 2020/21 National Paediatric Diabetes Audit identified 29,000 children and young people with type 1 diabetes and 973 with type 2 being managed within a Paediatric Diabetes Unit.

Much of the general care for type 2 diabetes is the same as for type 1 diabetes, although the initial management is different. Being overweight or

obese when associated with type 2 diabetes brings an increased risk of renal complications and problems such as hypertension and dyslipidaemia. These differences in management and complications need guidance specific to type 2 diabetes. A variety of genetic conditions (such as maturity-onset diabetes in the young) and other conditions (such as cystic fibrosis-related diabetes) may also lead to diabetes in children and young people, but the care of these diverse conditions is beyond the scope of this guideline.

This guideline recommends attempting to reach a glycated haemoglobin (HbA1c) level near the normal range and near normoglycaemia. This is to further reduce the long-term risks associated with diabetes. Tight management may be achieved by intensive insulin management (multiple daily injections or insulin pump therapy) from diagnosis, accompanied by carbohydrate counting. Newer technology such as continuous subcutaneous glucose monitoring may also help children and young people to have better blood glucose management, although this is not currently recommended for all children and young people with type 2 diabetes.

By implementing the strict blood glucose management recommended in this guideline, improvements can be made to diabetes care that reduce the impact of the condition on the future health of children and young people.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the NICE webpage on diabetes.

For details of the guideline committee see the committee member list.

Update information

April 2023: This guideline is an update of NICE guideline NG18 (published August 2015) and will replace it. We have reviewed the evidence on pharmacological agents for improving glycaemic control in children and young people with type 2 diabetes.

Recommendations are marked **[2023]** if the evidence has been reviewed.

In recommendations shaded in grey and ending **[…amended 2023]**, we have made changes that could affect the intent without reviewing the evidence. Yellow shading is used to highlight these changes, and reasons for the changes are given in table 1.

Table 1 Recommendations that have been deleted

Recommendation in current guideline	Comment

Table 2 Amended recommendation wording (change to intent) without an evidence review

Recommendation in current guideline	Recommendation in updated guideline	Reason for change

ISBN: