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

Clinical Guideline <…>
Appendices
December 2014

Draft for Consultation
Commissioned by the National Institute for Health and Care Excellence
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## Diagnosis and management of type 1 diabetes in children and young people

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

#### A.1 Recommendations to be deleted

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

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

<table>
<thead>
<tr>
<th>Recommendation in 2004 guideline</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document. (1.1.2.5)</td>
<td>This recommendation has been deleted because the new 2015 recommendations on DKA give detailed advice on the need for referral to hospital when DKA is suspected or confirmed, and DKA is always treated in hospital.</td>
</tr>
<tr>
<td>Children and young people with type 1 diabetes should be informed that the use of multiple daily insulin injection regimens or continuous subcutaneous insulin infusion (or insulin pump therapy) will not prolong the partial remission phase, although these forms of therapy may be appropriate for optimising glycaemic control, especially in young people. (1.1.3.2)</td>
<td>Replaced by: Take into account the personal and family circumstances of the child or young person with type 1 diabetes and discuss their personal preferences with them and their family members or carers (as appropriate) when choosing an insulin regimen. (1.2.19) Offer children and young people with type 1 diabetes multiple daily insulin injection regimens from diagnosis. If a multiple daily insulin injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). (1.2.20)</td>
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</tbody>
</table>
| Children and young people with newly diagnosed type 1 diabetes should be offered a structured programme of education covering the aims of insulin therapy, delivery of insulin, self-monitoring of blood glucose, the effects of diet, physical activity and intercurrent illness on glycaemic control, and the detection and management of hypoglycaemia. (1.1.4.1) | Replaced by: Offer children and young people with type 1 diabetes and their family members or carers (as appropriate) a continuing programme of education from diagnosis. Ensure that the programme includes the following core topics: - insulin therapy, including its aims, how it works and its mode of delivery - blood glucose monitoring, including targets for blood glucose control (blood glucose and HbA1c levels) - the effects of diet, physical activity and intercurrent illness on blood glucose control - managing intercurrent illness (‘sick-day
<table>
<thead>
<tr>
<th>Recommendation in 2004 guideline</th>
<th>Comment</th>
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<tbody>
<tr>
<td><strong>Tailor the education programme to each child or young person with type 1 diabetes and their family members or carers (as appropriate), taking account of issues such as:</strong></td>
<td><strong>Tailor the education programme to each child or young person with type 1 diabetes and their family members or carers (as appropriate), taking account of issues such as:</strong></td>
</tr>
<tr>
<td>- personal preferences</td>
<td>- personal preferences</td>
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<tr>
<td>- emotional wellbeing</td>
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<td>- age and maturity</td>
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<td>- current and future social circumstances</td>
<td>- current and future social circumstances</td>
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<tr>
<td>- life goals. (1.2.1)</td>
<td>- life goals. (1.2.1)</td>
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Children and young people with type 1 diabetes and their families should be offered timely and ongoing opportunities to access information about the development, management and effects of type 1 diabetes. The information provided should be accurate and consistent and it should support informed decision-making. (1.2.1.1)

Replaced by:

Offer children and young people with type 1 diabetes and their family members or carers (as appropriate) a continuing programme of education from diagnosis. Ensure that the programme includes the following core topics:

- insulin therapy, including its aims, how it works and its mode of delivery
- blood glucose monitoring, including targets for blood glucose control (blood glucose and HbA1c levels)
- the effects of diet, physical activity and intercurrent illness on blood glucose control
- managing intercurrent illness (‘sick-day rules’, including monitoring of blood ketones [beta-hydroxybutyrate])
- detecting and managing hypoglycaemia, hyperglycaemia and ketosis. (1.2.1)

Children and young people with type 1 diabetes and their families should be offered opportunities to discuss particular issues and to ask questions at each clinic visit. (1.2.1.2)

Replaced by:

Encourage children and young people with type 1 diabetes and their family members or carers (as appropriate) to discuss any concerns or raise any questions they have with their diabetes team. (1.2.5)

The method of delivering education and content will depend on the individual and should be appropriate for the child’s or young person’s age, maturity, culture, wishes and existing knowledge within the family. (1.2.1.3)

Replaced by:

Tailor the education programme to each child or young person with type 1 diabetes and their family members or carers (as appropriate), taking account of issues such as:

- personal preferences
- emotional wellbeing
- age and maturity
- cultural considerations
- existing knowledge
<table>
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<tr>
<th>Recommendation in 2004 guideline</th>
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<tr>
<td><strong>Pre-school and primary school children with type 1 diabetes</strong> should be offered the most appropriate individualised regimens to optimise their glycaemic control. (1.2.2.1)</td>
<td>Replaced by: Offer children and young people with type 1 diabetes multiple daily insulin injection regimens from diagnosis. If a multiple daily insulin injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). (1.2.20)</td>
</tr>
<tr>
<td><strong>Young people with type 1 diabetes</strong> should be offered multiple daily injection regimens to help optimise their glycaemic control. (1.2.2.2)</td>
<td>Replaced by: Offer children and young people with type 1 diabetes multiple daily insulin injection regimens from diagnosis. If a multiple daily insulin injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). (1.2.20)</td>
</tr>
<tr>
<td>Multiple daily injection regimens should be offered only as part of a package of care that involves continuing education, dietary management, instruction on the use of insulin delivery systems and blood glucose monitoring, emotional and behavioural support, and medical, nursing and dietetic expertise in paediatric diabetes, because this improves glycaemic control. (1.2.2.3)</td>
<td>The contents of this recommendation are covered by new recommendations throughout the guideline.</td>
</tr>
<tr>
<td><strong>Children and young people using multiple daily injection regimens</strong> should be informed that they may experience an initial increase in the risk of hypoglycaemia and short-term weight gain. (1.2.2.4)</td>
<td>This recommendation has been deleted because the GDG considered that multiple daily injection regimens improve blood glucose control so reference to hypoglycaemia was no longer appropriate. The group did not identify evidence to indicate that weight gain is an important adverse event.</td>
</tr>
<tr>
<td><strong>Young people who do not achieve satisfactory glycaemic control with multiple daily injection regimens</strong> should be offered additional support and, if appropriate, alternative insulin therapy (once-, twice- or three-times daily mixed insulin regimens or continuous subcutaneous insulin infusion using an insulin pump). (1.2.2.6)</td>
<td>Replaced by: If a child or young person with type 1 diabetes does not achieve satisfactory blood glucose control:</td>
</tr>
<tr>
<td><strong>Young people with type 1 diabetes who have</strong></td>
<td>Replaced by:</td>
</tr>
<tr>
<td>Recommendation in 2004 guideline</td>
<td>Comment</td>
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<tr>
<td>difficulty adhering to multiple daily injection regimens should be offered twice-daily injection regimens. (1.2.2.7)</td>
<td>Take into account the personal and family circumstances of the child or young person with type 1 diabetes and discuss their personal preferences with them and their family members or carers (as appropriate) when choosing an insulin regimen. (1.2.19)</td>
</tr>
<tr>
<td>Offer children and young people with type 1 diabetes multiple daily insulin injection regimens from diagnosis. If a multiple daily insulin injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). (1.2.20)</td>
<td>Offer children and young people with type 1 diabetes multiple daily insulin injection regimens from diagnosis. If a multiple daily insulin injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). (1.2.20)</td>
</tr>
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</table>
| Continuous subcutaneous insulin infusion (or insulin pump therapy) is recommended as an option for people with type 1 diabetes provided that:  
  - multiple-dose insulin therapy (including, where appropriate, the use of insulin glargine) has failed; and  
  - those receiving the treatment have the commitment and competence to use the therapy effectively. (1.2.2.8) | Replaced by:  
Take into account the personal and family circumstances of the child or young person with type 1 diabetes and discuss their personal preferences with them and their family members or carers (as appropriate) when choosing an insulin regimen. (1.2.19) |
| Continuous subcutaneous insulin infusion therapy should be initiated only by a trained specialist team, which should normally comprise a physician with a specialist interest in insulin pump therapy, a diabetes specialist nurse and a dietitian. (1.2.2.9) | Replaced by:  
Offer children and young people with type 1 diabetes multiple daily insulin injection regimens from diagnosis. If a multiple daily insulin injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). (1.2.20) |
| Established users of continuous subcutaneous insulin infusion therapy should have their insulin management reviewed by their specialist team so that a decision can be made about whether a trial or a switch to multiple-dose insulin incorporating insulin glargine would be appropriate. (1.2.2.11) | Replaced by:  
Offer children and young people with type 1 diabetes multiple daily insulin injection regimens from diagnosis. If a multiple daily insulin injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). (1.2.20) |

Children and young people with type 1 diabetes

The part of the recommendation referring to
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<th>Recommendation in 2004 guideline</th>
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<tr>
<td>should be offered the most appropriate insulin preparations (rapid-acting insulin analogues, short-acting insulins, intermediate-acting insulins, long-acting insulin analogues or biphasic insulins) according to their individual needs and the instructions in the patient information leaflet supplied with the product, with the aim of obtaining an HbA1c level of less than 7.5% without frequent disabling hypoglycaemia and maximising quality of life. (1.2.3.1)</td>
<td>patient information leaflets has been deleted, as the GDG felt that healthcare professionals would be expected to take account of this information regardless. In addition, the text on HbA1c target levels has been deleted, as this is covered by the new 2015 recommendations on HbA1c target levels. The GDG considered that the remainder of the 2004 recommendation was no longer relevant. There is already a recommendation about providing rapid-acting insulin analogues from the 2004 guideline (1.2.30), and children and young people using multiple daily insulin or mixed insulin regimens would invariably receive specific preparations according their needs.</td>
</tr>
<tr>
<td><strong>Children and young people with type 1 diabetes who use insulin preparations containing intermediate-acting insulin should be informed that these preparations should be mixed before use according to the instructions in the patient information leaflet supplied with the product. (1.2.3.4)</strong></td>
<td>This recommendation has been deleted because mixing of insulins by the patient is no longer part of clinical practice.</td>
</tr>
</tbody>
</table>
| Children and young people with type 1 diabetes and their families should be informed that the target for long-term glycaemic control is an HbA1c level of less than 7.5% without frequent disabling hypoglycaemia and that their care package should be designed to attempt to achieve this.(1.2.6.1) | Replaced by: 
Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that an HbA1c target level of 48 mmol/mol (6.5%) or lower is ideal to minimise the risk of long-term complications. (1.2.68) 
Explain to children and young people with type 1 diabetes who have an HbA1c level above the ideal target of 48 mmol/mol (6.5%) and their family members or carers (as appropriate) that any reduction in HbA1c level reduces the risk of long-term complications. (1.2.69) 
Agree an individualised lowest achievable HbA1c target with each child or young person with type 1 diabetes and their family members or carers (as appropriate) to achieve and maintain their individual agreed HbA1c target level. (1.2.70) 
Support children and young people with type 1 diabetes and their family members or carers (as appropriate) to achieve and maintain their individual agreed HbA1c target level. (1.2.71) |
| Current HbA1c measurements should be made available in outpatient clinics because their availability can lead to immediate changes in insulin therapy and/or diet and so reduce the need for follow-up appointments. (1.2.6.3) | The GDG considered that this recommendation was no longer necessary because it is no longer difficult to get the results of HbA1c tests promptly in practice. |
| Children and young people with type 1 diabetes and their families should be informed that aiming to achieve low levels of HbA1c can lead to increased risks of hypoglycaemia and that high | Replaced by: 
Explain the benefits of safely achieving and maintaining the lowest attainable HbA1c to children and young people with type 1 diabetes |
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<tbody>
<tr>
<td>levels of HbA1c can lead to increased risks of long-term microvascular complications. (1.2.6.4)</td>
<td>and their family members or carers (as appropriate). (1.2.67)</td>
</tr>
<tr>
<td>Children and young people with HbA1c levels consistently above 9.5% should be offered additional support by their diabetes care teams to help them improve their glycaemic control because they are at increased risk of developing diabetic ketoacidosis and long-term complications. (1.2.6.5)</td>
<td>Replaced by: Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that an HbA1c target level of 48 mmol/mol (6.5%) or lower is ideal to minimise the risk of long-term complications. (1.2.68)</td>
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<td></td>
<td>Explain to children and young people with type 1 diabetes who have an HbA1c level above the ideal target of 48 mmol/mol (6.5%) and their family members or carers (as appropriate) that any reduction in HbA1c level reduces the risk of long-term complications. (1.2.69)</td>
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<td>Support children and young people with type 1 diabetes and their family members or carers (as appropriate) to achieve and maintain their individual agreed HbA1c target level. (1.2.71)</td>
</tr>
<tr>
<td>Children and young people with type 1 diabetes should be encouraged to use blood glucose measurements for short-term monitoring of glycaemic control because this is associated with reduced levels of glycated haemoglobin. Urine glucose monitoring is not recommended because it is less effective and is associated with lower patient satisfaction. (1.2.6.6)</td>
<td>Replaced by: Advise children and young people with type 1 diabetes and their family members or carers (as appropriate) to routinely perform at least 5 capillary blood glucose tests per day. (1.2.59)</td>
</tr>
</tbody>
</table>
| Children and young people with type 1 diabetes and their families should be informed that the optimal targets for short-term glycaemic control are a pre-prandial blood glucose level of 4–8 mmol/litre and a post-prandial blood glucose level of less than 10 mmol/litre. (1.2.6.7) | Replaced by: Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that the optimal target ranges for short-term blood glucose control are:  
  - fasting blood glucose level of 4–7 mmol/litre (or 5–7 mmol/litre for young people intending to drive the following morning)  
  - a blood glucose level of 4–7 mmol/litre before meals  
  - a blood glucose level of 5–9 mmol/litre after meals. (1.2.55)                                                                                                                 |
| Children and young people with type 1 diabetes and their families should be encouraged to perform frequent blood glucose monitoring as part of a continuing package of care that includes dietary management, continued education and regular contact with their diabetes care teams. (1.2.6.8) | Replaced by: Advise children and young people with type 1 diabetes and their family members or carers (as appropriate) to routinely perform at least 5 capillary blood glucose tests per day. (1.2.59)                                                                 |
|                                                                                                                                                 | Advise children and young people with type 1 diabetes and their family members or carers (as appropriate) that more frequent testing may be needed in some circumstances, for example during intercurrent illness. (1.2.60)                                                                 |

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| **Children and young people with type 1 diabetes who are trying to optimise their glycaemic control and/or have intercurrent illness should be encouraged to measure their blood glucose levels more than four times per day.** (1.2.6.12) | Replaced by: Advise children and young people with type 1 diabetes and their family members or carers (as appropriate) to routinely perform at least 5 capillary blood glucose tests per day. (1.2.59)  
Advise children and young people with type 1 diabetes and their family members or carers (as appropriate) that more frequent testing may be needed in some circumstances, for example during intercurrent illness. (1.2.60) |
| **Children and young people with type 1 diabetes who have persistent problems with hypoglycaemia unawareness or repeated hypoglycaemia or hyperglycaemia should be offered continuous glucose monitoring systems.** (1.2.6.14) | Replaced by: Offer ongoing unblinded ('real-time') continuous glucose monitoring with alarms to children and young people with type 1 diabetes who have:  
- frequent severe hypoglycaemia or  
- impaired awareness of hypoglycaemia associated with adverse consequences (for example, seizures or anxiety). (1.2.63)  
Consider intermittent (unblinded ['real-time'] or blinded ['retrospective']) continuous glucose monitoring to help improve blood glucose control in children and young people who continue to have hyperglycaemia despite insulin adjustment and additional support. (1.2.65) |
| **Children and young people with type 1 diabetes should be offered blood glucose monitors with memories (as opposed to monitors without memories) because these are associated with improved patient satisfaction.** (1.2.6.15) | This recommendation has been deleted because blood glucose monitors now routinely have memory functions. |
| **Children and young people with type 1 diabetes should be encouraged to develop a good working knowledge of nutrition and how it affects their diabetes.** (1.2.7.3) | Replaced by: Support children and young people with type 1 diabetes and their family members or carers (as appropriate) to develop a good working knowledge of nutrition and how it affects their diabetes. (1.2.34) |
| **Children and young people with type 1 diabetes and their families should be informed of the importance of healthy eating in reducing the risk of cardiovascular disease (including foods with a low glycaemic index, fruit and vegetables, and types and amounts of fats), and means of making appropriate nutritional changes in the period after diagnosis and according to need and interest at intervals thereafter.** (1.2.7.4) | Replaced by: Explain regularly to children and young people with type 1 diabetes and their family members or carers (as appropriate) how healthy eating (including eating foods with a low glycaemic index, fruit and vegetables, and appropriate types and amounts of fats) can reduce their risk of cardiovascular disease, and support them to adjust their food choices accordingly. (1.2.35) |
| **Children and young people with type 1 diabetes should be encouraged to consider eating a bedtime snack. The nutritional composition and timing of all snacks should be discussed with the diabetes care team.** (1.2.7.5) | Replaced by: Encourage children and young people with type 1 diabetes and their family members or carers (as appropriate) to discuss the nutritional composition and timing of snacks with the diabetes team. (1.2.40) |
| **Children and young people using multiple daily injection regimens should be offered education** | Replaced by: Offer children and young people with type 1 diabetes and their family members or carers (as appropriate) education and support to help them to:  
- self-monitor blood glucose levels (at least 5 times per day)  
- understand the importance of these results  
- understand the meaning of changes in blood glucose levels. (1.2.36)  
Children and young people with type 1 diabetes and their family members or carers (as appropriate) should be advised on the importance of recording their blood glucose levels at the following times: (1.2.37)  
- before the two main meals (breakfast and dinner)  
- before bedtime  
- before exercise  
- when symptoms may indicate a need to check their blood glucose levels. (1.2.38) |

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### Recommendation in 2004 guideline

about insulin and dietary management as part of their diabetes care package, to enable them to adjust their insulin dose to reflect their carbohydrate intake. (1.2.7.6)

### Comment

diabetes and their family members or carers (as appropriate) a continuing programme of education from diagnosis. Ensure that the programme includes the following core topics:

- insulin therapy, including its aims, how it works and its mode of delivery
- blood glucose monitoring, including targets for blood glucose control (blood glucose and HbA1c levels)
- the effects of diet, physical activity and intercurrent illness on blood glucose control
- managing intercurrent illness (‘sick-day rules’, including monitoring of blood ketones [beta-hydroxybutyrate])
- detecting and managing hypoglycaemia, hyperglycaemia and ketosis. (1.2.1)

Offer level 3 carbohydrate-counting education from diagnosis to children and young people with type 1 diabetes who are using multiple daily injections or insulin pump therapy, and to their family members or carers (as appropriate), and repeat the offer at intervals thereafter. (1.2.37)

Children and young people with type 1 diabetes, their parents and other carers should be informed that exercise should be undertaken with caution if blood glucose levels are greater than 17 mmol/litre in the presence of ketosis. (1.2.8.9)

### Replaced by:

When DKA is suspected in a child or young person with known diabetes (see recommendation 1.4.4) measure the blood ketones (beta-hydroxybutyrate), using a near-patient method if available. If the level is elevated, immediately send them to a hospital with acute paediatric facilities. (1.4.5)

When DKA is suspected in a child or young person with known diabetes (see recommendation 1.4.4) and it is not possible to measure the blood ketones (beta-hydroxybutyrate) using a near-patient method, immediately send them to a hospital with acute paediatric facilities. (1.4.6)

Parents and, where appropriate, school nurses and other carers should be offered education on the administration of glucagon.(1.3.1.7)

This recommendation has been deleted as it was no longer relevant in light of amendments to other recommendations from the 2004 guideline.

Young people with type 1 diabetes should be offered alcohol education programmes.(1.2.9.2)

### Replaced by:

Offer children and young people with type 1 diabetes and their family members or carers (as appropriate) a continuing programme of education from diagnosis. Ensure that the programme includes the following core topics:

- insulin therapy, including its aims, how it works and its mode of delivery
- blood glucose monitoring, including targets for blood glucose control (blood glucose and HbA1c levels)
- the effects of diet, physical activity and
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<tr>
<td>Intercurrent illness on blood glucose control</td>
<td>Tailor the education programme to each child or young person with type 1 diabetes and their family members or carers (as appropriate), taking account of issues such as:</td>
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<tr>
<td>• Managing intercurrent illness ('sick-day rules', including monitoring of blood ketones [beta-hydroxybutyrate])</td>
<td>• personal preferences</td>
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<tr>
<td>• Detecting and managing hypoglycaemia, hyperglycaemia and ketosis. (1.2.1)</td>
<td>• emotional wellbeing</td>
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<td>• age and maturity</td>
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<td>• cultural considerations</td>
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<td>• current and future social circumstances</td>
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<td>• life goals. (1.2.2)</td>
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| Parents and, where appropriate, school nurses and other carers should be offered education on the administration of glucagon. (1.3.1.7) | This recommendation has been deleted as it was no longer relevant in light of amendments to other recommendations from the 2004 guideline. |

| Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes. (1.3.2.1) | This recommendation is no longer necessary as the recognition and management of DKA has now been covered in detail by the 2015 update. |

| Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children's ward. (1.3.2.2) | Replaced by: |
| | Children and young people with DKA should be managed appropriately and should be cared for in a facility that can provide the level of monitoring and care for DKA specified in section 1.4 of this guideline. (1.4.16) |
| | Children and young people with DKA should be cared for either on a high-dependency unit, or on a general paediatric ward with one-to-one nursing, if: |
| | • they are younger than 2 years or |
| | • they have severe DKA (blood pH below 7.1). (1.4.17) |

| Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit. (1.3.2.3) | Replaced by: |
| | Children and young people with DKA should be managed appropriately and should be cared for in a facility that can provide the level of monitoring and care for DKA specified in section 1.4 of this guideline. (1.4.16) |
| | Children and young people with DKA should be cared for either on a high-dependency unit, or on a general paediatric ward with one-to-one nursing, if: |
| | • they are younger than 2 years or |
| | • they have severe DKA (blood pH below 7.1). (1.4.17) |

<p>| Children with diabetic ketoacidosis who are | Replaced by: |</p>
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| younger than 2 years of age should be managed in a paediatric intensive care unit. (1.3.2.4) | Children and young people with DKA should be cared for in a facility that can provide the level of monitoring and care for DKA specified in section 1.4 of this guideline. (1.4.16) Children and young people with DKA should be cared for either on a high-dependency unit, or on a general paediatric ward with one-to-one nursing, if:  
- they are younger than 2 years  
- they have severe DKA (blood pH below 7.1). (1.4.17) |
| Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose. (1.3.2.5) | Replaced by: Treat DKA with oral fluids and subcutaneous insulin only if the child or young person is alert, not nauseated or vomiting, and not clinically dehydrated. (1.4.22) |
| Children and young people with type 1 diabetes and their families should be offered clear guidance and protocols (‘sick-day rules’) for the management of type 1 diabetes during intercurrent illness. (1.3.4.1) | Replaced by: Provide each child and young person with type 1 diabetes and their family members or carers (as appropriate) with clear individualised oral and written advice (‘sick-day rules’) about managing type 1 diabetes during intercurrent illness or episodes of hyperglycaemia, including:  
- monitoring blood glucose  
- monitoring blood ketones (beta-hydroxybutyrate)  
- adjusting their insulin regimen  
- food and fluid intake  
- when to seek further advice or help. Revisit the advice with the child or young person and their family members or carers (as appropriate) at least annually. (1.2.54) |
| Children and young people with type 1 diabetes should have short-acting insulin or rapid-acting insulin analogues and blood and/or urine ketone testing strips available for use during intercurrent illness. (1.3.4.2) | Replaced by: Provide children and young people with type 1 diabetes with rapid-acting insulin analogues for use during intercurrent illness or episodes of hyperglycaemia. (1.2.30) Provide each child and young person with type 1 diabetes and their family members or carers (as appropriate) with clear individualised oral and written advice (‘sick-day rules’) about managing type 1 diabetes during intercurrent illness or episodes of hyperglycaemia, including:  
- monitoring blood glucose  
- monitoring blood ketones (beta-hydroxybutyrate)  
- adjusting their insulin regimen  
- food and fluid intake |
### Recommendation in 2004 guideline | Comment
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when to seek further advice or help. Revisit the advice with the child or young person and their family members or carers (as appropriate) at least annually. (1.2.54) | 
Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that it is important to ensure that blood ketone testing strips are not used after the specified (‘use-by’) date. (1.2.74) |
Routine screening for elevated blood lipid levels and/or neurological function is not recommended for children and young people with type 1 diabetes. (1.3.5.2) | The GDG considered that monitoring for dyslipidaemia or neurological function in children and young people with type 1 diabetes is not part of current practice and so a recommendation was unnecessary. |
Parents of pre-school children with type 1 diabetes should be informed that persistent hypoglycaemia, in particular in association with seizures, is associated with a small but definite risk of long-term neurocognitive dysfunction.(1.4.4.1) | This recommendation has been deleted because advice on preventing and treating hypoglycaemia was considered more important. Assessment for cognitive difficulties is still covered by the following 2004 recommendation: Diabetes teams should consider referring children and young people with type 1 diabetes who have frequent hypoglycaemia and/or recurrent seizures for assessment of cognitive function, particularly if these occur at a young age. (1.2.85) |
Children and young people with type 1 diabetes, especially young people using multiple daily injection regimens, should be offered structured behavioural intervention strategies because these may improve psychological well-being and glycaemic control. (1.4.7.2) | Replaced by: Offer specific family-based behavioural interventions, such as behavioural family systems therapy, if there are difficulties with diabetes-related family conflict. (1.2.100) Consider a programme of behavioural intervention therapy for children and young people with type 1 diabetes in whom there are concerns about psychological wellbeing in order to improve:  
- health-related quality of life - for example, counselling or cognitive behavioural therapy (CBT), including CBT focused on quality of life  
- adherence to diabetes treatment - for example, motivational interviewing or multi-systemic therapy  
- glycaemic control in children and young people with high HbA1c levels (HbA1c above 69 mmol/mol (above 8.5%)) - for example, multi-systemic therapy  
- self-esteem - for example, support strategies such as mentoring  
- depression - for example, motivational interviewing. (1.2.101) |
Young people with type 1 diabetes should be offered specific support strategies, such as mentoring and self-monitoring of blood glucose levels supported by problem solving, to improve | Replaced by: Consider a programme of behavioural intervention therapy for children and young people with type 1 diabetes in whom there are...
### A.2 Amended recommendation wording (change to meaning)

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

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

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

<table>
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| their self-esteem and glycaemic control. (1.4.7.3) | concerns about psychological wellbeing in order to improve:  
- health-related quality of life - for example, counselling or cognitive behavioural therapy (CBT), including CBT focused on quality of life  
- adherence to diabetes treatment - for example, motivational interviewing or multi-systemic therapy  
- glycaemic control in children and young people with high HbA1c levels (HbA1c above 69 mmol/mol (above 8.5%)) - for example, multi-systemic therapy  
- self-esteem - for example, support strategies such as mentoring  
- depression - for example, motivational interviewing. (1.2.101) | |
| Families of children and young people with type 1 diabetes should be offered specific support strategies (such as behavioural family systems therapy) to reduce diabetes-related conflict between family members. (1.4.7.4) | Replaced by: Offer specific family-based behavioural interventions, such as behavioural family systems therapy, if there are difficulties with diabetes-related family conflict. (1.2.100) | |
| Teaching staff should be informed about the potential effects of type 1 diabetes on cognitive function and educational attainment (1.5.1.3) | This recommendation has been deleted because it was considered more important to assess children and young people at increased risk of cognitive function disorders than to raise concerns about all children and young people with type 1 diabetes. This is covered in the following 2004 recommendation:  
Diabetes teams should consider referring children and young people with type 1 diabetes who have frequent hypoglycaemia and/or recurrent seizures for assessment of cognitive function, particularly if these occur at a young age. (1.2.85) | |
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<tr>
<td>The diagnosis of type 1 diabetes in children and young people should be based on the criteria specified in the 1999 World Health Organization report on the diagnosis and classification of diabetes mellitus.[1]</td>
<td>Be aware that the characteristics of type 1 diabetes include:</td>
<td>The WHO updated their report on the diagnosis and classification of diabetes in 2006. In addition, this recommendation has been split into 2 recommendations to make it easier to understand. ‘Symptoms and signs’ has been replaced with ‘characteristics’ as the GDG felt this was a more accurate term for the list of conditions in this recommendation.</td>
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<td>The symptoms and signs of type 1 diabetes include:</td>
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<td>hyperglycaemia (random blood glucose more than 11 mmol/litre), polyuria, polydipsia and weight loss. (1.1.1.1)</td>
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<tr>
<td>Children and young people with suspected type 1 diabetes should be offered immediate (same day) referral to a multidisciplinary paediatric diabetes care team that has the competencies needed to confirm diagnosis and to provide immediate care. (1.1.1.2)</td>
<td>Refer children and young people with suspected type 1 diabetes immediately (on the same day) to a multidisciplinary paediatric diabetes care team with the competencies needed to confirm diagnosis and to provide immediate care. (1.1.2)</td>
<td>The action was changed from ‘offer’ to ‘refer’, as the 2012 NICE guidelines manual used to develop this update has a specific definition of the word ‘offer’ that was not used when the original 2004 guideline was published.</td>
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| Consideration should be given to the possibility of other types of diabetes (such as early-onset type 2 diabetes, other insulin resistance syndromes, maturity-onset diabetes in the young and molecular/ enzymatic abnormalities) in children and young people with suspected type 1 diabetes who:  
- have a strong family history of diabetes  
- are obese at presentation  
- are of black or Asian origin  
- have an insulin requirement of less than 0.5 units/kg body weight/day outside a partial remission phase  
- have no insulin requirement  
- rarely or never produce ketone bodies in the urine (ketonuria) during episodes of hyperglycaemia  
- show evidence of insulin resistance (for example, acanthosis nigricans)  
- have associated features, such as eye disease, deafness, or another systemic illness or syndrome. (1.1.1.3) | Think about the possibility of type 2 diabetes in children and young people with suspected diabetes who:  
- have a strong family history of diabetes  
- are obese at presentation  
- are of black or Asian family origin  
- have no insulin requirement, or have an insulin requirement of less than 0.5 units/kg body weight/day after the partial remission phase  
- show evidence of insulin resistance (for example, acanthosis nigricans). (1.1.5) | This recommendation has been split into two, as the GDG felt that type 2 diabetes should be considered separately from the rarer conditions now that it is covered in this guideline. In addition, not all of the factors listed applied to type 2 diabetes or to the rarer conditions. Because of this, the GDG felt that separating them into two lists makes it clearer which factors apply to which condition. In the second recommendation, ‘eye’ disease’ has been replaced with ‘retinitis pigmentosa’, as the GDG felt that ‘eye disease’ was not specific enough and could be mistaken for diabetic retinopathy. |
| Think about the possibility of type 2 diabetes in children and young people with suspected diabetes who:  
- have a strong family history of diabetes  
- are obese at presentation  
- are of black or Asian origin  
- have no insulin requirement, or have an insulin requirement of less than 0.5 units/kg body weight/day after the partial remission phase  
- show evidence of insulin resistance (for example, acanthosis nigricans). (1.1.5) | Think about the possibility of other types of diabetes other than types 1 or 2 (such as other insulin resistance syndromes, maturity-onset diabetes in the young and molecular/ enzymatic abnormalities) in children and young people with suspected diabetes who have any of the following features:  
- rarely or never produce ketone bodies in the urine (ketonuria) during episodes of hyperglycaemia  
- have associated features, such as retinitis pigmentosa, deafness, or another systemic illness or syndrome. (1.1.6) | |

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<tr>
<td>Young people with type 1 diabetes should be encouraged to attend clinics on a regular basis (three or four times per year) because regular attendance is associated with good glycaemic control. (1.5.2.1)</td>
<td>Encourage young people with type 1 diabetes to attend clinic 4 times a year because regular contact is associated with good blood glucose control. (1.2.3)</td>
<td>The recommended number of contacts has been updated to reflect the Paediatric Diabetes Best Practice Tariff Criteria. In addition, 4 clinic attendances is standard in current clinical practice.</td>
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<tr>
<td>Children and young people with type 1 diabetes and their families should be informed that, as for other children, regular dental examinations[2] and eye examinations (every 2 years) are recommended. (1.3.5.4)</td>
<td>Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that like others they are advised to have • regular dental examinations (see the NICE guideline on dental recall) • an eye examination by an optician every 2 years. (1.2.4)</td>
<td>An explanation has been added to the bullet on eye examination to make it clear this refers to standard eye tests rather than retinopathy monitoring. In addition, 'recommended' has been changed to 'advised to have' as part of the editorial changes to make this sentence active.</td>
</tr>
<tr>
<td>Children and young people with type 1 diabetes and their families should be informed that the Department of Health recommends immunisation against pneumococcal infection for children and young people with diabetes over the age of 2 months. (1.2.11.2)</td>
<td>Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that the Department of Health's Green Book recommends immunisation against pneumococcal infection for children and young people with diabetes who need insulin or oral hypoglycaemic medicines. (1.2.17)</td>
<td>This recommendation has been updated to reflect guidance from the Department of Health's Green Book.</td>
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<tr>
<td>Children and young people with newly diagnosed type 1 diabetes</td>
<td>Explain to children and young people with newly diagnosed type 1 diabetes and their</td>
<td>This recommendation has been updated to reflect guidance from the Department of Health's Green Book.</td>
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<td>Children and young people with type 1 diabetes using insulin injection regimens should be offered needles that are of an appropriate length for their body fat (short needles are appropriate for children and young people with less body fat; longer needles are appropriate for children and young people with more body fat). (1.2.4.2)</td>
<td>Provide children and young people with type 1 with insulin injection needles that are of an appropriate length for their body fat. (1.2.27)</td>
<td>The information on what needle length is appropriate for a child has been deleted from this recommendation, as the GDG felt that this was well known and did not need defining in the recommendation.</td>
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<tr>
<td>Children and young people with type 1 diabetes should be offered: • annual foot care reviews • investigation of the state of injection sites at each clinic visit. (1.3.5.3)</td>
<td>Offer children and young people with type 1 diabetes a review of injection sites at each clinic visit. (1.2.29)</td>
<td>The text on foot care has been removed from this recommendation, as it is covered by the new NICE guideline on diabetic foot care.</td>
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<td>should be informed that they may experience a partial remission phase (or 'honeymoon period') during which a low dosage of insulin (0.5 units/kg body weight/day) may be sufficient to maintain an HbA1c level of less than 7%. (1.1.3.1)</td>
<td>family members or carers (as appropriate) that they may experience a partial remission phase (a 'honeymoon period') during which a low dosage of insulin (0.5 units/kg body weight/day) may be sufficient to maintain an HbA1c level of less than 48 mmol/mol (6.5%). (1.2.25)</td>
<td>The information on what needle length is appropriate for a child has been deleted from this recommendation, as the GDG felt that this was well known and did not need defining in the recommendation.</td>
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| Children and young people with type 1 diabetes and their families should be informed that they have the same basic nutritional requirements as other children and young people. The food choices of children and young people should provide sufficient energy and nutrients for optimal growth and development, with total daily energy intake being distributed as follows:  
  - carbohydrates – more than 50%  
  - protein – 10–15%  
  - fat – 30–35%.  
  The consumption of five portions of fruit and vegetables per day is also recommended. Neonates, infants and pre-school children require individualised dietary assessment to determine their energy needs. (1.2.7.2) | Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that children and young people with type 1 diabetes have the same basic nutritional requirements as other children and young people. Children and young people’s food should provide sufficient energy and nutrients for optimal growth and development. (1.2.36) | The text on total daily energy intake distribution and eating 5 portions of fruit and vegetables per day has been removed from this recommendation, as the 2015 recommendation 1.2.41 covers this. In addition, the specific energy intake levels were removed, as these are applicable to all children and not just those with type 1 diabetes. |
| Children and young people with type 1 diabetes should have their height and weight measured and plotted on an appropriate growth chart and their body mass index calculated at each clinic visit. The purpose of measuring and plotting height and weight and calculating body mass index is to check for normal growth and/or significant changes in weight because these may reflect changing glycaemic control. (1.3.5.5) | At each clinic visit for children and young people with type 1 diabetes:  
  - measure height and weight and plot on an appropriate growth chart  
  - calculate body mass index.  
  Check for normal growth and/or significant changes in weight because these may reflect changing blood glucose control. (1.2.45) | This recommendation has been heavily edited for clarity, and the second part of the recommendation has been rewritten to make it easier to follow. |
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<tr>
<td>Children and young people with type 1 diabetes and their families should be informed about the effects of exercise on blood glucose levels and about strategies for preventing exercise-induced hypoglycaemia during and/or after physical activity. (1.2.8.4)</td>
<td>Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) about the effects of exercise on blood glucose levels and about strategies for avoiding hypo- or hyperglycaemia during or after physical activity. (1.2.49)</td>
<td>The term 'exercise-induced' has been removed from this recommendation, as the GDG felt that the cause of hypoglycaemia did not need stating here. In addition, hyperglycaemia caused by exercise has been added to this recommendation, as this is also a complication that children and young people with type 1 diabetes and their family members or carers (as appropriate) should be aware of. In addition, this recommendation has been expanded to include family members or carers (as appropriate), as they may also be involved in the child or young person’s treatment.</td>
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<tr>
<td>Children and young people with type 1 diabetes should be offered testing of their HbA1c levels two to four times per year (more frequent testing may be appropriate if there is concern about poor glycaemic control).</td>
<td>Offer children and young people with type 1 diabetes measurement of their HbA1c level 4 times a year (more frequent testing may be appropriate if there is concern about poor blood glucose control). (1.2.72)</td>
<td>The recommended number of measurements has been updated to reflect the</td>
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<td>(1.2.6.2)</td>
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<td>Paediatric Diabetes Best Practice Tariff Criteria. In addition, 4 measurements a year is standard in current clinical practice.</td>
</tr>
<tr>
<td>Children and young people with type 1 diabetes, their parents and other carers should be informed that they should always have access to an immediate source of carbohydrate (glucose or sucrose) and blood glucose monitoring equipment for immediate confirmation and safe management of hypoglycaemia. (1.3.1.1)</td>
<td>Explain to children and young people with type 1 diabetes and their family members or carers (as appropriate) that they should always have access to an immediate source of fast-acting glucose and blood glucose monitoring equipment for immediate confirmation and safe management of hypoglycaemia. (1.2.77)</td>
<td>The type of carbohydrate suitable for safe management of hypoglycaemia has been changed from 'glucose or sucrose' to 'fast-acting glucose', as the GDG felt this was what was recommended in current practice.</td>
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<td>Parents and, where appropriate, school nurses and other carers should have access to glucagon for subcutaneous or intramuscular use in an emergency, especially when there is a high risk of severe hypoglycaemia. (1.3.1.6)</td>
<td>Family members or carers and, where appropriate, school nurses and other carers should be trained and equipped to give intramuscular glucagon for severe hypoglycaemia in an emergency. (1.2.78)</td>
<td>Subcutaneous glucagon has been removed from this recommendation, as the GDG did not think this was used in current practice. The recommendation has been re worded to make it clear that intramuscular glucagon would only be given for severe hypoglycaemia. In addition, ‘have access’ has been replaced with ‘trained and equipped’, as the GDG felt that this was an important point that was left out of the original recommendation.</td>
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<tr>
<td>Children and young people with mild to moderate hypoglycaemia should be treated as follows.</td>
<td>Immediately treat mild to moderate hypoglycaemia in children and young people as follows.</td>
<td>This recommendation has been reworded and reordered to make it easier to understand. In addition, the type of carbohydrate suitable for safe management of hypoglycaemia has been changed from 'glucose or sucrose' to 'fast-acting glucose', as the GDG felt this was what was recommend in current practice.</td>
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<td>• Take immediate action.</td>
<td>• Give fast-acting glucose (for example, 10–20 g) by mouth (liquid carbohydrate may be taken more easily than solid).</td>
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<tr>
<td>• The first line of treatment should be the consumption of rapidly absorbed simple carbohydrate (for example, 10–20 g carbohydrate given by mouth).</td>
<td>• Be aware that fast-acting glucose may need to be given in frequent small amounts, because hypoglycaemia can cause vomiting.</td>
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<tr>
<td>• The simple carbohydrate should raise blood glucose levels within 5–15 minutes.</td>
<td>• Recheck blood glucose levels within 15 minutes (fast-acting glucose should raise blood glucose levels within 5–15 minutes).</td>
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<tr>
<td>• Carbohydrate given in liquid form may be taken more easily.</td>
<td>• As symptoms improve or normoglycaemia is restored, give oral complex long-acting carbohydrate to maintain blood glucose levels, unless the child or young person is:</td>
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<tr>
<td>• It may be appropriate to give small amounts of rapidly absorbed simple carbohydrate frequently because hypoglycaemia may cause vomiting.</td>
<td>o about to have a snack or meal</td>
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<td>• As symptoms improve or normoglycaemia is restored additional complex long-acting carbohydrate should be given orally to maintain blood glucose levels unless a snack or meal is imminent.</td>
<td>o receiving a continuous subcutaneous insulin infusion. (1.2.79)</td>
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<tr>
<td>• Additional complex long-acting carbohydrate is not required for children and young people using continuous subcutaneous insulin infusion.</td>
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<td>• Blood glucose levels should be rechecked within 15 minutes. (1.3.1.4)</td>
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| Children and young people with severe hypoglycaemia should be treated as follows.  
- In a hospital setting, 10% intravenous glucose should be used when rapid intravenous access is possible (up to 500 mg/kg body weight – 10% glucose is 100 mg/ml).  
- Outside hospital, or where intravenous access is not practicable, intramuscular glucagon or concentrated oral glucose solution (e.g. Hypostop) may be used.  
- Children and young people over 8 years old (or body weight more than 25 kg) should be given 1 mg glucagon.  
- Children under 8 years old (or body weight less than 25 kg) should be given 500 micrograms of glucagon.  
- Blood glucose levels should respond within 10 minutes.  
- As symptoms improve or normoglycaemia is restored, in children and young people who are sufficiently awake, additional complex long-acting carbohydrate should be given orally to maintain blood glucose levels. | Treat severe hypoglycaemia in children and young people who are in hospital and in whom rapid intravenous access is possible by giving 10% intravenous glucose. Give a maximum dose of 500 mg/kg body weight (equivalent to a maximum of 5 ml/kg). (1.2.80)  
- Treat severe hypoglycaemia in children and young people who are not in hospital or who do not have rapid intravenous access available as follows.  
- Use intramuscular glucagon or concentrated oral glucose solution (for example, Glucogel®). Do not use oral glucose solution if the level of consciousness is reduced as this could be dangerous.  
- If using intramuscular glucagon:  
  - give children and young people over 8 years old (or who weigh more than 25 kg) 1 mg glucagon.  
  - give children under 8 years old (or who weigh less than 25 kg) 500 micrograms of glucagon. | This recommendation has been reworded, reordered, and split into 2 separate recommendations to make it easier to understand. In addition, the action in the section on intramuscular glucagon and concentrated oral glucose solution has changed from ‘may be used’ to ‘Use’. This is because the GDG felt that these 2 were the only standard treatment options rather than 2 options out of several, as was suggested by the original wording. The reference to ‘Hypostop’ has been changed to ‘Glucogel’, as the GDG felt that this was the preparation commonly used in clinical practice. A warning on using oral glucose solution in children with reduced levels of consciousness has been added, as the GDG felt that |
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| • Some children and young people may continue to have reduced consciousness for several hours after a severe hypoglycaemic episode, and repeat blood glucose measurements will be required to determine whether further glucose is necessary.  
• Medical assistance should be sought for children and young people whose blood glucose levels fail to respond and those in whom symptoms persist for more than 10 minutes. (1.3.1.5) | • Seek medical assistance if blood glucose levels do not respond or symptoms persist for more than 10 minutes.  
• As symptoms improve or normoglycaemia is restored, and once the child or young person is sufficiently awake, give oral complex long-acting carbohydrate to maintain blood glucose levels.  
• Recheck the blood glucose repeatedly in children and young people who have persistently reduced consciousness after a severe hypoglycaemic episode, to determine whether further glucose is needed. (1.2.81) | The term 'nocturnal hypoglycaemia' has been changed to 'hypoglycaemia while sleeping', as the GDG did not think the original term was common in clinical practice. |
<p>| Young people with type 1 diabetes should be informed about the specific effects of alcohol consumption on glycaemic control, particularly the risk of (nocturnal) hypoglycaemia. (1.2.9.1) | Explain to young people with type 1 diabetes the effects of alcohol consumption on blood glucose control, and in particular that there is an increased risk of hypoglycaemia including hypoglycaemia while sleeping. (1.2.82) | |
| Non-adherence to therapy should be considered in children and young people with type 1 diabetes who have poor glycaemic control, especially in adolescence. (1.4.6.1) | Think about the possibility of non-adherence to therapy in children and young people with type 1 diabetes who have poor blood glucose control, especially in adolescence. (1.2.86) | The action was changed from 'consider' to 'think about', as the 2012 NICE guidelines manual used to develop this update has a specific definition of the word 'consider' that was not used when the original 2004 guideline was published. |
| Diabetes care teams should be aware that children and young people with type 1 diabetes have a greater risk of emotional and behavioural problems than other children and young people. | Diabetes teams should be aware that children and young people with type 1 diabetes have a greater risk of emotional and behavioural difficulties. (1.2.93) | This recommendation has been amended, as the original suggested |</p>
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<td>Young people with ‘brittle diabetes’ (that is, those who present with frequent episodes of diabetic ketoacidosis over a relatively short time) should have their emotional and psychological well-being assessed. (1.4.6.3)</td>
<td>Assess the emotional and psychological well-being of young people with type 1 diabetes who present with frequent episodes of diabetic ketoacidosis. (1.2.95)</td>
<td>The term ‘brittle diabetes’ has been removed from this recommendation, as the GDG felt that this term was no longer commonly used in clinical practice.</td>
</tr>
<tr>
<td>Children and young people with type 1 diabetes and their families should be offered timely and ongoing access to mental health professionals because they may experience psychological disturbances (such as anxiety, depression, behavioural and conduct disorders and family conflict) that can impact on the management of diabetes and well-being. (1.4.7.5)</td>
<td>Offer children and young people with type 1 diabetes and their family members or carers (as appropriate) timely and ongoing access to mental health professionals because they may experience psychological problems (such as anxiety, depression, behavioural and conduct disorders and family conflict) that can impact on the management of diabetes and well-being.</td>
<td>A cross-reference to the NICE guidelines on depression in children and young people and antisocial behaviour and conduct disorders in children and young people has been added for information.</td>
</tr>
<tr>
<td>Diabetes care teams should be aware that children and young people with type 1 diabetes, in particular young women, have an increased risk of eating disorders. (1.4.3.1)</td>
<td>Diabetes teams should be aware that children and young people with type 1 diabetes, in particular young women, have an increased risk of eating disorders.</td>
<td>A cross-reference to the NICE guideline on eating disorders has been added for information.</td>
</tr>
<tr>
<td>Diabetes care teams should be aware that children and young people with eating disorders</td>
<td>Be aware that children and young people with type 1 diabetes who have eating disorders</td>
<td>The terms ‘persistent’</td>
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| people with type 1 diabetes who have eating disorders may have associated problems of persistent hyperglycaemia, recurrent hypoglycaemia and/or symptoms associated with gastric paresis. (1.4.3.2) | may have associated difficulties with • poor blood glucose control (both hyperglycaemia and hypoglycaemia) • symptoms of gastroparesis. (1.2.106) | hyperglycaemia' and 'recurrent hypoglycaemia' have been replaced with the text on poor blood glucose control, covering both hyperglycaemia and hypoglycaemia. This is because the GDG felt that these two complications are both indicative of 'poor blood glucose control', so it would be simpler to use this phrase in the recommendation. 
In addition, the phrase 'symptoms associated with gastric paresis' has been changed, as the GDG felt that the use of 'associated' made this recommendation vague. 'gastric paresis' has been changed to 'gastroparesis', as this is the term currently used in practice. |

Children and young people with type 1 diabetes in whom eating disorders are
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<td>disorders are identified by their diabetes care team should be offered joint management involving their diabetes care team and child mental health professionals. (1.4.3.3)</td>
<td>identified, offer joint management involving their diabetes team and child mental health professionals. (1.2.107)</td>
<td>Ion has been amended as healthcare professionals outside of the diabetes team (such as GPs) can also identify eating disorders.</td>
</tr>
<tr>
<td>Children and young people with type 1 diabetes and their families should be informed that, as for other children, regular dental examinations[3] and eye examinations (every 2 years) are recommended. (1.3.5.4)</td>
<td>Explain to children and young people with type 2 diabetes and their family members or carers (as appropriate) that like others they are advised to have: • regular dental examinations[4] • an eye examination by an optician every 2 years. (1.3.3)</td>
<td>An explanation has been added to the bullet on eye examination to make it clear this refers to standard eye tests rather than retinopathy monitoring. ‘recommende d’ has been changed to ‘advised to have’ as part of the editorial changes to make this sentence active. In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.</td>
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<tr>
<td>Children and young people with type 1 diabetes and their families should be offered information about the existence of and means of contacting local and/or national diabetes support groups and organisations, and the potential benefits of membership. This should be done in the time following diagnosis and periodically thereafter. (1.5.1.1)</td>
<td>Give children and young people with type 2 diabetes and their family members or carers (as appropriate) information about local and/or national diabetes support groups and organisations, and the potential benefits of membership. Give this information after diagnosis and regularly afterwards. (1.3.5)</td>
<td>NICE has made editorial changes to the original wording to clarify the action to be taken (no change to meaning): a verb has been added, or the verb used has been changed. In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.</td>
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<tr>
<td>Children and young people with type 1 diabetes and their families should be advised how to obtain information about benefits in relation to government disability support. (1.5.1.4)</td>
<td>Explain to children and young people with type 2 diabetes and their family members or carers (as appropriate) how to find information about possible benefits from government disability support. (1.3.6)</td>
<td>The word ‘possible’ has been added, as the benefits available to children and young people with type 2 diabetes can be different to those available to children and young people with type 1 diabetes. In addition, this recommendation originally only applied</td>
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<td>Children and young people with type 1 diabetes and their families should be informed that the Department of Health[5] recommends annual immunisation against influenza for children and young people with diabetes over the age of 6 months. (1.2.11.1)</td>
<td>Explain to children and young people with type 2 diabetes and their family members or carers (as appropriate) that the Department of Health’s Green Book recommends annual immunisation against influenza for children and young people with diabetes. (1.3.12)</td>
<td>These recommendations originally only applied to type 1 diabetes in children and young people, but have been included in the section of this guideline on type 2 diabetes as they are applicable to this population.</td>
</tr>
<tr>
<td>Children and young people with type 1 diabetes and their families should be informed that the Department of Health[7] recommends immunisation</td>
<td>Explain to children and young people with type 2 diabetes and their family members or carers (as appropriate) that the Department of Health’s Green Book recommends immunisation against pneumococcal infection</td>
<td>This recommendation has been updated to reflect</td>
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<td>against pneumococcal infection for children and young people with diabetes over the age of 2 months. (1.2.11.2)</td>
<td>for children and young people with diabetes who need insulin or oral hypoglycaemia medicines. (1.3.13)</td>
<td>guidance from the Department of Health’s Green Book.</td>
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In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.

In addition, ‘over the age of 2 months’ has been taken out of this recommendation, as type 2 diabetes normally only occurs in young people or adults, and never in children under 2 months.
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<tr>
<td>Children and young people with type 1 diabetes should have their height and weight measured and plotted on an appropriate growth chart and their body mass index calculated at each clinic visit. The purpose of measuring and plotting height and weight and calculating body mass index is to check for normal growth and/or significant changes in weight because these may reflect changing glycaemic control. (1.3.5.5)</td>
<td>At each clinic visit for children and young people with type 2 diabetes: • measure height and weight and plot on an appropriate growth chart • calculate body mass index. Check for normal growth and/or significant changes in weight because these may reflect changing blood glucose control. (1.3.20)</td>
<td>This recommendation has been heavily edited for clarity, and the second part of the recommendation has been rewritten to make it easier to follow. In addition, this recommendation originally only applied to type 1 diabetes in children and young people, but has been included in the section of this guideline on type 2 diabetes as it is applicable to this population.</td>
</tr>
<tr>
<td>Diabetes care teams should be aware that children and young people with type 1 diabetes have a greater risk of emotional and behavioural problems than other children and young people. (1.4.1.1)</td>
<td>Diabetes teams should be aware that children and young people with type 2 diabetes have a greater risk of emotional and behavioural difficulties. (1.3.31)</td>
<td>This recommendation has been amended, as the original suggested that children and young people with diabetes have a greater risk of emotional and behavioural problems than all other children and young people, which is not the case. In addition, this</td>
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<td>recommendat ion originally only applied to type 1 diabetes in children and young people, but has been amended to include type 2 diabetes as it is applicable to this population.</td>
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<td><strong>Recommendation in current guideline</strong></td>
<td><strong>Reason for change</strong></td>
<td>This recommendat ion has been split into 2 recommendat ions to make the differences in care for the 2 populations clearer. In addition, this recommendat ion originally only applied to type 1 diabetes in children and young people, but has been amended to include type 2 diabetes as it is applicable to this population.</td>
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<tr>
<td><strong>Children with type 1 diabetes who are younger than 2 years of age and children and young people who have social or emotional difficulties, or who live a long way from hospital should be offered inpatient initial management. (1.1.2.6)</strong></td>
<td><strong>Offer initial inpatient management to children with diabetes who are aged under 2 years. (1.5.5)</strong></td>
<td><strong>Think about initial inpatient management for children and young people with diabetes if there are social or emotional factors that would make home-based management inappropriate, or if they live a long distance from the hospital. (1.5.6)</strong></td>
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<tr>
<td><strong>1.2.21, 1.2.23, 1.2.24</strong></td>
<td><strong>The terms 'preprandial' and 'postprandial' have been changed to 'pre-meal', 'before meals', and 'after meals' when appropriate, as the GDG felt that these</strong></td>
<td><strong>The terms 'preprandial' and 'postprandial' have been changed to 'pre-meal', 'before meals', and 'after meals' when appropriate, as the GDG felt that these</strong></td>
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<td>terms are simpler and more commonly used.</td>
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<tr>
<td>1.2.21, 1.2.22, 1.2.23, 1.2.24, 1.2.25, 1.2.39, 1.2.50</td>
<td>These recommendations have been expanded to include family members or carers (as appropriate), as they may also be involved in the child or young person's treatment.</td>
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<tr>
<td>1.2.6, 1.2.22, 1.2.33, 1.2.92, 1.2.96, 1.2.109, 1.4.64, 1.5.7, 1.5.12</td>
<td>NICE has made editorial changes to the original wording to clarify the action to be taken (no change to meaning): a verb has been added, or the verb used has been changed.</td>
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<td>1.3.7, 1.3.8, 1.3.9, 1.3.10, 1.3.11, 1.3.16, 1.3.21, 1.3.29, 1.3.30, 1.3.32, 1.3.34, 1.3.35, 1.3.36, 1.3.37, 1.3.38, 1.5.1, 1.5.2, 1.5.3, 1.5.4, 1.5.5, 1.5.6, 1.5.8, 1.5.9, 1.5.10</td>
<td>These recommendations originally only applied to type 1 diabetes in children and young people, but have been included in the section of this guideline on type 2 diabetes as they are applicable to this population.</td>
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</table>

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

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

<table>
<thead>
<tr>
<th>Recommendation in 2004 guideline</th>
<th>Recommendation in current guideline</th>
<th>Reason for change</th>
</tr>
</thead>
</table>

Recommendations have been edited into the direct style (in line with current NICE style for recommendations in clinical guidelines) where possible. Yellow highlighting has not been applied to these changes. Where applicable, terminology has been made consistent within the guideline and with terminology that will be used in other updates of NICE guidelines on diabetes (diabetes in pregnancy [publication expected February 2015], type 1 diabetes and type 2 diabetes [publication expected August 2015]) – for example, ‘impaired awareness of hypoglycaemia’ rather than ‘hypoglycaemia unawareness’; ‘blood glucose control’ rather than ‘glycaemic control’.

1.2.9 This recommendation has been updated to use modern disability terminology.

1.2.22 (CSII or insulin pump) is specified for clarity (original wording did not mention insulin pumps).

1.2.97, 1.3.35 The term ‘psychological disturbances’ has been rephrased to ‘psychological problems’ to avoid putting a negative emphasis on mental health conditions.

1.2.98, 1.3.36 The term ‘assessment of psychological dysfunction’ has been rephrased to ‘psychological assessment’ to avoid putting a negative emphasis on mental health assessment and treatment.

1.2.21, 1.2.22, 1.2.23, 1.2.76, 1.2.79, 1.2.80, 1.2.81, 1.2.87, 1.2.88, 1.2.95 Type 1 diabetes is specified for clarity (original wording had ‘diabetes’ or did not specify diabetes at all).
Appendix B: 2015 update scope

NATIONAL INSTITUTE FOR HEALTH AND
CLINICAL EXCELLENCE
SCOPE

1 Guideline title

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

1.1 Short title

Diabetes in children and young people

2 The remit

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

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

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

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

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

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

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

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

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

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

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

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

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

3 Clinical need for the guideline

3.1 Epidemiology

3.1.1 Type 1 diabetes

a) Type 1 diabetes is an autoimmune disorder resulting in the destruction of insulin-producing cells in the pancreas. It is predominantly diagnosed in children and young people and inevitably needs insulin replacement treatment.

b) Around 26,500 children and young people in the UK are estimated to have type 1 diabetes needing insulin replacement therapy.

c) Most children and young people diagnosed with type 1 diabetes do not have a family member with the condition, although there may be related disorders such as thyroid or rheumatoid disease in the family. However, a family history of type 1 diabetes does increase a child’s risk of developing type 1 diabetes. For children with an identical twin with type 1 diabetes, the risk of developing the disorder is 1 in 3, for children with a father with type 1 diabetes the risk is 1 in 16, and for children with a mother with type 1 diabetes the risk is 1 in 40. By comparison, the population risk is roughly 1 in 500, although this varies with geographical location.
d) Children and young people with type 1 diabetes have poorer glucose control and the higher rates of acute metabolic complications such as diabetic ketoacidosis in comparison with children and young people with type 2 diabetes. Nine per cent of children and young people with diabetes experienced at least 1 episode of diabetic ketoacidosis in 2009–2010.

e) Systems of surveillance for the early detection of complications in children and young people with type 1 diabetes are important, as is effective management of late complications when they occur.

f) Good blood glucose control is known to prevent or delay the long-term complications of both type 1 and type 2 diabetes.

3.1.2 Type 2 diabetes

g) In 2011, around 300 children and young people in the UK had a confirmed diagnosis of type 2 diabetes.

h) Type 2 diabetes is initially an insulin-resistant state, the primary treatment for which is weight loss and exercise. Pharmacological measures to increase insulin sensitivity or to increase insulin release can be added to lifestyle interventions, but insulin may be needed because of the continuing failure of insulin secretion. Like type 1 diabetes, type 2 diabetes has a significant impact on lifestyle in the short term, and is associated with major long-term complications and reduced life expectancy.

i) Obesity is the most common risk factor for type 2 diabetes. Type 2 diabetes is more common in people of South Asian, Chinese, black African and African–Caribbean origin. In Europeans, type 2 diabetes in children is associated with the most severe degrees of obesity.

j) People from the most deprived socioeconomic backgrounds are 2.5 times more likely than average to have type 2 diabetes at any given age.
3.2 **Current practice**

a) Fewer than 20% of children and young people with diabetes receive the basic care recommended by NICE guidelines.

b) Current standard care for children and young people with diabetes includes patient education, dietary advice, psychological support and management of complications.

c) Standard care for children and young people with type 1 diabetes also includes insulin therapy.

d) For children and young people with type 2 diabetes, first-line care often includes advice on the need for weight loss and the importance of adopting a healthy lifestyle. Metformin may also be used to improve glycaemic control by increasing insulin sensitivity. If good glycaemic control is not achieved then additional insulin or other agents may be needed.

e) The aim of patient education is to enable children and young people and their parents or carers to live a normal life and minimise the risk of complications. It includes advice on diet, improving glycaemic control and how complications are managed.

f) Management of hypoglycaemia depends on its severity. Hospital care may be needed if the child or young person is unresponsive or unconscious, but some children and young people can be cared for at home.

h) Children and young people with type 1 diabetes are monitored for growth and pubertal development, blood pressure, injection site
complications, thyroid disease and coeliac disease. Long-term glycaemic control is monitored using haemoglobin A1c (HbA1c). From the age of 12 years they are also monitored for retinopathy and nephropathy by the measurement of microalbuminuria. Rare associated conditions (juvenile cataracts, necrobiosis lipoidica, rheumatoid disease and Addison’s disease, among others) may also be considered.

i) Children and young people with type 1 or type 2 diabetes receive annual foot care reviews from the age of 12 years. Minor problems (ingrown toenails or verrucas) are common and may be treated by a chiropodist. Serious foot problems are very rare in children and young people.

j) Psychological and social issues are also important to consider at each clinic visit, and treatment or advice is given where necessary.

k) There is a process of transition so that from the age of 13 years, young people are prepared for eventual transfer to adult care. This includes agreed protocols and joint clinics if possible. Young people are given time to familiarise themselves with this process and it is only completed when they are ready to move to adult services. The timing of transition depends on the young person’s physical development, emotional maturity, stability of health, other life changes and local circumstances.

l) Since the publication of Type 1 diabetes (NICE clinical guideline 15), new evidence has been published (or is anticipated) to warrant reconsideration of the following areas of care for children and young people with type 1 diabetes:

- structured education programmes
- behavioural interventions to improve adherence
- insulin regimens (multiple daily injections versus mixed insulin injections)
- strategies for glucose and ketone monitoring
• dietetic advice
• recognition and management of diabetic ketoacidosis
• recognition of complications and comorbidities.

m) Consideration is also being given to the following areas of care for children and young people with type 2 diabetes based on clinical priorities and likely availability of evidence:

• structured education programmes
• behavioural interventions to improve adherence
• dietetic advice
• weight management
• metformin monotherapy
• targets for HbA1c
• recognition and management of diabetic ketoacidosis
• recognition of complications and comorbidities.

4 The guideline

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

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

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

4.1 Population

4.1.1 Groups that will be covered
a) Children and young people (younger than 18 years) with type 1 diabetes.
b) Children and young people (younger than 18 years) with type 2 diabetes (new 2012).

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

- children and young people with an ethnicity associated with a high prevalence of diabetes
- disabilities (including learning disabilities)
- children and young people with comorbidities (medical or psychological conditions)
- children and young people with poor educational achievement.

4.1.2 Groups that will not be covered

a) Young women with diabetes who wish to conceive or who are pregnant.

b) Children and young people with other forms of diabetes mellitus (for example, monogenic diabetes and cystic fibrosis-related diabetes) (new 2012).

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

d) Adults (aged 18 years and older) with type 2 diabetes.

4.2 Healthcare setting

All settings in which NHS care is received or commissioned.

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

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

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

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

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

Areas from the original guideline that will be updated

a) The role of c-peptide and antibody testing in the diagnosis of type 1 and type 2 diabetes.

b) Structured education programmes for children and young people with type 1 diabetes.

c) Behavioural interventions to improve adherence in children and young people with type 1 diabetes.

d) Multiple daily injections versus mixed insulin injections in children and young people with type 1 diabetes.

e) HbA1c targets for children and young people with type 1 diabetes.

f) Glucose monitoring strategies in children and young people with type 1 diabetes, including:
  • blood glucose targets
  • frequency of intermittent testing (finger-prick read by meter)
  • continuous glucose monitoring with retrospective (intermittent) versus real-time (long-term) adjustment of treatment.
g) Blood ketone monitoring compared with urine ketone monitoring in children and young people with type 1 diabetes.

h) Dietetic advice, including carbohydrate counting and glycaemic index, for children and young people with type 1 diabetes.

i) Recognition and management of diabetic ketoacidosis in children and young people with type 1 diabetes:

- recognition based on symptoms, signs and biochemical abnormalities
- immediate management at presentation (for example, maintenance of airway, breathing and circulation or the potential need for a nasogastric tube to prevent pulmonary aspiration)
- clinical assessment and investigations at presentation to guide management
- fluid management, including:
  - assessment of dehydration
  - route of administration
  - rate and volume of administration
  - choice of fluid
  - other additives (for example, glucose, potassium and bicarbonate)
- insulin therapy, including:
  - timing
  - route of administration
  - dosage
- anticoagulant prophylaxis to prevent venous thrombosis
- clinical monitoring (to assess the response to treatment and to look for evidence of cerebral oedema), including:
  - general observations (for example, heart and respiratory rate and blood pressure)
  - body weight
  - hydration status
- fluid balance
- neurological observations
- electrocardiographic (ECG) monitoring
- laboratory monitoring (to assess the response to treatment and to look for evidence of hypokalaemia), including:
  - blood glucose
  - blood or urine ketones
  - serum urea and electrolytes
  - acid/base status.

j) Recognition of complications and comorbidities in children and young people with type 1 diabetes (retinopathy and nephropathy).

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

k) Structured education programmes for children and young people with type 2 diabetes.

l) Behavioural interventions to improve adherence in children and young people with type 2 diabetes.

m) Dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes.

n) Weight management in children and young people with type 2 diabetes who are overweight or obese to improve glycaemic control.

o) Metformin monotherapy for children and young people with type 2 diabetes.

p) HbA1c targets for children and young people with type 2 diabetes.

q) Recognition and management of diabetic ketoacidosis in children and young people with type 2 diabetes (the specific aspects to be...
covered for this area will be the same as those in section 4.3.1, point h).

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

4.3.2 Clinical issues that will not be covered

Areas from the original guideline that will not be updated

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

a) All aspects of diagnosis and initial management in children and young people other than those listed in section 4.3.1, including:
   - location of initial management after diagnosis
   - advice on the natural history of type 1 diabetes.

b) All aspects of ongoing management other than those listed in section 4.3.1, including:
   - insulin preparations, including new short- and long-acting insulins
   - methods of delivering insulin
   - metformin in addition to insulin for type 1 diabetes
   - exercise
   - advice on alcohol, smoking and recreational drugs
   - long-distance travel
   - immunisation.

c) All aspects of complications and associated conditions other than those listed in section 4.3.1, including:
   - hypoglycaemia
   - care during surgery
• monitoring for complications and comorbidities of type 1 diabetes other than those specified.

d) All aspects of psychological and social issues other than those listed in section 4.3.1, including:
   • emotional and behavioural problems, anxiety, depression and eating disorders
   • cognitive disorders
   • behavioural and conduct disorders
   • psychosocial support
   • adolescence.

e) Continuity of care, including:
   • communication between organisations
   • transition from paediatric to adult care.

Areas not covered by the original guideline or the update

f) Management of hypoglycaemia unawareness in children and young people with type 1 diabetes.

g) Glycaemic monitoring strategies for children and young people with type 2 diabetes.

h) Treatment for children and young people with type 2 diabetes in whom glycaemic control is not maintained with metformin.

i) Bariatric surgery for children and young people with type 2 diabetes.

j) Monitoring for complications and comorbidities of type 2 diabetes other than those specified in section 4.3.1.

k) Management of complications and comorbidities of type 1 or type 2 diabetes.
l) Contraceptive, pre-pregnancy and conception advice for children and young people with type 1 or type 2 diabetes.

m) Foot care for children and young people with type 1 or type 2 diabetes.

4.4 Main outcomes

a) Glycaemic control.

b) Any adverse effects of interventions used to manage type 1 or type 2 diabetes.

c) Health-related quality of life (validated questionnaire), for example, diabetes-specific health-related quality of life.

d) Complications of diabetes.

e) Mortality.

f) Psychological outcomes.

g) Patient satisfaction.

4.5 Review questions

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

Type 1 diabetes

- What is the effectiveness of c-peptide and antibody tests to distinguish type 1 and type 2 diabetes?
- What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?
- What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 1 diabetes?
• What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

• What is the optimal HbA1c target for children and young people with type 1 diabetes?

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

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

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

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

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

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

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

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

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

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

• What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?
• When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?

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

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

• Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:
  – general observations (for example, heart and respiratory rate and blood pressure)
  – body weight
  – hydration status
  – fluid balance
  – neurological observations
  – ECG monitoring?

• Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:
  – blood glucose
  – blood or urine ketones
  – serum urea or electrolytes
  – acid/base status?

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

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

**Type 2 diabetes**

• What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?
• What is the effectiveness of behavioural interventions to promote engagement with clinical services in children and young people with type 2 diabetes?

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

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

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

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

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

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

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

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

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

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

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

• How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?
• What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?

• Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:
  - general observations (for example, heart and respiratory rate and blood pressure)
  - body weight
  - hydration status
  - fluid balance
  - neurological observations
  - ECG monitoring?

• Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:
  - blood glucose
  - blood or urine ketones
  - serum urea or electrolytes
  - acid/base status?

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

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

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

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

4.6 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and
analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see 'Further information').

4.7 Status

Scope
This is the final scope.

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

5 Related NICE guidance

5.1 Published guidance

Related NICE guidance
- Preventing type 2 diabetes: risk identification and interventions for individuals at high risk. NICE public health guidance 38 (2012).
- Anxiety. NICE clinical guideline 113 (2011).
- Depression with a chronic physical health problem. NICE clinical guideline 91 (2010).
- Type 2 diabetes. NICE clinical guideline 87 (2009).
- Medicines adherence. NICE clinical guideline 76 (2009).
- Promoting physical activity for children and young people. NICE public health guidance 17 (2009).
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- **Obesity.** NICE clinical guideline 43 (2006).
- **Four commonly used methods to increase physical activity.** NICE public health guidance 2 (2006).
- **Type 2 diabetes. footcare.** NICE clinical guideline 10 (2004).

5.2 **Guidance under development**

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

- Lipid modification (update). NICE clinical guideline. Publication date to be confirmed.
- Buccal insulin for the management of type 1 diabetes. NICE technology appraisal guidance. Publication date to be confirmed.

6 **Further information**

Information on the guideline development process is provided in the following documents, available from the NICE website:
• ‘How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS’

• ‘The guidelines manual’

Information on the progress of the guideline will also be available from the NICE website.
Appendix C: Stakeholder organisations

C.1 Original (2004) stakeholder organisations

A. Menarini Diagnostics Ltd
Abbott Laboratories Limited (BASF/Knoll)
Afiya Trust
African and Caribbean Diabetes Association
Ambulance Service Association
Association of British Clinical Diabetologists
Association of British Health-Care Industries
Association of Clinical Biochemists
Association of the British Pharmaceuticals Industry
AstraZeneca UK Ltd
Atkins Nutritional Inc
Aventis Pasteur MSD
Aventis Pharma
Blood Pressure Association
Bournemouth Diabetes and Endocrine Centre
British Association of Prosthetists and Orthotists
British Association of Sport and Exercise Sciences
British Dietetic Association
British Geriatrics Society Special Interest Group in Diabetes
British Hypertension Society
British In Vitro Diagnostics Association
British Medical Association
British National Formulary
British Psychological Society
British Society for Paediatric Endocrinology and Diabetes
British Society of Periodontology
BUPA
Chartered Society of Physiotherapy
Cheshire West PCT and Ellesmere Port & Neston PCT Diabetes NSF LIT
Commission for Health Improvement
College of Optometrists
Coloplast Limited
Community District Nurses Association
ConvaTec
Department of Health
Depression Alliance
Diabetes UK
Eli Lilly and Company Ltd
Faculty of Dental Surgery
Faculty of Public Health
Fibroid Network Charity
General Medical Council
Health Development Agency
Heart UK
Institute of Sport and Recreation Management
Insulin Dependent Diabetes Trust
Johnson & Johnson Medical
Kidney Alliance
LifeScan
Limbless Association
Long Term Medical Conditions Alliance
Maternity Health Links
Medicines and Healthcare products Regulatory Agency
Medtronic Limited
Merck Sharp & Dohme
National Association of Theatre Nurses
Type 1 diabetes
National Council for Disabled People, Black, Minority and Ethnic Community
National Public Health Service
Newcastle PCT
NHS Information Authority
NHS Quality Improvement Scotland
Norfolk and Norwich University Hospital NHS Trust
Novo Nordisk Limited
Ortho Biotech
Patient Involvement Unit for NICE
Pfizer Limited
Prodigy
Provalis Diagnostics Ltd
Roche Diagnostics Limited
Royal College of Anaesthetists
Royal College of General Practitioners
Royal College of General Practitioners Wales
Royal College of Midwives
Royal College of Nursing
Royal College of Ophthalmologists
Royal College of Paediatrics and Child Health
Royal College of Pathologists
Royal College of Physicians of London
Royal College of Psychiatrists
Royal College of Surgeons of England
Royal National Institute of the Blind
Royal Pharmaceutical Society of Great Britain
Scottish Intercollegiate Guidelines Network
Sheffield Teaching Hospitals NHS Trust
Society of Chiropodists and Podiatrists
The Royal Society of Medicine
Tissue Viability Nurses Association
Tissue Viability Society
TOAST (The Obesity Awareness and Solutions Trust)
UK National Screening Committee
UK Pain Society
UK Thalassaemia Society
Welsh Assembly Government (formerly National Assembly for Wales)
Westmeria Healthcare Ltd
Guideline Development Group membership and acknowledgements
C.2 2015 update

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

Appendix D: Declarations of interest

D.1 2015 update

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

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

Table 1: GDG members' declarations of interest

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

**GDG member**

<table>
<thead>
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<th>Interest</th>
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<tbody>
<tr>
<td>on the management of diabetes at the 40th ISPAD conference in Toronto, Canada in September 2014; invited speaker at the ISPAD annual meeting 2012 and received funding from Roche towards accommodation expenses; invited speaker (on the topic of exercise and diabetes management) at the Juvenile Diabetes Research Foundation (JDRF) 'Type 1 diabetes discovery weekend' and received funding from JDRF towards travel expenses, the conference was supported by industry sponsorship; received educational grant (£250) from Novo Nordisk to cover the cost of ISPAD conference registration fee, the conference was supported by industry sponsorship</td>
</tr>
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</table>

**Non-personal pecuniary**

- Co-applicant for the following Health Technology Assessment (HTA) funded trials: Child and Adolescent Structured Competencies Approach to Diabetes Education (CASCADE), randomised controlled trial (RCT) of continuous subcutaneous insulin infusion compared to multiple daily injection regimens in children and young people at diagnosis of type 1 diabetes (Subcutaneous Insulin, Pumps or Injections (SCIP!)); organised an educational meeting on the topic of ‘exercise in diabetes’. Funds were received from Novo Nordisk to cover the costs of food and the venue. Francesca Annan did not receive these funds directly

**Personal non-pecuniary**

- Member of British Dietetic Association, Diabetes Management & Education Group (DMEG), Diabetes UK, ISPAD, Sports Dietitians UK; regular teaching commitments related to nutritional management of diabetes, and exercise and diabetes at University of York, University of Warwick, Coventry University, Birmingham Children’s Hospital; contributed to ISPAD guidelines on nutritional management and exercise; wrote articles on exercise and diabetes management and nutritional management of diabetes for Complete Nutrition and Diabetes Care for Children & Young People; presentations at national and international meetings on exercise and diabetes management; reviewed patient information content of Diabetes UK publications and pharmaceutical company literature (Lilly and Roche); chair of Paediatric Sub Group of Diabetes Management and Education Group (a specialist group of The British Dietetic Association) from April 2013; member of the writing group for ISPAD consensus guidelines

**Jo Dalton**

<table>
<thead>
<tr>
<th>Personal pecuniary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current post as paediatric diabetes specialist nurse funded by a diabetes charity within the Royal London Hospital</td>
</tr>
</tbody>
</table>

**Personal non-pecuniary**

- Member of the guideline development group (GDG) for the 2004 NICE guideline on type 1 diabetes in children and young people; member of the Royal College of Nursing (RCN), ISPAD, Primary Care Diabetes Society (PCDS), professional member of Diabetes UK, attended a study day funded by Medtronic on a topic that is not specific to the guideline scope (continuous subcutaneous insulin infusion therapy); registered for a symposium funded by Novo Nordisk in Leicester on paediatric diabetes in October 2014 but did not attend
### Declarations of interest

<table>
<thead>
<tr>
<th>GDG member</th>
<th>Interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jacqueline Double</td>
<td><strong>Personal pecuniary</strong> Honorarium from NHS Diabetes as Chair of national Parent Reference Group; invited speaker at 2 Friends For Life conferences and received free travel and food, the conferences were supported by industry sponsorship; received funding to cover travel expenses to attend a meeting in Australia funded by a number of commercial sources; gave a presentation at an IDF meeting in Melbourne. Travel expenses were paid by the organisation. <strong>Personal family interest</strong> Husband received funding to cover travel expenses from Children with Diabetes (a US not-for-profit organisation) to attend a Family Conference in the USA. <strong>Personal non-pecuniary</strong> Spoke for NHS Technology Adoption Centre (NTAC) and NHS Diabetes; ran workshops on schools, advocacy and mother’s emotional needs; member of Diabetes UK and JDRF; director of INPUT (a patient-run organisation that advocates for access to insulin pumps and diabetes technology in the UK) until December 2012; member of UK Children with Diabetes Advocacy Group.</td>
</tr>
<tr>
<td>Sarah Eaton</td>
<td><strong>Non-personal pecuniary</strong> Member of conference planning team for conferences organised by Diabetes UK and the Universities of York and Huddersfield. The conferences are sponsored by a number of pharmaceutical companies but Sarah Eaton does not receive any funding personally and is not responsible for management of the funds. <strong>Personal non-pecuniary</strong> Attended GP education meetings funded by Ashfield In2 Focus, Bayer Healthcare, Boehringer Ingelheim, HRA Pharma, Napp Pharmaceuticals, Pfizer, Reckit Benckiser; professional member of Diabetes UK, volunteer for Diabetes UK children’s care events; member of team (also involving Diabetes UK, University of Huddersfield and University of York) planning a conference on new developments in diabetes management in primary care.</td>
</tr>
<tr>
<td>Julie Edge (Chair of the diabetic ketoacidosis (DKA) subgroup)</td>
<td><strong>Personal pecuniary</strong> Honoraria for writing on type 1 diabetes for the British National Formulary for Children; honoraria for writing on type 1 diabetes for Practical Diabetes; attended the ISPAD annual meeting in Gothenburg as invited speaker and received expenses (travel, registration, 3 nights’ hotel accommodation and one evening meal) from ISPAD; received funding from the IDF to cover the cost of travel and accommodation expenses incurred when attending their meeting in Melbourne; received funding from the Australia Paediatric Society to cover registration and travel expenses to speak on the topic of cerebral oedema in children and young people with DKA at their Diabetes Meeting, the event was funded by a number of commercial sources; received funding from Diabetes UK to cover travel expenses to attend their Diabetes UK conference. <strong>Non-personal pecuniary</strong> Julie Edge holds managerial responsibility for departmental funding from Oxford Medical Diagnostics for a research project on a device not directly linked to any of the topics in.</td>
</tr>
<tr>
<td>GDG member</td>
<td>Interest</td>
</tr>
<tr>
<td>------------</td>
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</tr>
<tr>
<td></td>
<td>the scope, from Aventis, Novo Nordisk, and Roche for sponsorship of educational meetings, and from the British Heart Foundation, Diabetes UK, JDRF, National Institute for Health Research Comprehensive Clinical Research Network (NIHR CCRN) via the Comprehensive Local Research Networks (CLRN)s and Thames Valley Diabetes Research Network (TVRN) for the following research projects for which Julie Edge is the local principle investigator: Adolescent Type 1 Diabetes Cardio-Renal Intervention Trial (AdDIT); Diabetes Genome Anatomy Project (DGAP); and studies about insulin for diabetes including an RCT of continuous subcutaneous insulin infusion compared to multiple daily injection regimens in children and young people at diagnosis of type 1 diabetes (SCIPI); holds managerial responsibility for departmental funding from Advanced Therapeutics, Ánimas/LifeScan (part of Johnson and Johnson), Glucomen, Lilly, Novo Nordisk and Roche for sponsorship of educational meetings in 2013; holds managerial responsibility for departmental funding from Advanced Therapeutics, Aventis, Novo Nordisk and Roche for sponsorship of educational meetings in 2014; received funding from Novo Nordisk to cover travel expenses to attend and speak at a symposium (also funded by Novo Nordisk) in Leicester on paediatric diabetes in October 2014.</td>
</tr>
<tr>
<td></td>
<td>Personal non-pecuniary</td>
</tr>
<tr>
<td></td>
<td>Involved over many years in research on the management of DKA; lectured and prepared guidelines on DKA; member of Association of Children's Diabetes Clinicians (ACDC), BSPE, Diabetes UK and ISPAD; member of the writing group for ISPAD consensus guidelines; attended a half-day training course organised by Medtronic about continuous intravenous insulin therapy pumps; author of a paper looking at the timing of insulin therapy which was included in the guideline systematic review for the same topic; joint author on a paper looking at the rate of fluid administration which was included in the guideline systematic review for the same topic.</td>
</tr>
<tr>
<td>Nikhil Gokani</td>
<td>Personal pecuniary</td>
</tr>
<tr>
<td></td>
<td>Payment received for systematic reviewing work not directly linked to any of the topics in the guideline scope.</td>
</tr>
<tr>
<td></td>
<td>Personal non-pecuniary</td>
</tr>
<tr>
<td></td>
<td>Supporting member of Diabetes UK and member of its groups and committees; contingent PhD candidate in public health and law; member of the National Diabetes Audit Partnership Board; member of Royal College of Physicians (RCP) joint specialty committee on endocrinology and diabetes.</td>
</tr>
<tr>
<td>William Lamb</td>
<td>Personal pecuniary</td>
</tr>
<tr>
<td></td>
<td>Honoraria from Practical Diabetes for writing an article about adolescent diabetes and from Medtronic Ltd for lecturing on continuous glucose monitoring; honoraria from eMedicine.com (part of Medscape from WebMD) for writing and updating articles about diabetes and DKA; attended an educational meeting organised by Francesca Annan on the topic of exercise in diabetes, the meeting was sponsored by Novo Nordisk and travel expenses were paid by the conference organisers; received payment for medico-legal</td>
</tr>
</tbody>
</table>
GDG member | Interest
---|---
work (expert testimony and a report) in a case pertaining to paediatric diabetes care that was not specific to the scope of the guideline (neglect); received funding to cover travel expenses to speak at a conference on diabetes and exercise, the conference was sponsored by a number of insulin pump manufacturers; received funding from university employer to cover travel expenses to speak at a training course on the use of insulin pumps, the course was sponsored by a number of insulin pump manufacturers

Professional member of Diabetes UK; member of ACDC, BSPED and ISPAD; volunteer for Diabetes UK and JDRF; associate editor of Clinical Diabetes; attended meetings supported by various industry sponsors unknown to William Lamb as part of continuing professional development. Spoke at JDRF ‘Type 1 diabetes discovery weekend’, the event was supported by industry sponsorship but William Lamb received no funding

Carol Metcalfe | Personal pecuniary
Received funding from Novo Nordisk to attend the Diabetes UK annual Professional Conference in March 2014 and from Eli Lilly to attend the Eli Lilly National Paediatric Diabetes Meeting in May 2014; received funding from Roche to cover accommodation costs while attending a study day (also funded by Roche) on a topic that is not specific to the guideline scope (continuous subcutaneous insulin infusion therapy); received funding from Novo Nordisk to cover accommodation expenses while attending a symposium (also funded by Novo Nordisk) in Leicester on paediatric diabetes in October 2014

Claire Pesterfield | Non-personal pecuniary
Addenbrookes Charitable Trust will receive honoraria from Abbott, Animas, Roche and Medtronic for Claire Pesterfield presenting clinical case studies regarding diabetes care and preparing 2 articles for publication (1 about an education event (sports day) for Diabetes Care of Children and Young People and the other about management of neonatal diabetes for Diabetes Management)

Volunteer for Diabetes UK; IDF young leader programme mentor; wrote article about parental attitudes to a closed-loop blood glucose trial for Diabetes Technology and Therapeutics (2010); co-founder and director of Team Blood Glucose, a not-for-profit social enterprise that provides peer support and education resources to encourage people with or at risk of diabetes to participate in exercise

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

<table>
<thead>
<tr>
<th>Staff member</th>
<th>Interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarah Bailey</td>
<td>No interests declared</td>
</tr>
<tr>
<td>Frauke Becker</td>
<td>No interests declared</td>
</tr>
<tr>
<td>Zosia Beckles</td>
<td>No interests declared</td>
</tr>
<tr>
<td>Rupert Franklin</td>
<td>No interests declared</td>
</tr>
<tr>
<td>Yelan Guo</td>
<td>No interests declared</td>
</tr>
<tr>
<td>Paul Jacklin</td>
<td>No interests declared</td>
</tr>
</tbody>
</table>
Table 3: Expert advisers’ declarations of interest

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

Appendix E: Review protocols

E.1 Diagnosis

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

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

Question for compatibility with the evidence review for the adult’s guideline

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

### 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 or 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 does uncertainty exist, and what should be done when uncertainty exists?

### Population

Young people with all types of diabetes

- Young people is defined as aged at least 11 years and younger than 18 years
- Diabetes types are: type 1 diabetes, type 2 diabetes, latent autoimmune diabetes of adulthood (LADA) and maturity onset diabetes of the young (MODY)

### Subgroups

The following groups will be considered separately if data are available:

- Young people

### 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
- Other (zinc transporter 8 (ZnT8), islet-specific glucose-6-phosphatase catalytic subunit (IGRP), anti-ZnT8)

### Outcomes

- Presence of marker (number or percentage of participants with marker)
- Concentration of marker (ug/ml)
- Change in marker over time (number or percentage of participants with marker)
- Change in concentration of marker over time (ug/ml)

### Importance of outcomes

**Critical outcomes**
- Not relevant

### Study design

All study types

### Population size and directness

Studies will be excluded if any of the following apply.

- The population is mixed, with no young people 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
### Diagnosis

| Sample size restrictions. We will exclude studies if any of the following apply.  
  | • Adults and young people with sample size of N < 50 if we retrieve > 20 studies that have been conducted in young people and adults separately  
  | • Young people with a sample size of N < 50 if there are > 20 young people studies retrieved  
| Setting | All settings (as per scope)  
| Search strategy | Search will be restricted to studies published since the original guideline for type 1 diabetes in adults (2003). If only a few studies are found, then we will extend the search to all years  
| Review strategy | 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
Diagnosis – health economic evidence

Objectives
To identify economic studies relevant to the review question set out above

Criteria
Populations, interventions and comparators as specified in the individual review protocol above. Must be a relevant economic study design (cost-utility analysis, cost-benefit analysis, cost-effectiveness analysis, cost-consequence analysis, comparative cost analysis)

Search strategy
An economic study search was undertaken using population specific terms and an economic study filter

Review strategy
Each study is assessed using the NICE economic evaluation checklist - NICE guidelines manual (2009 edition)

Inclusion/exclusion criteria
- If a study is rated as both 'Directly applicable' and 'Minor limitations' (using the NICE economic evaluation checklist) then it should be included in the guideline. An evidence table should be completed and it should be included in the economic profile
- If a study is rated as either 'Not applicable' or 'Very serious limitations' then it should be excluded from the guideline. It should not be included in the economic profile and there is no need to include an evidence table
- If a study is rated as 'Partially applicable' and/or 'Potentially serious limitations' then there is discretion over whether it should be included. The health economist should make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the GDG if required. The ultimate aim being to include studies that are helpful for decision making in the context of the guideline and current NHS setting. Where exclusions occur on this basis, this should be noted in the relevant section of the guideline with references.

Also exclude:
- unpublished reports unless submitted as part of a call for evidence
- abstract-only studies
- letters
- editorials
- reviews of economic evaluations
- foreign language articles

Where there is discretion
The health economist should be guided by the following hierarchies.

Setting:
- UK NHS
- OECD countries with predominantly public health insurance systems (for example, France, Germany, and Sweden)
- OECD countries with predominantly private health insurance systems (for example, the USA, and Switzerland)
- Non-OECD settings (always 'Not applicable')

Economic study type:
- cost-utility analysis
- other type of full economic evaluation (cost-benefit analysis, cost-effectiveness analysis, cost-consequence analysis)
- comparative cost analysis
- non-comparative cost analyses including cost of illness studies (always 'Not applicable')

Year of analysis:
- the more recent the study, the more applicable it is

Quality and relevance of effectiveness data used in the economic analysis:
### E.2 Type 1 diabetes – education

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

<table>
<thead>
<tr>
<th><strong>Type 1 diabetes – education</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Existing recommendation(s) in 2004 guideline</strong></td>
</tr>
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<td></td>
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<tr>
<td><strong>Review question for update</strong></td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
</tr>
</tbody>
</table>
### Type 1 diabetes – education

| Type 1 diabetes. Structured education programmes deliver information to the child or young person, or their family, with the intention of improving outcomes and using a process which includes (see ISPAD Clinical Practice Consensus Guidelines 2009, Chapter 5 (Diabetes education in children and adolescents)):
| http://www.ispad.org/content/ispad-clinical-practice-consensus-guidelines-2009

- a structured, agreed, written curriculum
- use of trained educators
- quality assurance
- audit

| Language | English
---|---
| Study design | Systematic reviews and randomised controlled trials (RCTs) only

Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion. The next step might be to include systematic reviews of RCTs and nonrandomised comparative studies (but not individual nonrandomised studies).

| Status | Published articles indexed since the searches for the 2004 guideline were completed

This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles).

| Population | Children and young people with type 1 diabetes

The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years.

This review question will focus solely on ‘patient’ education (that is, education of healthcare professionals will be excluded).

| Intervention or index test | Structured education programmes specific to type 1 diabetes (education aimed at children and young people or their families)

A useful reference (systematic review) for educational and behavioural interventions is AHQR 2008 (Evidence report 166 http://www.ahrq.gov/clinic/tp/diabeticp.htm)

Possible search terms (based on AHQR 2008 systematic review plus GDG suggestions):
- education
- game
- information
- instruction
- intervention
- knowledge
## Type 1 diabetes – education

<table>
<thead>
<tr>
<th>Comparators or reference standard</th>
<th>Alternative models of structured education</th>
<th>Usual care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual care</td>
<td></td>
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</tbody>
</table>

**Physical outcomes**
- Glycaemic control
  - HbA1c (minimum follow-up 6 months after completion of primary intervention)
- Severe hypoglycaemic episodes
- Diabetic ketoacidosis (DKA; number of episodes)
- Adherence to diabetes management (including self-management)
- Adherence to education intervention

**Psychosocial outcomes**
- Health-related quality of life
- Children and young people’s and families’ satisfaction with intervention (education intervention)
- Risk-taking behaviours (such as smoking; this is of such importance that it has been included as an exceptional eighth outcome for data extraction)

This review should cover:
- all settings (diabetes clinics, schools, etc), while recognising that recommendations will be limited to the clinical practice context
- all forms of delivery of education (for example, one-to-one, brief, face-to-face, and remote (telemedicine, including text messaging))

Names of studies that might be relevant (not to be used as search terms):
- KICk-OFF (based on DAFNE)
- the ‘German model’ (see separate list of useful references)

**Clinical outcomes**

<table>
<thead>
<tr>
<th>Comparato r or reference standard</th>
<th>Alternative models of structured education</th>
<th>Usual care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual care</td>
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</tr>
</tbody>
</table>

The priority outcomes selected by the GDG are different to those for the review question on general behavioural interventions because psychosocial outcomes are more relevant there.

The GDG initially identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required. The minimum duration of follow-up was subsequently relaxed to cover follow-up from baseline (rather than completion of the primary intervention) to allow inclusion of clinically relevant evidence.

HbA1c minimally important difference (MID) is 0.5 percentage.
### Type 1 diabetes – education

<table>
<thead>
<tr>
<th>Health economic outcomes</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>This question was prioritised for health economic analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health-related quality of life and quality adjusted life years (QALYs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adherence to education intervention</td>
<td></td>
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</tr>
</tbody>
</table>

Severe hypoglycaemic episodes defined according to either of the following criteria. International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose) ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3) No long-term interventions needed to be prioritised as outcomes because HbA1c will determine these

| Other criteria for inclusion/exclusion of studies | None | | |

Studies that evaluate education programmes for healthcare professionals will be excluded (see above)

Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this (although the availability of such studies is not expected). Note that there are age-specific structured education programmes (mainly for young people)

Subgroup analysis according to the presence of associated conditions

| | | | |
| | | | |
### Type 1 diabetes – education

<table>
<thead>
<tr>
<th>Search strategies</th>
<th>See separate document</th>
<th>NCC-WCH technical team to search the PsycINFO bibliographic database for this review question (in addition to the standard bibliographic databases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review strategies</td>
<td>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence</td>
<td>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence</td>
</tr>
<tr>
<td>Equality</td>
<td>Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)</td>
<td>The notes above relating to subgroup analysis by associated conditions, language and cultural considerations reflect the importance of equalities issues in this question</td>
</tr>
</tbody>
</table>

such as autism spectrum disorder or learning difficulties, and according to language and culture-specific interventions would be useful if the evidence allows this.
E.3 Type 1 diabetes – behavioural interventions

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

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

<table>
<thead>
<tr>
<th><strong>Review question for update</strong></th>
<th>What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 1 diabetes?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objectives</strong></td>
<td>To determine the effectiveness of behavioural interventions in improving outcomes for children and young people with type 1 diabetes. The question is sufficiently broad to cover interventions aimed at families and healthcare professionals as well as those aimed at the child or young person. The GDG prioritised behavioural interventions that should be addressed in this question as follows.</td>
</tr>
<tr>
<td></td>
<td>- Family therapy (including behavioural family systems therapy (BFST)): this is always delivered to one family unit but it can include separate sessions with different members (individuals/groups) within the unit</td>
</tr>
<tr>
<td></td>
<td>- Cognitive behavioural therapy (CBT): this can be delivered one-to-one or in groups. The intervention focuses on recognising specific triggers for maladaptive behaviour and bringing about changes to behaviour</td>
</tr>
<tr>
<td></td>
<td>- Motivational interviewing: this can be delivered one-to-one or in groups. The intervention focuses on general exploration of ambivalence around maladaptive behaviours and what the person wants to do or should do. The</td>
</tr>
</tbody>
</table>
### Type 1 diabetes – behavioural interventions

<table>
<thead>
<tr>
<th>Intervention developed insight into maladaptive behaviour</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Counselling: this is delivered one-to-one but the content of interventions termed counselling may vary</td>
</tr>
<tr>
<td>• Mentoring: this can be delivered one-to-one or in groups. The mentor is typically older than the person receiving mentoring or is influential in the community</td>
</tr>
<tr>
<td>• Peer support: this can be delivered one-to-one or in groups. The intervention typically involves people of similar age to the person receiving peer support</td>
</tr>
</tbody>
</table>

#### Language

- **English**

#### Study design

- **Systematic reviews and randomised controlled trials (RCTs) only**

Study designs other than RCTs will be considered for any of the prioritised interventions only if no RCT evidence is identified for inclusion for that intervention. The next step might be to include systematic reviews of RCTs and nonrandomised comparative studies (but not individual nonrandomised studies).

#### Status

- **Published articles indexed since the searches for the 2004 guideline were completed**

This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles). The aim is to retain general recommendations that have not become outdated and to add specific recommendations about behavioural interventions if relevant.

#### Population

- **Children and young people with type 1 diabetes**

The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years.

#### Intervention or index test

- **Behavioural interventions specific to the management of type 1 diabetes in children and young people (this could involve interventions aimed at families and healthcare professionals as well as those aimed at the child or young person)**

- **Family therapy (include only validated therapies such as BFST – expert adviser to advise in relation to search results); it is likely that RCTs will be available for this type of intervention**

- **CBT; it is likely that RCTs will be available for this type of intervention**

Use the terms specific to the prioritised behavioural interventions when conducting the searches for this question. Useful reference (systematic review) for educational and behavioural interventions is AHQR 2008 (Evidence report 166 http://www.ahrq.gov/clinic/tp/diabedtp.htm). The following search terms from the
### Type 1 diabetes – behavioural interventions

- Motivational interviewing: it is possible that RCTs will be available for this intervention, although it is more likely to have been used in young people and adults rather than children
- Counselling: it is possible that RCTs will be available for this type of intervention
- Mentoring: there may be no RCTs evaluating this type of intervention
- Peer support: there may be no RCTs evaluating this type of intervention

AHRO 2008 systematic review were considered by the GDG and expert adviser as part of the prioritisation of behavioural interventions for this question but they were not selected for the reasons given and they should not be used as search terms for this question:

- adherence (an outcome not an intervention)
- behavioural therapy (poorly defined so not a priority)
- biofeedback (more relevant to the question relating to education programmes)
- cognitive therapy (not a priority because it focuses on awareness of behaviour but not changing behaviour)
- conjoint therapy (refers to any two therapies joined together)
- educational therapy (will be addressed in the education question)
- psychological interventions (not specific)
- psychological therapy (not specific)
- solution-focused therapy (not specific – refers to any therapy that focuses on solutions rather than problems; several of the prioritised interventions are solution-focused)
- therapy (not specific)

This review should cover:

- all settings (diabetes clinics, schools, etc), while recognising that recommendations will be limited to the clinical practice context
- all forms of delivery of the prioritised behavioural interventions (for example, one-to-one, brief, face-to-face, and remote (telemedicine))

Names of studies that might be relevant (not to be used as search terms):

- DEPICTED (motivational interviewing and agenda-setting for healthcare professionals)
- CASCADE (incomplete but expected to report during the guideline development period)
- FACTS (see, for example, the Diabetes UK and Juvenile Diabetes Foundation websites)
### Type 1 diabetes – behavioural interventions

<table>
<thead>
<tr>
<th>Comparators or reference standard</th>
<th>Physical outcomes</th>
<th>Usual care in this context usually includes education, no therapy, provision of information leaflets or multimedia (DVDs, CDs, websites, apps)</th>
</tr>
</thead>
<tbody>
<tr>
<td>An alternative behavioural intervention listed above</td>
<td>Physical outcomes</td>
<td>The GDG initially identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required. The minimum duration of follow-up was subsequently relaxed to cover follow-up from baseline (rather than completion of the primary intervention) to allow inclusion of clinically relevant evidence</td>
</tr>
<tr>
<td>An alternative and well defined behavioural intervention not listed above (expert adviser to advise on what is well defined in relation to search results)</td>
<td>Physical outcomes</td>
<td>The GDG noted that change in body mass index (BMI) standard deviation score (SDS) would be more important than DKA for the corresponding question for type 2 diabetes</td>
</tr>
<tr>
<td>Any other intervention aimed at changing a specific behaviour, a range of behaviours, or psychosocial adjustment to diabetes self-management</td>
<td>Physical outcomes</td>
<td>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</td>
</tr>
<tr>
<td>Usual care (this will be the most common comparator)</td>
<td>Physical outcomes</td>
<td>Severe hypoglycaemic episodes defined according to either of the following criteria.</td>
</tr>
</tbody>
</table>

#### Physical outcomes
- **Glycaemic control**
  - HbA1c (minimum follow-up 6 months after completion of primary intervention)
  - Adherence to diabetes management (the scope requires this; to include self-management)
- **Adverse events** (for example, severe hypoglycaemic episodes, diabetic ketoacidosis (DKA) or self-harm)

#### Psychosocial outcomes
- **Health-related quality of life**
- **Children and young people’s and families’ satisfaction with intervention**
- **Depression or anxiety**
- **School performance or attendance** (this will be very important for this question)
- **Risk-taking behaviours** (such as smoking; this is of such importance that it has been included as an exceptional eighth outcome for data extraction)

#### Comparators or reference standard

- **Behavioural interventions**
  - Usual care (this will be the most common comparator)
  - An alternative and well defined behavioural intervention not listed above (expert adviser to advise on what is well defined in relation to search results)
  - Any other intervention aimed at changing a specific behaviour, a range of behaviours, or psychosocial adjustment to diabetes self-management

#### Clinical outcomes

**Physical outcomes**
- **Glycaemic control**
  - HbA1c (minimum follow-up 6 months after completion of primary intervention)
  - Adherence to diabetes management (the scope requires this; to include self-management)
- **Adverse events** (for example, severe hypoglycaemic episodes, diabetic ketoacidosis (DKA) or self-harm)

**Psychosocial outcomes**
- **Health-related quality of life**
- **Children and young people’s and families’ satisfaction with intervention**
- **Depression or anxiety**
- **School performance or attendance** (this will be very important for this question)
- **Risk-taking behaviours** (such as smoking; this is of such importance that it has been included as an exceptional eighth outcome for data extraction)
## Type 1 diabetes – behavioural interventions

<table>
<thead>
<tr>
<th>Health economic outcomes</th>
<th>No long-term interventions needed to be prioritised as outcomes because HbA1c will determine these</th>
</tr>
</thead>
<tbody>
<tr>
<td>This question was not prioritised for health economic analysis</td>
<td>This question was rated as a medium (but not high) priority for health economic analysis, but it could be considered if resources allow, especially as there are parallels with the question on structured education packages, which was selected as a high priority for health economic analysis</td>
</tr>
<tr>
<td>Health-related quality of life and quality adjusted life years (QALYs)</td>
<td>GDG to note that, although mortality is not prioritised as a clinical outcome, health economic modelling incorporating data on mortality might be relevant through the link between hyperglycaemia and mortality</td>
</tr>
<tr>
<td>Adherence to treatment</td>
<td>It would only be necessary to consider the cost effectiveness of behavioural interventions if there were some evidence of clinical benefit. If behavioural interventions have a mixture of harms and benefits then a QALY approach could facilitate the appropriate trade-off. There may also be a need to model longer-term QALY gains or losses from intermediate trial or study outcomes (for example, changes in weight)</td>
</tr>
<tr>
<td>It may be possible attach a QALY to various long-term complications – this could be a longer list than the seven outcomes considered for the GRADE profiles</td>
<td></td>
</tr>
<tr>
<td>Other criteria for inclusion/exclusion of studies</td>
<td>None</td>
</tr>
<tr>
<td>Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this (although the availability of such studies is not expected). Subgroup analysis by ages within these groups would also be useful if it is feasible</td>
<td></td>
</tr>
<tr>
<td>Evidence tables should document who delivered the intervention(s), the frequency of contact with healthcare or other relevant professionals to deliver the intervention(s), and process evaluation information</td>
<td></td>
</tr>
<tr>
<td>Search strategies</td>
<td>See separate document</td>
</tr>
<tr>
<td>NCC-WCH technical team to search the PsycINFO bibliographic database for this review question (in addition to the standard bibliographic databases)</td>
<td></td>
</tr>
<tr>
<td>Review strategies</td>
<td>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided</td>
</tr>
<tr>
<td><strong>Type 1 diabetes – behavioural interventions</strong></td>
<td></td>
</tr>
<tr>
<td>:--</td>
<td></td>
</tr>
<tr>
<td>following weeding</td>
<td></td>
</tr>
<tr>
<td>Evidence tables and an evidence profile will be used to summarise the evidence</td>
<td></td>
</tr>
<tr>
<td><strong>Equality</strong></td>
<td></td>
</tr>
<tr>
<td>Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)</td>
<td></td>
</tr>
</tbody>
</table>
### E.4 Type 1 diabetes – multiple daily injections

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

<table>
<thead>
<tr>
<th><strong>Type 1 diabetes – multiple daily injections</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Existing recommendation(s) in 2004 guideline</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Review question for update</strong></td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
</tr>
<tr>
<td><strong>Language</strong></td>
</tr>
<tr>
<td><strong>Study design</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Status</strong></td>
</tr>
<tr>
<td><strong>Population</strong></td>
</tr>
</tbody>
</table>

The 2004 guideline contains the following definitions:
- pre-school children – children aged 1 year or older, and younger than 5 years
- primary school children – children aged 5 years or older, and younger than 11 years
- young people – people aged 11 years or older, and younger than 18 years

Although this is an update of part of a review question considered in the 2004 guideline, no date limit will be applied to searches to ensure that all relevant articles are identified and allow extraction of data in the form of GRADE profiles.

The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years.

Exclude studies involving children.
<table>
<thead>
<tr>
<th>Type 1 diabetes – multiple daily injections</th>
<th>or young people with type 2 diabetes unless the results for children and young people with type 1 diabetes are reported separately</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention or index test</td>
<td>Multiple daily injections of insulin, with or without carbohydrate counting</td>
</tr>
<tr>
<td></td>
<td>The definition of multiple daily injections will be four or more injections per day using unmixed insulin (meaning insulins that are not mixed in the syringe)</td>
</tr>
<tr>
<td></td>
<td>The 2004 guideline defines multiple daily injections as follows: the person has injections of short-acting insulin or rapid-acting insulin analogue before meals, together with one or more separate daily injections of intermediate-acting insulin or long-acting insulin analogue</td>
</tr>
<tr>
<td></td>
<td>Evidence tables should record additional care received (carbohydrate counting, advice, monitoring, etc)</td>
</tr>
<tr>
<td></td>
<td>Any articles in which four or more injections were given but it was not clear from the title or abstract whether mixed or unmixed insulin was used should be ordered and discussed with the GDG</td>
</tr>
<tr>
<td></td>
<td>The GDG noted that studies in which short-term intensive insulin treatment is used from diagnosis are not relevant for this question</td>
</tr>
<tr>
<td></td>
<td>Report the following types of studies separately:</td>
</tr>
<tr>
<td></td>
<td>• those in which all participants are studied from diagnosis</td>
</tr>
<tr>
<td></td>
<td>• those in which all participants receive a change in treatment simultaneously</td>
</tr>
<tr>
<td></td>
<td>• those in which selected children and young people receive a change in treatment (for example, because usual treatment has failed)</td>
</tr>
<tr>
<td>Comparator or reference standard</td>
<td>Fewer than four injections or occasions of injecting per day. Predominantly mixed insulin regimens – combinations of insulins with different durations of action given in a single injection – also includes regimens where such insulins are given in separate injections but at the same time. Two injections given at the same time will count</td>
</tr>
<tr>
<td></td>
<td>The definition of a mixed insulin regimen will be one in which fewer than four injections per day using mixed insulin (meaning insulin with different durations of action mixed in the syringe) are administered</td>
</tr>
</tbody>
</table>
### Type 1 diabetes – multiple daily injections

as one mixed injection

25:75 and 30:70 mixes are currently available in the UK, but studies involving other mixes (for example, 40:60) or free-mixed insulin are also eligible for inclusion.

The 2004 guideline defines fewer than four injections per day as follows: injections of short-acting insulin or rapid-acting insulin analogue mixed with intermediate-acting insulin. The insulin preparations may be mixed by the patient at the time of injection.

For example, mixtures of 25-30% short-acting analogue with an intermediate insulin (such as Humalog mix25)

Any articles in which fewer than four injections were given but it was not clear from the title or abstract whether mixed or unmixed insulin was used should be ordered and discussed with the GDG.

### Clinical outcomes

#### Physical outcomes

- Glycaemic control
  - HbA1c (minimum follow-up 6 months)
  - Severe hypoglycaemic episodes
  - Diabetic ketoacidosis (DKA; number of episodes)
- Adherence to diabetes management (including self-management)
- Changes in body mass index (BMI) standard deviation score (SDS)

#### Psychosocial outcomes

- Health-related quality of life
- Children and young people’s and families’ satisfaction with intervention

The GDG considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes.

HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)

Severe hypoglycaemic episodes defined according to either of the following criteria.

- International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose)
- ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or
### Type 1 diabetes – multiple daily injections

| **Health economics outcomes** | This question was prioritised for health economic analysis  
Health-related quality of life (measured using quality adjusted life years (QALYs))  
Adherence to diabetes management (including self-management)  
It may be possible attach a QALY weight to various long-term complications – this could be a longer list than the seven outcomes considered for GRADE profiles |
| **Other criteria for inclusion/exclusion of studies** | Exclude studies with <10 participants in total |
| **Search strategies** | See separate document |
| **Review strategies** | Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)  
A list of excluded studies will be provided following weeding  
Evidence tables and an evidence profile will be used to summarise the evidence |
| **Equality** | Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012) |

unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)

BMI SDS minimally important difference is 0.5 for weight-loss interventions and 0 for all other interventions

平等与健康经济结果

健康相关生活质量（用质量调整寿命年（QALYs）衡量）

遵循糖尿病管理（包括自我管理）

可能将QALY权重附加到各种长期并发症上——这可能是比考虑的七个结果更长的列表。

**其他标准**

排除总参与者<10的研究

**实验策略**

- 根据描述在NICE指南手册（2012年11月）中的过程评估质量。
- 列出排除的研究。
- 证据表格和证据概要将被用于总结证据。

**平等**

按照描述在NICE指南手册（2012年11月）中的过程评估平等性问题。
Type 1 diabetes – HbA1c targets

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

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

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Comparator or reference standard</th>
<th>Clinical outcomes</th>
</tr>
</thead>
</table>
| Specified target value for HbA1c or HbA1c values achieved (recorded) | Comparisons to be made between outcomes according to target values for HbA1c and/or HbA1c values achieved (recorded) | Physical outcomes  
- Glycaemic control  
  o Severe hypoglycaemic episodes (frequency)  
  o Nocturnal hypoglycaemic episodes (frequency)  
  o Any hypoglycaemic episode (however defined; frequency)  
- Contact with the diabetes care team as a measure of healthcare utilisation  

Psychosocial outcomes  
- Health-related quality of life  
- Children and young people’s and families’ satisfaction with intervention (acceptability and comfort associated with testing, and anxiety or stress associated with trying to meet specific targets would be reflected here, but these were not expected to be reported frequently enough to warrant consideration as separate outcomes)  

The GDG used the review protocol for the question related to blood glucose monitoring for type 1 diabetes as the starting point for the outcomes to be considered for this question  
- Outcomes related to hypoglycaemia were prioritised for inclusion because the risk of hypoglycaemia is important with type 1 diabetes; this contrasts with the corresponding protocol for HbA1c targets for type 2 diabetes where the risk of long-term complications is more important  
- The GDG identified a minimum follow-up period of 4 months after completion of the primary intervention for all prioritised outcomes. Include further follow-up if reported, for example, if a top-up intervention is required  
- Severe hypoglycaemic episodes defined according to either of the following criteria.  
  - International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose)  
  - ISPAD 2000 grade 2 or 3 – the
<table>
<thead>
<tr>
<th><strong>Type 1 diabetes – HbA1c targets</strong></th>
<th>child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health economic outcomes</td>
<td>This question was not prioritised for health economic analysis</td>
</tr>
<tr>
<td>Other criteria for inclusion/exclusion of studies</td>
<td>None</td>
</tr>
<tr>
<td>Search strategies</td>
<td>See separate document</td>
</tr>
<tr>
<td>Review strategies</td>
<td>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence</td>
</tr>
<tr>
<td>Equality</td>
<td>Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)</td>
</tr>
</tbody>
</table>
### E.6 Type 1 diabetes – blood glucose targets

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

<table>
<thead>
<tr>
<th>Type 1 diabetes – blood glucose targets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Existing recommendation(s) in 2004 guideline</strong></td>
</tr>
<tr>
<td><strong>Review question for update</strong></td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
</tr>
<tr>
<td><strong>Language</strong></td>
</tr>
<tr>
<td><strong>Study design</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Status</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Population</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
### Type 1 diabetes – blood glucose targets

<table>
<thead>
<tr>
<th>Pay attention</th>
<th>have published blood glucose targets as search terms:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• American Diabetes Association (ADA)</td>
</tr>
<tr>
<td></td>
<td>• Australasian Paediatric Endocrine Group (APEG)</td>
</tr>
<tr>
<td></td>
<td>• International Society for Pediatric and Adolescent Diabetes (ISPAD)</td>
</tr>
</tbody>
</table>

The GDG may be interested in:

- recommending more intensive blood glucose control than the 2004 guideline (for example, reducing the upper limit of the target range, and/or narrowing the target range)
- considering the timing and frequency of monitoring relative to meals, etc
- setting different targets depending on the insulin regimen used and for different age groups

<table>
<thead>
<tr>
<th>Comparator or reference standard</th>
<th>Comparisons to be made between outcomes according to target ranges for blood glucose and/or blood glucose values achieved (recorded)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Clinical outcomes</th>
<th>Physical outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Glycaemic control</td>
</tr>
<tr>
<td></td>
<td>o HbA1c (minimum follow-up 6 months)</td>
</tr>
<tr>
<td></td>
<td>o Severe hypoglycaemic episodes</td>
</tr>
<tr>
<td></td>
<td>o Nocturnal hypoglycaemic episodes</td>
</tr>
<tr>
<td></td>
<td>o Diabetic ketoacidosis (DKA; number of episodes)</td>
</tr>
<tr>
<td></td>
<td>• Contact with the diabetes care team as a measure of healthcare utilisation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Psychosocial outcomes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Health-related quality of life</td>
<td></td>
</tr>
<tr>
<td>• Children and young people’s and families’ satisfaction with intervention (acceptability and comfort associated with testing, and anxiety or stress associated with trying to meet specific targets would be reflected here, but these were not expected to be reported frequently enough to warrant consideration as separate outcomes)</td>
<td></td>
</tr>
</tbody>
</table>

The GDG identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required.

HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)

Severe hypoglycaemic episodes defined according to either of the following criteria.
### Type 1 diabetes – blood glucose targets

- **International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009** – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose)
- **ISPAD 2000 grade 2 or 3** – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)

<table>
<thead>
<tr>
<th>Health economic outcomes</th>
<th>This question was not prioritised for health economic analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other criteria for inclusion/exclusion of studies</td>
<td>None</td>
</tr>
<tr>
<td>Search strategies</td>
<td>See separate document</td>
</tr>
</tbody>
</table>
| Review strategies | Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)  
A list of excluded studies will be provided following weeding  
Evidence tables and an evidence profile will be used to summarise the evidence |
| Equality | Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012) |
### E.7 Type 1 diabetes – blood glucose monitoring

**Review questions:**

- How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?
- What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?
- What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?

#### Type 1 diabetes – blood glucose monitoring – frequency of finger prick testing

<table>
<thead>
<tr>
<th>Existing recommendation(s) in 2004 guideline</th>
<th>Children and young people with type 1 diabetes and their families should be encouraged to perform frequent blood glucose monitoring as part of a continuing package of care that includes dietary management, continued education and regular contact with their diabetes care teams.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Children and young people with type 1 diabetes who are trying to optimise their glycaemic control and/or have intercurrent illness should be encouraged to measure their blood glucose levels more than four times per day.</td>
</tr>
<tr>
<td></td>
<td>Children and young people with type 1 diabetes should be encouraged to monitor their blood glucose levels before and after exercise so that they can:</td>
</tr>
<tr>
<td></td>
<td>• identify when changes in insulin or food intake are necessary</td>
</tr>
<tr>
<td></td>
<td>• learn the glycaemic response to different exercise conditions</td>
</tr>
<tr>
<td></td>
<td>• be aware of exercise-induced hypoglycaemia</td>
</tr>
<tr>
<td></td>
<td>• be aware that hypoglycaemia may occur several hours after prolonged exercise.</td>
</tr>
<tr>
<td></td>
<td>Young people with type 1 diabetes who drink alcohol should be informed that they should:</td>
</tr>
<tr>
<td></td>
<td>• eat food containing carbohydrate before and after drinking</td>
</tr>
<tr>
<td></td>
<td>• monitor their blood glucose levels regularly and aim to keep the levels within the recommended range by</td>
</tr>
<tr>
<td></td>
<td>• eating food containing carbohydrate.</td>
</tr>
<tr>
<td></td>
<td>Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no...</td>
</tr>
<tr>
<td></td>
<td>The GDG commented that 5 tests a day or more is considered to be good practice and so this should be the comparison for RCTs (5 or more per day compared with 4 or fewer)</td>
</tr>
</tbody>
</table>
## Type 1 diabetes – blood glucose monitoring – frequency of finger prick testing

<table>
<thead>
<tr>
<th>Review question for update</th>
<th>How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objectives</strong></td>
<td>To identify the optimal frequency of capillary blood glucose testing (at any site) in children and young people with type 1 diabetes. The question is designed to identify which frequency (or range of frequencies) of testing is associated with optimal glycaemic control and thus a reduced risk of long-term complications</td>
</tr>
</tbody>
</table>

Notes from GDG:
- frequent blood glucose testing helps to mitigate against hypoglycaemia unawareness
- blood glucose level- anxiety is related to excessive testing
- excessive testing can be more expensive than continuous glucose monitoring, and so clinicians often use excessive testing as a rationale for requesting funding for continuous monitoring systems

<table>
<thead>
<tr>
<th>Language</th>
<th>English</th>
</tr>
</thead>
</table>

### Study design

- Systematic reviews and randomised controlled trials (RCTs) and observational studies

Studies that may be of interest:
- Hvidore (name of a town in Denmark – pan-European audit)
- Hanas (Swedish author) may also be relevant
- DPV study (German)
- Type 1 exchange study (USA)

### Status

- Published articles (no limitation on year of publication)

The original guideline did not consider non-comparative, observational studies and so no date limit will be applied to searches

### Population

- Children and young people with type 1 diabetes

### Intervention or index test

- RCTs: 5 or more finger-prick tests per day
- Observational studies: frequency varies with lower limit of 0 tests per day and no upper limit

It is not expected that there will be RCTs that fully answer this question and so no restriction in study design will be applied to the literature searches. This reflects the following considerations:
- there are unlimited possibilities in terms of the frequency of testing
- it might be difficult ethically to randomise any participants to just a few tests
- including observational studies will allow consideration of no testing at all, which would never be recommended practice

### Comparator or reference standard

- RCTs: 4 or fewer finger-prick tests per day
- Observational studies: different frequencies of testing

### Clinical

- Physical outcomes

The GDG selected 7 outcomes and...
Type 1 diabetes – blood glucose monitoring – frequency of finger prick testing

| outcomes | agreed to use them across the three questions relating to blood glucose monitoring (with the exception of DKA which is used in this question but is replaced in the CGMS questions by mean blood glucose levels):

- frequency of finger-prick (capillary) testing,
- sustained use of continuous subcutaneous glucose monitoring with real-time adjustment of insulin treatment versus intermittent use of continuous subcutaneous glucose monitoring with retrospective adjustment of insulin treatment, and
- finger-prick (capillary) testing versus continuous subcutaneous glucose monitoring

Continuous subcutaneous glucose monitoring may be associated with very good control (low HbA1c) yet may also occur as part of the management of type 1 diabetes in children and young people with poor long-term control

The GDG considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes

HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)

Severe hypoglycaemic episodes defined according to either of the following criteria.

- International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose)
- ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or
### Type 1 diabetes – blood glucose monitoring – frequency of finger prick testing

<table>
<thead>
<tr>
<th>Health economics outcomes</th>
<th>This question was prioritised for health economic analysis Health-related quality of life (measured using quality adjusted life years (QALYs)) In particular, risk of complications or accidents resulting from mild or severe hypoglycaemic episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this (frequency of testing is likely to depend on age)</td>
<td></td>
</tr>
<tr>
<td>Other criteria for inclusion/exclusion of studies</td>
<td>None</td>
</tr>
<tr>
<td>Search strategies</td>
<td>See separate document</td>
</tr>
<tr>
<td>Review strategies</td>
<td>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence</td>
</tr>
<tr>
<td>Equality</td>
<td>Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)</td>
</tr>
<tr>
<td>School regulations can be a barrier to uptake, which creates variations in practice The GDG noted that it can be helpful if spare pens, meters and strips are available in schools</td>
<td></td>
</tr>
</tbody>
</table>

### Type 1 diabetes – blood glucose monitoring – finger prick testing versus continuous glucose monitoring

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

**Question for update**  
Glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?

- Can be used daily or just at night. Monitoring devices are often supplied by the diabetes care team for short-term use (4-5 days) for trouble-shooting multiple daily injection regimens, for example, to get an idea of when hypoglycaemia occurs (often at night). More recently, they have been made available to the child or young person for long-term use.
- The child or young person may not see the results that are recorded – the results may be transmitted to the diabetes care team and analysed retrospectively.
- This question covers all forms of finger-prick testing and continuous glucose monitoring.

**Objectives**  
To identify the circumstances in which children and young people with type 1 diabetes should be offered continuous subcutaneous glucose monitoring in addition to capillary blood testing (finger-prick testing).

- NICE has confirmed that evidence relating to insulin pumps that perform a continuous glucose monitoring function can be considered in this review (alongside evidence relating to standalone continuous glucose monitoring devices). The guideline will not be able to make any specific recommendations in relation to insulin pumps and the review should avoid commenting on individual insulin pumps. The guideline will be able to cross-reference to the NICE technology appraisal (TA) 151 on insulin pump therapy for diabetes where appropriate (see [http://publications.nice.org.uk/continuous-subcutaneous-insulin-infusion-for-the-treatment-of-diabetes-mellitus-ta151](http://publications.nice.org.uk/continuous-subcutaneous-insulin-infusion-for-the-treatment-of-diabetes-mellitus-ta151)).

**Language**  
English

**Study design**  
Systematic reviews and randomised controlled trials (RCTs) only


The following studies might be relevant to this question:
- Pickup 2011 (meta-analysis based on individual patient data – see BMJ 2011;343:d3805 doi: 10.1136/bmj.d3805)
- Bergenstal 2010 (multicentre)
<table>
<thead>
<tr>
<th>Status</th>
<th>Published articles indexed since the searches for the 2004 guideline were completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>Children and young people with type 1 diabetes</td>
</tr>
</tbody>
</table>
| Intervention or index test | Any form of continuous subcutaneous glucose monitoring, including:  
  - sustained use of continuous subcutaneous glucose monitoring (providing real-time, ongoing output)  
  - continuous subcutaneous glucose monitoring performed intermittently and analysed retrospectively without the child or young person seeing the measurements |
| Comparator or reference standard | Any form of capillary blood glucose testing, including:  
  - finger-prick testing  
  - testing at another anatomical site  
  - any frequency of testing |
| Clinical outcomes | Physical outcomes  
  - Glycaemic control  
    - HbA1c (minimum follow-up 6 months – if not available then use 3-month follow-up)  
    - mean blood glucose levels  
    - severe hypoglycaemic episodes  
    - nocturnal hypoglycaemic episodes  
  - Adherence to diabetes management (including self-management)  
Psycho-social outcomes  
  - Health-related quality of life |


This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles), although it is unlikely that many of them will be relevant because technology has moved on. Short-term use and loan of monitoring devices is, however, still relevant.

In all instances, finger-prick testing needs to be used alongside continuous subcutaneous glucose monitoring for the purposes of calibrating the continuous monitoring device.

Note to NCC-WCH: all monitoring methods that involve a subcutaneous cannula are of interest in this question, but evidence relating to any version of glucowatch (which is now obsolete) should be excluded.

Self-monitoring of blood glucose (SMBG) is standard term in clinical practice and research articles.

The GDG agreed that all frequencies of SMBG will be included.

The GDG selected 7 outcomes and agreed to use these across the three questions relating to blood glucose monitoring (with the exception of mean blood glucose levels which would be excluded from the frequency question and replaced with DKA):  
- frequency of finger-prick (capillary) testing,  
- sustained use of continuous subcutaneous glucose monitoring with real-time
### Type 1 diabetes – blood glucose monitoring – finger prick testing versus continuous glucose monitoring

<table>
<thead>
<tr>
<th>Children and young people’s and families’ satisfaction with intervention (impact of pain to be reflected here)</th>
<th>adjustment of insulin treatment versus intermittent use of continuous subcutaneous glucose monitoring with retrospective adjustment of insulin treatment, and</th>
</tr>
</thead>
<tbody>
<tr>
<td>finger-prick (capillary) testing versus continuous subcutaneous glucose monitoring</td>
<td>Continuous subcutaneous glucose monitoring may be associated with very good control (low HbA1c) yet may also occur as part of the management of type 1 diabetes in children and young people with poor long-term control</td>
</tr>
</tbody>
</table>

The GDG considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes.

HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)

Severe hypoglycaemic episodes defined according to either of the following criteria.

- International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose)
- ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with
<table>
<thead>
<tr>
<th><strong>Type 1 diabetes – blood glucose monitoring – finger prick testing versus continuous glucose monitoring</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis and management of type 1 diabetes in children and young people</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Review protocols</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Health economics outcomes</strong></td>
<td>This question was prioritised for health economic analysis</td>
</tr>
<tr>
<td></td>
<td>Health-related quality of life (measured using quality adjusted life years (QALYs))</td>
</tr>
<tr>
<td></td>
<td>In particular, risk of complications or accidents resulting from mild or severe hypoglycaemic episodes</td>
</tr>
<tr>
<td></td>
<td>or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)</td>
</tr>
<tr>
<td><strong>Other criteria for inclusion/exclusion of studies</strong></td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this</td>
</tr>
<tr>
<td></td>
<td>Subgroup analysis for insulin pump therapy versus multiple daily injections would be of interest</td>
</tr>
<tr>
<td></td>
<td>Subgroup analysis based on how continuous subcutaneous glucose monitoring is used (sustained versus intermittent) would be of interest</td>
</tr>
<tr>
<td><strong>Search strategies</strong></td>
<td>See separate document</td>
</tr>
<tr>
<td></td>
<td>A single search for evidence will be undertaken across the three questions relating to blood glucose monitoring</td>
</tr>
<tr>
<td><strong>Review strategies</strong></td>
<td>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</td>
</tr>
<tr>
<td></td>
<td>A list of excluded studies will be provided following weeding</td>
</tr>
<tr>
<td></td>
<td>Evidence tables and an evidence profile will be used to summarise the evidence</td>
</tr>
<tr>
<td><strong>Equality</strong></td>
<td>Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)</td>
</tr>
<tr>
<td></td>
<td>The possibility of providing spare pens, meters, strips and continuous subcutaneous glucose monitoring devices to keep in school was raised by the GDG</td>
</tr>
<tr>
<td><strong>Type 1 diabetes – blood glucose monitoring – intermittent versus real-time continuous glucose monitoring</strong></td>
<td></td>
</tr>
<tr>
<td>--------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td><strong>Existing recommendation(s) in 2004 guideline</strong></td>
<td>Children and young people with type 1 diabetes who have persistent problems with hypoglycaemia unawareness or repeated hypoglycaemia or hyperglycaemia should be offered continuous glucose monitoring systems.</td>
</tr>
<tr>
<td>Updating needs to be clear about which children and young people would benefit from using continuous glucose monitoring systems</td>
<td></td>
</tr>
<tr>
<td><strong>Review question for update</strong></td>
<td>What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?</td>
</tr>
</tbody>
</table>
| **Objectives** | To identify the optimal use of continuous subcutaneous glucose monitoring (sustained use with real-time adjustment versus intermittent use with retrospective adjustment) in children and young people with type 1 diabetes. The question focuses on the comparative effectiveness in children and young people with type 1 diabetes of:  
- sustained continuous subcutaneous glucose monitoring (providing real-time, ongoing output and adjustment to insulin treatment where appropriate), and  
- continuous subcutaneous glucose monitoring performed intermittently with retrospective adjustment of insulin treatment.  
- In all instances, finger-prick testing needs to be used alongside continuous subcutaneous glucose monitoring for the purposes of calibrating the continuous monitoring device. |
| **NICE** has confirmed that evidence relating to insulin pumps that perform a continuous glucose monitoring function can be considered in this review (alongside evidence relating to standalone continuous glucose monitoring devices). The guideline will not be able to make any specific recommendations in relation to insulin pumps and the review should avoid commenting on individual insulin pumps. The guideline will be able to cross-reference to the NICE technology appraisal (TA) 151 on insulin pump therapy for diabetes where appropriate (see http://publications.nice.org.uk/continuous-subcutaneous-insulin-infusion-for-the-treatment-of-diabetes-mellitus-ta151) |
| **Language** | English |
| **Study design** | Systematic reviews and randomised controlled trials (RCTs) only |
| **A 2012 Cochrane review 'Continuous glucose monitoring systems for type 1 diabetes mellitus' contains seven RCTs** |
### Type 1 diabetes – blood glucose monitoring – intermittent versus real-time continuous glucose monitoring

<table>
<thead>
<tr>
<th>Status</th>
<th>Published articles indexed since the searches for the 2004 guideline were completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Status</td>
<td>This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles), although it is unlikely that many of them will be relevant because technology has moved on. Short-term use and loan of monitoring devices is, however, still relevant.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Population</th>
<th>Children and young people with type 1 diabetes</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Intervention or index test</th>
<th>Sustained use of continuous subcutaneous glucose monitoring (providing real-time, ongoing output)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Comparator or reference standard</th>
<th>Continuous subcutaneous glucose monitoring performed intermittently and analysed retrospectively without the child or young person seeing the measurements</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Clinical outcomes</th>
<th>Physical outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Glycaemic control</td>
</tr>
<tr>
<td></td>
<td>o HbA1c (minimum follow-up 6 months)</td>
</tr>
<tr>
<td></td>
<td>o Mean blood glucose levels</td>
</tr>
<tr>
<td></td>
<td>o Severe hypoglycaemic episodes</td>
</tr>
<tr>
<td></td>
<td>o Nocturnal hypoglycaemic episodes</td>
</tr>
<tr>
<td></td>
<td>• Adherence to diabetes management (including self-management)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Psycho-social outcomes</th>
<th>• Health-related quality of life</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Children and young people’s and families’ satisfaction with intervention (impact of pain to be reflected here)</td>
</tr>
</tbody>
</table>

The GDG selected 7 outcomes and agreed to use these across the three questions relating to blood glucose monitoring (with the exception of mean blood glucose levels which would be excluded from the frequency question and replaced with DKA):

- frequency of finger-prick (capillary) testing,
- sustained use of continuous subcutaneous glucose monitoring with real-time adjustment of insulin treatment versus intermittent use of continuous subcutaneous glucose monitoring with retrospective adjustment of insulin treatment, and
- finger-prick (capillary) testing versus continuous subcutaneous glucose monitoring

Continuous subcutaneous glucose monitoring may be associated with very good control (low HbA1c) yet may also occur as part of the management of type 1 diabetes in children and young people with poor long-term outcomes.
### Type 1 diabetes – blood glucose monitoring – intermittent versus real-time continuous glucose monitoring

<table>
<thead>
<tr>
<th>control</th>
</tr>
</thead>
<tbody>
<tr>
<td>The GDG considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes</td>
</tr>
<tr>
<td>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</td>
</tr>
<tr>
<td>Severe hypoglycaemic episodes defined according to either of the following criteria.</td>
</tr>
<tr>
<td>- International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose)</td>
</tr>
<tr>
<td>- ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)</td>
</tr>
</tbody>
</table>

### Health economics outcomes

<table>
<thead>
<tr>
<th>Health economics outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>This question was prioritised for health economic analysis</td>
</tr>
<tr>
<td>Health-related quality of life (measured using quality adjusted life years (QALYs))</td>
</tr>
<tr>
<td>In particular, risk of complications or accidents resulting from mild or severe hypoglycaemic episodes</td>
</tr>
</tbody>
</table>

### Other criteria for inclusion/exclusion of studies

<table>
<thead>
<tr>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this</td>
</tr>
<tr>
<td>Type 1 diabetes – blood glucose monitoring – intermittent versus real-time continuous glucose monitoring</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Search strategies</td>
</tr>
<tr>
<td>A single search for evidence will be undertaken across the three questions relating to blood glucose monitoring</td>
</tr>
<tr>
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<td>A list of excluded studies will be provided following weeding</td>
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<tr>
<td>Evidence tables and an evidence profile will be used to summarise the evidence</td>
</tr>
<tr>
<td>Equality</td>
</tr>
<tr>
<td>The possibility of providing spare devices to keep in school was raised by the GDG</td>
</tr>
</tbody>
</table>
### E.8 Type 1 diabetes – blood ketone monitoring

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

| **Type 1 diabetes – blood ketone monitoring** |
|---|---|---|
| **Existing recommendation(s) in 2004 guideline** | Children and young people with type 1 diabetes should have short-acting insulin or rapid-acting insulin analogues and blood and/or urine ketone testing strips available for use during intercurrent illness. | The 2004 guideline also includes a recommendation for further research to evaluate the role of blood ketone monitoring in preventing diabetic ketoacidosis (DKA) in children and young people with type 1 diabetes. |
| **Review question for update** | What is the effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of DKA? |
| **Objectives** | To compare the clinical and cost effectiveness of blood ketone monitoring and urine ketone monitoring in the prevention or early detection of DKA in children and young people with type 1 diabetes. The question relates to home monitoring of ketones (rather than monitoring in hospital during treatment for DKA). It should include consideration of the frequency of monitoring, and the potential use of ketone monitoring will be interpreted more broadly than in relation to intercurrent illness. Comparisons between monitoring during intercurrent illness and at other times, depending on the insulin regimen being used (and especially when using insulin pump therapy), will be considered if the evidence allows |
| **Language** | English |
| **Study design** | Systematic reviews and randomised controlled trials (RCTs) Comparative observational studies (including cohort and case-control studies) | Study designs other than RCTs will be considered only if no RCT evidence is identified for inclusion |
| **Status** | Published articles indexed since the searches for the 2004 guideline were completed | This is an update of part of a review question considered in the 2004 guideline. The studies included in the 2004 guideline will need to be considered for inclusion in the update review (involving extraction of data in the form of GRADE profiles) |
| **Population** | Children and young people with type 1 diabetes | The guideline scope |
| Type 1 diabetes – blood ketone monitoring | defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years |
| Intervention or index test | Blood ketone monitoring | Beta-hydroxybutyrate, ketosis, and acetoacetate might be useful search terms |
| Comparator or reference standard | Urine ketone monitoring | Historically urine ketone monitoring would have been usual practice |
| Clinical outcomes | Physical outcomes | The GDG noted that use of out-of-date testing strips would constitute a lack of adherence and such practice should be discouraged. The group did not prioritise adherence to diabetes management (including self-management) as an outcome for extraction initially because it was unlikely to be reported in clinical studies. The group did, however, note that discouraging the use of out-of-date testing strips might be discussed in the evidence to recommendations section of the guideline |
| | • Development of DKA (number of episodes) | Due to the sparsity of evidence identified for inclusion, the NCC-WCH technical team extracted data on adherence to diabetes management (percentage of time the test was used during sick days) |
| | • Severity of DKA (measured by pH at admission) | |
| | • Hospital admission rates | |
| | • Mortality | |
| | • Contact with the diabetes care team (for example, to interpret ketone measurements and determine appropriate action) as a measure of healthcare utilization | |
| | • Adherence to diabetes management (including self-management) | |
| | Psychosocial outcomes | |
| | • Health-related quality of life | |
| | • Children and young people’s and families’ satisfaction with intervention | |
| Health economics outcomes | This question was prioritised for health economic analysis | Full recovery usually occurs with appropriate management, although a risk of long-term intellectual impairment may occur even in children and young people without cerebral oedema. DKA is the most common form of diabetic related death in children and young |
| | Health-related quality of life (measured using quality adjusted life years (QALYs)) | |
| | Hospitalisation episodes | |
### Type 1 diabetes – blood ketone monitoring

| Type 1 diabetes – blood ketone monitoring | people with a 2-5% mortality from cases

Most of the potential QALY gain from monitoring is, therefore, likely to arise from averted mortality, although there is additionally some long-term morbidity from neurological deficits in about 35% of children and young people who survive an episode of cerebral oedema

In addition to the QALY gain, cost-effectiveness will be dependent on monitoring averting expensive episodes of hospitalisation

| Other criteria for inclusion/exclusion of studies | None |

NCC-WCH to inform the team developing the type 1 diabetes in adults guideline whether studies involving home ketone monitoring report numbers of hospital admissions (this outcome was prioritised for consideration in this question). The team developing the type 1 diabetes in adults guideline would also like to know whether studies involving monitoring of ketones in hospital report severity or length of stay, but this relates to ketone monitoring during treatment for DKA, which will be covered in this guideline by the questions relating to management of DKA

| Search strategies | See separate document |

| Review strategies | Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)
A list of excluded studies will be provided following weeding
Evidence tables and an evidence profile will be used to summarise the evidence |

<p>| Equality | Equalities issues with be assessed according to |</p>
<table>
<thead>
<tr>
<th><strong>Type 1 diabetes – blood ketone monitoring</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>processes described in NICE guidelines manual</td>
</tr>
<tr>
<td>(November 2012)</td>
</tr>
</tbody>
</table>
E.9 Type 1 diabetes – dietary advice

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

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

<table>
<thead>
<tr>
<th>Type 1 diabetes – dietary advice – carbohydrate counting</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Existing recommendation(s) in 2004 guideline</strong></td>
</tr>
<tr>
<td>Children and young people with type 1 diabetes and their families should be informed that they have the same basic nutritional requirements as other children and young people. The food choices of children and young people should provide sufficient energy and nutrients for optimal growth and development, with total daily energy intake being distributed as follows:</td>
</tr>
<tr>
<td>• carbohydrates – more than 50%</td>
</tr>
<tr>
<td>• protein – 10–15%</td>
</tr>
<tr>
<td>• fat – 30–35%.</td>
</tr>
<tr>
<td>The consumption of five portions of fruit and vegetables per day is also recommended. Neonates, infants and pre-school children require individualised dietary assessment to determine their energy needs.</td>
</tr>
<tr>
<td>Children and young people using multiple daily injection regimens should be offered education about insulin and dietary management as part of their diabetes care package, to enable them to adjust their insulin dose to reflect their carbohydrate intake.</td>
</tr>
<tr>
<td>The 2004 guideline does not make specific recommendations about carbohydrate counting, but it includes the recommendations listed which refer to carbohydrate intake as a percentage of the total diet and adjusting insulin doses to reflect carbohydrate intake.</td>
</tr>
<tr>
<td><strong>Review question for update</strong></td>
</tr>
<tr>
<td>What is the effectiveness of dietetic advice using carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes?</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
</tr>
<tr>
<td>To determine whether dietetic advice using carbohydrate counting is effective in children and young people with type 1 diabetes. The term carbohydrate counting is taken here to mean the calculation of insulin:carbohydrate ratios, as used with multiple daily injection regimens or insulin pump therapy (that is, level 3 carbohydrate counting in the American Dietetic Association classification)</td>
</tr>
<tr>
<td>The American Dietetic Association classifies approaches to carbohydrate counting using the following three levels (see Gillespie et al, 1998 and Rabasa-Lhoret et al, 1999)</td>
</tr>
<tr>
<td>• Level 1 – consistent carbohydrate intake. At this level the patient is introduced to the fundamental concept that carbohydrate is the food component that raises blood glucose. A consistent intake of carbohydrate is encouraged based on predefined quantities of food</td>
</tr>
<tr>
<td>Note that dietary management using glycaemic index, which can be used with or without carbohydrate counting, is considered in a separate review question</td>
</tr>
<tr>
<td>References for the American Dietetic Association classification are as follows:</td>
</tr>
<tr>
<td>• Rabasha-Lhoret R, Garon J, Langelier H et al. Effects of meal carbohydrate content on insulin requirements in Type 1 diabetic patients treated with Ultralente-Regular) insulin regimen. Diabetes Care 1999:</td>
</tr>
</tbody>
</table>
### Type 1 diabetes – dietary advice – carbohydrate counting

- **Level 2** – pattern management principles. At this level, patients continue to eat regular carbohydrate, use a consistent baseline insulin dose and monitor blood glucose levels frequently. They recognise patterns of blood glucose response to carbohydrate (and other food) intake, and changes that occur with insulin and exercise. They learn to adjust their insulin dose, or change carbohydrate intake or timing of exercise, to meet blood glucose targets.

- **Level 3** – insulin:carbohydrate ratios. At this level, which is appropriate for people on multiple daily injection regimens or insulin pump therapy, calculation of insulin:carbohydrate ratios are individualised according to age, sex, pubertal status, duration of diabetes, time of day, and activity. Adjustment of pre-meal insulin according to the estimated carbohydrate content of the meal or snack is then undertaken using the specified insulin:carbohydrate ratios.

The GDG clarified that level 3 carbohydrate counting is used only with multiple daily injection regimens and insulin pump therapy.

<table>
<thead>
<tr>
<th>Language</th>
<th>English</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study design</td>
<td>Systematic reviews and randomised controlled trials (RCTs) only</td>
</tr>
<tr>
<td>Status</td>
<td>Published articles (no limitation on year of publication)</td>
</tr>
<tr>
<td>Population</td>
<td>Children and young people with type 1 diabetes</td>
</tr>
<tr>
<td>Intervention or index test</td>
<td>Dietetic advice involving carbohydrate counting (level 3 in the American Dietetic Association classification)</td>
</tr>
<tr>
<td></td>
<td>Include studies only if dietetic advice includes direct contact and training with healthcare professionals (for example, providing an information leaflet is not enough)</td>
</tr>
<tr>
<td></td>
<td>Exclude studies in which advice about carbohydrate counting is given, but insulin is not adjusted according to carbohydrate intake (level 3 carbohydrate counting implies participants will be using multiple daily injection regimens or insulin pump therapy)</td>
</tr>
<tr>
<td></td>
<td>Evidence tables should document the insulin regimen in the intervention and comparison groups</td>
</tr>
</tbody>
</table>
### Type 1 diabetes – dietary advice – carbohydrate counting

<table>
<thead>
<tr>
<th>Comparators or reference standard</th>
<th>Usual care</th>
<th>Usual care could include dietetic advice which does not incorporate specific advice about carbohydrate counting, including levels 1 and 2 in the American Dietetic Association classification</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>NCC-WCH technical team to clarify with the GDG whether specific interventions and comparators are relevant to this question once the search has been completed and/or weeded; the appropriate focus may depend on the conclusions from the multiple daily injections review question</td>
</tr>
</tbody>
</table>

#### Clinical outcomes

<table>
<thead>
<tr>
<th>Physical outcomes</th>
<th>Health-related quality of life</th>
<th>Children and young people’s and families’ satisfaction with intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycaemic control</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c (minimum follow-up 6 months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe hypoglycaemic episodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postprandial hyperglycaemia (for example, glucose excursions or larger area under the glucose concentration curve)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adherence to diabetes management (including self-management)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changes in body mass index (BMI) standard deviation score (SDS)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Psychosocial outcomes

- Health-related quality of life
- Children and young people’s and families’ satisfaction with intervention

The GDG selected the same priority outcomes for the questions on carbohydrate counting and glycaemic index, and the outcomes selected were the same as those for the question on multiple daily injection regimens except that postprandial hyperglycaemia was substituted for diabetic ketoacidosis (DKA).

The GDG considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes.

HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol).

Severe hypoglycaemic episodes defined according to either of the following criteria.

- International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose).
### Type 1 diabetes – dietary advice – carbohydrate counting

<table>
<thead>
<tr>
<th><strong>Type 1 diabetes – dietary advice – carbohydrate counting</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)</td>
</tr>
</tbody>
</table>

### Health economic outcomes

<table>
<thead>
<tr>
<th><strong>Health economic outcomes</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>This question was prioritised for health economic analysis, but only in connection with the question on multiple daily injections</td>
</tr>
<tr>
<td>Health-related quality of life and quality adjusted life years (QALYs)</td>
</tr>
<tr>
<td>Adherence to diabetes management (including self-management)</td>
</tr>
<tr>
<td>It may be possible attach a QALY to various long-term complications – long-term outcomes are not prioritised per se but might be affected through glycaemic control</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Health economic outcomes</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>GDG to note that, although mortality is not prioritised as a clinical outcome, health economic modelling incorporating data on mortality might be relevant through the link between hypoglycaemia and mortality</td>
</tr>
</tbody>
</table>

### Other criteria for inclusion/exclusion of studies

<table>
<thead>
<tr>
<th><strong>Other criteria for inclusion/exclusion of studies</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allow this (although the availability of such studies is not expected)</td>
</tr>
</tbody>
</table>

### Search strategies

<table>
<thead>
<tr>
<th><strong>Search strategies</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>See separate document</td>
</tr>
</tbody>
</table>

### Review strategies

<table>
<thead>
<tr>
<th><strong>Review strategies</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</td>
</tr>
<tr>
<td>A list of excluded studies will be provided following weeding</td>
</tr>
<tr>
<td>Evidence tables and an evidence profile will be used to summarise the evidence</td>
</tr>
</tbody>
</table>

### Equality

<table>
<thead>
<tr>
<th><strong>Equality</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)</td>
</tr>
</tbody>
</table>

### Type 1 diabetes – dietary advice – glycaemic index

<table>
<thead>
<tr>
<th><strong>Type 1 diabetes – dietary advice – glycaemic index</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Existing recommendation(s) in 2004 guideline</strong></td>
</tr>
<tr>
<td>Children and young people with type 1 diabetes and their families should be informed of the importance of healthy eating in reducing the risk of cardiovascular disease (including foods with a low glycaemic index, fruit and vegetables, and types and amounts of fats), and means of making appropriate nutritional changes in the period after diagnosis and according to need and interest at intervals thereafter.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Type 1 diabetes – dietary advice – glycaemic index</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Children and young people using multiple daily</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Type 1 diabetes – dietary advice – glycaemic index</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>The 2004 guideline does not make specific recommendations about glycaemic intake in children and young people, but it includes the recommendations listed which refer to the importance of foods with low glycaemic index as part of a healthy diet, and adjusting insulin doses to reflect carbohydrate intake</td>
</tr>
</tbody>
</table>
**Type 1 diabetes – dietary advice – glycaemic index**

<table>
<thead>
<tr>
<th>Review question for update</th>
<th>What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objectives</td>
<td>To determine whether dietetic advice using glycaemic index is effective in children and young people with type 1 diabetes in terms of maintaining glycaemic control. The GDG noted that knowledge about foods with a low glycaemic index and those with a high glycaemic index could be relevant for the update.</td>
</tr>
<tr>
<td>Language</td>
<td>English</td>
</tr>
<tr>
<td>Study design</td>
<td>Systematic reviews and randomised controlled trials (RCTs) only</td>
</tr>
<tr>
<td>Status</td>
<td>Published articles (no limitation on year of publication)</td>
</tr>
<tr>
<td>Population</td>
<td>Children and young people with type 1 diabetes</td>
</tr>
<tr>
<td>Intervention or index test</td>
<td>Dietetic advice taking account of the glycaemic index of carbohydrates</td>
</tr>
</tbody>
</table>
| Comparator or reference standard | Dietetic advice that does not take account of glycaemic index  
Carbohydrate counting without taking account of glycaemic index |

The type 1 diabetes in adults guideline update includes a parallel question for which the initial systematic review was undertaken by the NCC-WCH team; material differences between the two reviews are indicated here.

- Expect more evidence for this question than for carbohydrate counting
- Evidence tables should document the insulin regimen and whether or not carbohydrate counting was used
- Articles to consider include:
Diagnosis and management of type 1 diabetes in children and young people
Review protocols

<table>
<thead>
<tr>
<th>Type 1 diabetes – dietary advice – glycaemic index</th>
<th>2003</th>
</tr>
</thead>
</table>

Clinical outcomes

Physical outcomes

- Glycaemic control
  - HbA1c (minimum follow-up 6 months)
  - Severe hypoglycaemic episodes
  - Postprandial hyperglycaemia (for example, glucose excursions or larger area under the glucose concentration curve)
- Adherence to diabetes management (including self-management)
- Changes in body mass index (BMI) standard deviation score (SDS)

Psychosocial outcomes

- Health-related quality of life
- Children and young people’s and families’ satisfaction with intervention

The GDG for diabetes in children and young people selected the same priority outcomes for the review questions on carbohydrate counting and glycaemic index, and the outcomes selected were the same as those for the question on multiple daily injection (MDI) regimens except that postprandial hyperglycaemia was substituted for diabetic ketoacidosis (DKA).

The GDG for type 1 diabetes in adults selected the same priority outcomes as for children and young people, except that nocturnal hypoglycaemia was substituted for changes in BMI SDS. The latter was considered to be more important in children and young people with type 1 diabetes across the questions about dietetic advice and MDI regimens because any dietetic intervention might affect weight gain, whereas daytime food intake is unlikely to result in nocturnal hypoglycaemia because food intake will be covered by administration of short-acting insulin that will generally have little effect during sleep.

The GDG for diabetes in children and young people considered that, in this question, a minimum follow-up period of 6 months in both treatment arms would be needed for measurement of HbA1c and a minimum follow-up period of 4 months in both treatment arms would be needed for the other outcomes. The same approach was used in the question related to adults with type 1 diabetes.
### Type 1 diabetes – dietary advice – glycaemic index

<table>
<thead>
<tr>
<th><strong>Type 1 diabetes – dietary advice – glycaemic index</strong></th>
<th><strong>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Severe hypoglycaemic episodes defined according to either of the following criteria.</td>
</tr>
<tr>
<td></td>
<td>- International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose)</td>
</tr>
<tr>
<td></td>
<td>- ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose; grade 3)</td>
</tr>
</tbody>
</table>

### Health economic outcomes

<table>
<thead>
<tr>
<th><strong>Health economic outcomes</strong></th>
<th><strong>This question was not prioritised for health economic analysis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Health-related quality of life and quality adjusted life years (QALYs)</td>
</tr>
<tr>
<td></td>
<td>Adherence to diabetes management (including self-management)</td>
</tr>
<tr>
<td></td>
<td>It may be possible attach a QALY to various long-term complications – long-term outcomes are not prioritised per se but might be affected through glycaemic control</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Other criteria for inclusion/exclusion of studies</strong></th>
<th><strong>None</strong></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th><strong>Search strategies</strong></th>
<th><strong>See separate document</strong></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th><strong>Review strategies</strong></th>
<th><strong>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A list of excluded studies will be provided following weeding</td>
</tr>
</tbody>
</table>
### Type 1 diabetes – dietary advice – glycaemic index

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence tables and</td>
<td>Evidence tables and an evidence profile will be used to summarise the evidence</td>
</tr>
<tr>
<td>Equality</td>
<td>Equality issues with be assessed according to processes described in NICE guidelines manual (November 2012)</td>
</tr>
</tbody>
</table>
### E.10 Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

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

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

<table>
<thead>
<tr>
<th>Status</th>
<th>Published articles (no limitation on year of publication)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Although this is an update and expansion of a review question considered in the 2004 guideline, no date limit will be applied to searches for these specific review questions to ensure that all relevant articles are identified for both type 1 and 2 diabetes</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Population</th>
<th>Children and young people (in whom type 1 or type 2 diabetes may or may not have been recognised previously)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years</td>
<td></td>
</tr>
<tr>
<td>The GDG noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intervention or index test</th>
<th>Symptoms, signs and biochemical abnormalities that are suggestive of DKA and their predictive values individually or in combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms and signs</td>
<td></td>
</tr>
<tr>
<td>• polydypsia</td>
<td></td>
</tr>
<tr>
<td>• polyuria (possibly manifesting as bedwetting, that is, secondary enuresis)</td>
<td></td>
</tr>
<tr>
<td>• weight loss</td>
<td></td>
</tr>
<tr>
<td>• dehydration</td>
<td></td>
</tr>
<tr>
<td>• nausea or vomiting</td>
<td></td>
</tr>
<tr>
<td>The clinical problem is that DKA is not always recognised (rather than it being overdiagnosed)</td>
<td></td>
</tr>
<tr>
<td>The GDG agreed to consider the symptoms, signs and biochemical abnormalities listed in terms of their value as predictive features</td>
<td></td>
</tr>
<tr>
<td>The order in which the symptoms and signs are</td>
<td></td>
</tr>
</tbody>
</table>
### Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

<table>
<thead>
<tr>
<th>Symptom/Sign</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>currently listed reflects increasing severity of DKA; it might be useful to reflect this in the review</td>
</tr>
<tr>
<td>Respiratory distress</td>
<td></td>
</tr>
<tr>
<td>Altered level of consciousness</td>
<td></td>
</tr>
<tr>
<td>Biochemical abnormalities</td>
<td>GDG to consider tests (capillary blood glucose), recognition, prevention at diagnosis somewhere in the guideline (not directly this question)</td>
</tr>
<tr>
<td>Hyperglycaemia</td>
<td></td>
</tr>
<tr>
<td>Acidosis</td>
<td></td>
</tr>
<tr>
<td>Ketosis</td>
<td></td>
</tr>
</tbody>
</table>

### Comparators or reference standard

<table>
<thead>
<tr>
<th>Comparator or reference standard</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital-based diagnosis of DKA (based on pH or bicarbonate, blood glucose and blood or urine ketones)</td>
<td></td>
</tr>
</tbody>
</table>

### Clinical outcomes

<table>
<thead>
<tr>
<th>Description</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic test (predictive) accuracy (sensitivity, specificity and positive and negative likelihood ratios) applied to symptoms, signs and biochemical abnormalities individually or in groups</td>
<td>This will remain true provided the recommendations arising from these questions are restricted to giving a list of symptoms, signs and biochemical abnormalities to look out for, rather than interventions that should follow based on them</td>
</tr>
</tbody>
</table>

### Health economics outcomes

<table>
<thead>
<tr>
<th>Description</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>These questions were not prioritised for health economic analysis</td>
<td></td>
</tr>
</tbody>
</table>

### Other criteria for inclusion/exclusion of studies

<table>
<thead>
<tr>
<th>Description</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exclude studies with &lt;10 participants in total</td>
<td>Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation</td>
</tr>
<tr>
<td></td>
<td>Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this</td>
</tr>
</tbody>
</table>

### Search strategies

<table>
<thead>
<tr>
<th>Description</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>See separate document</td>
<td>A single search for evidence will be undertaken across the two questions</td>
</tr>
</tbody>
</table>

### Review strategies

<table>
<thead>
<tr>
<th>Description</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</td>
<td>The GDG’s view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first presentation</td>
</tr>
<tr>
<td>A list of excluded studies will be provided following weeding</td>
<td></td>
</tr>
<tr>
<td>Evidence tables and an evidence profile will be used to summarise the evidence</td>
<td></td>
</tr>
</tbody>
</table>

### Equality

<table>
<thead>
<tr>
<th>Description</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)</td>
<td></td>
</tr>
</tbody>
</table>
### Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs

<table>
<thead>
<tr>
<th>presentation with diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Communication problems (young children and neurodisabilities) might also be of relevance for this question</td>
</tr>
</tbody>
</table>
## E.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

### Review questions:
- What routine assessments and investigations should be used to guide management in children and young people who present with diabetic ketoacidosis?
- Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:
  - general observations (for example, heart and respiratory rate and blood pressure)
  - body weight
  - hydration status
  - fluid balance
  - neurological observations
  - electrocardiographic (ECG) monitoring?
- Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:
  - blood glucose
  - blood or urine ketones
  - serum urea or electrolytes
  - acid/base status?

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

<table>
<thead>
<tr>
<th>Management from diagnosis</th>
<th>Diabetic ketoacidosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document.</td>
<td>Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes.</td>
</tr>
<tr>
<td><strong>Diabetic ketoacidosis</strong></td>
<td></td>
</tr>
<tr>
<td>Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children’s ward.</td>
<td>Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit.</td>
</tr>
<tr>
<td>Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit.</td>
<td>Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 7.3)</td>
</tr>
</tbody>
</table>

All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness.

The guidelines published by the British Society for Paediatric Endocrinology and Diabetes (BSPED) were reproduced in an appendix of the 2004 guideline.

The 2004 guideline was specific to type 1 diabetes.

The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the GDG plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full GDG will ratify all conclusions and
Diagnosis and management of type 1 diabetes in children and young people
Review protocols

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

<table>
<thead>
<tr>
<th>Recommendations based on the DKA evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 nmol/litre, but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.</td>
</tr>
</tbody>
</table>

**Review question for update**

What routine assessments and investigations should be used to inform management in children and young people who present with DKA? Which of the following should be performed as clinical monitoring during treatment of DKA in children and young people:
- general observations (for example, heart and respiratory rate and blood pressure)
- body weight
- hydration status
- fluid balance
- neurological observations
- electrocardiographic (ECG) monitoring?

Which of the following laboratory investigations should be performed to monitor children and young people during treatment for DKA:
- blood glucose
- blood or urine ketones
- serum urea or electrolytes
- acid/base status?

**The review questions for type 1 and type 2 diabetes are identical**

The GDG needs to address assessment of, and typical degree of, dehydration somewhere, and volume of fluids for rehydration, and this protocol is intended to be broad enough to accommodate this.

The GDG might want to consider recommending the use of early warning scores.

**Objectives**

To identify the appropriate clinical assessments and laboratory investigations that should be performed in order to guide treatment for children and young people with DKA, and to monitor the response during treatment. The guideline scope requires the GDG to consider all of the following.
- Immediate management at presentation (for example, maintenance of airway, breathing and circulation or the potential need for a nasogastric tube to prevent pulmonary aspiration)
- Clinical assessment and investigations at presentation to guide management
- Fluid management, including:
  - assessment of dehydration
  - volume of administration
- Clinical monitoring (to assess the response to treatment and to look for evidence of cerebral oedema), including:
  - general observations (for example, heart and respiratory rate and blood pressure)
  - body weight
  - hydration status
  - fluid balance
  - neurological observations
  - ECG monitoring
- Laboratory monitoring (to assess the response to treatment and to look for evidence of...)

Other aspects of fluid management (route and rate of administration, choice of fluid, and additives) are addressed through separate questions and a different protocol.
| **Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations** |
|--------------------------------------------------|-------------------------------------------------------|
| hypokalaemia), including:                       | There are unlikely to be any RCTs for this question and so the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies |
| o blood glucose                                | No date limit will be applied to searches for these specific review questions to ensure that all relevant articles are identified for both type 1 and 2 diabetes |
| o blood or urine ketones                        | The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years |
| o serum urea and electrolytes                   | The GDG noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services |
| o acid/base status                              |                                                                 |

**Language** English

**Study design**

- Systematic reviews and randomised controlled trials (RCTs)
- Comparative observational studies (including cohort and case-control studies)

**Status**

- Published articles (no limitation on year of publication)

**Population**

- Children and young people with type 1 or type 2 diabetes (although the diabetes may not yet have been recognised, for example, if the child or young person is presenting for the first time with DKA)

**Intervention or index test**

- Any approach to clinical assessment and/or laboratory investigations for children and young people presenting with DKA or during treatment

**Notes**

- Immediate management at presentation (for example, maintenance of airway, breathing and circulation or the potential need for a nasogastric tube to prevent pulmonary aspiration)
- Clinical assessment and investigations at presentation to guide management

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

<table>
<thead>
<tr>
<th>Fluid management, including:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• assessment of dehydration</td>
</tr>
<tr>
<td>• volume of administration</td>
</tr>
<tr>
<td>• (other aspects of fluid management will be addressed through separate questions and a different protocol)</td>
</tr>
</tbody>
</table>

**Clinical monitoring (to assess the response to treatment and to look for evidence of cerebral oedema), including:**

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

**Laboratory monitoring (to assess the response to treatment and to look for evidence of hypokalaemia), including:**

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

The GDG noted that the following terminology might be helpful when selecting search terms

**Clinical assessment**

- General observations (vital signs):
  - temperature
  - level of consciousness
- Clinical signs of dehydration:
  - altered skin colour
  - sunken eyes
  - cold extremities
  - prolonged capillary refill time
  - dry mucous membranes
  - reduced skin turgor
  - reduced urine output
<table>
<thead>
<tr>
<th>Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Signs of deep vein thrombosis (including leg pain or swelling)</td>
<td></td>
</tr>
<tr>
<td>Laboratory investigations</td>
<td></td>
</tr>
<tr>
<td>• Blood ketones to include near-patient testing</td>
<td></td>
</tr>
<tr>
<td>• Plasma osmolality (tonicity)</td>
<td></td>
</tr>
<tr>
<td>The evidence identified for inclusion could provide guidance on the frequency and duration with which to perform laboratory investigations</td>
<td></td>
</tr>
<tr>
<td>Comparators or reference standard</td>
<td>Any other approach to clinical assessment and/or laboratory investigations for children and young people presenting with DKA or during treatment</td>
</tr>
<tr>
<td>There may be few comparative studies identified for inclusion, but where necessary the GDG will be able to use informal consensus based on knowledge and experience to formulate recommendations addressing all areas required by the scope</td>
<td></td>
</tr>
<tr>
<td>There may be comparative studies relating to blood ketone testing</td>
<td></td>
</tr>
<tr>
<td>Clinical outcomes</td>
<td>Physical outcomes</td>
</tr>
<tr>
<td>• Mortality</td>
<td></td>
</tr>
<tr>
<td>• Degree of dehydration confirmed by post-recovery weight</td>
<td></td>
</tr>
<tr>
<td>• Detection of hypovolaemia</td>
<td></td>
</tr>
<tr>
<td>• Detection of laboratory abnormalities:</td>
<td></td>
</tr>
<tr>
<td>o hypoglycaemia</td>
<td></td>
</tr>
<tr>
<td>o hypokalaemia</td>
<td></td>
</tr>
<tr>
<td>o hyponatraemia</td>
<td></td>
</tr>
<tr>
<td>o persistent acidosis</td>
<td></td>
</tr>
<tr>
<td>o persistent ketosis</td>
<td></td>
</tr>
<tr>
<td>• Detection of complications:</td>
<td></td>
</tr>
<tr>
<td>o cerebral oedema</td>
<td></td>
</tr>
<tr>
<td>o venous thrombosis</td>
<td></td>
</tr>
<tr>
<td>o aspiration</td>
<td></td>
</tr>
<tr>
<td>• Healthcare utilisation (for example, duration of admission, requirement for ventilation (as a proxy for severity of DKA or presence of cerebral oedema))</td>
<td></td>
</tr>
<tr>
<td>Note for NCC-WCH: Consider splitting outcomes by question but check first how much evidence is available for inclusion (that is, screen search results)</td>
<td></td>
</tr>
<tr>
<td>Include consideration of frequency of monitoring and intervals</td>
<td></td>
</tr>
<tr>
<td>GDG to consider changing terminology from 'hypokalaemia' to 'serum potassium concentration', etc in review questions related to DKA</td>
<td></td>
</tr>
<tr>
<td>Health economics outcomes</td>
<td>These questions were not selected as priorities for health economic analysis</td>
</tr>
<tr>
<td>Other criteria for inclusion/exclusion of studies</td>
<td>Exclude studies with &lt;10 participants in total</td>
</tr>
<tr>
<td>Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation</td>
<td></td>
</tr>
<tr>
<td><strong>Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations</strong></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td><strong>Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Search strategies</strong></td>
<td>See separate document</td>
</tr>
<tr>
<td><strong>Review strategies</strong></td>
<td>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence</td>
</tr>
<tr>
<td><strong>Equality</strong></td>
<td>Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)</td>
</tr>
</tbody>
</table>
E.12 Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

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

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

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

<table>
<thead>
<tr>
<th>Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Management from diagnosis</td>
</tr>
<tr>
<td>Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document.</td>
</tr>
</tbody>
</table>

Diabetic ketoacidosis
Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes.

Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children’s ward.

Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit.

Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit.

Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.

All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness.

The guidelines published by the British Society for Paediatric Endocrinology and Diabetes (BSPED) were reproduced in an appendix of the 2004 guideline.

The 2004 guideline was specific to type 1 diabetes.

The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the GDG plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full GDG will ratify all conclusions and recommendations based on the DKA evidence.
### Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

<table>
<thead>
<tr>
<th>Review question for update</th>
<th>Objectives</th>
<th>Language</th>
<th>Study design</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is the appropriate route of administration for fluids in children and young people with diabetic ketoacidosis? At what rate should children and young people with diabetic ketoacidosis be rehydrated? What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?</td>
<td>To determine the optimal fluid management regimen for children and young people with DKA. The review will address the following aspects of fluid management: • route of administration (‘route’ in the table of outcomes below) • rate of administration (‘rate’ in the table of outcomes below) • choice of fluid (including sodium chloride content; ‘fluid/sodium’ in the table of outcomes below) • other additives (for example, o glucose (‘glucose’ in the table of outcomes below) o potassium (‘potassium’ in the table of outcomes below) o bicarbonate (‘bicarbonate’ in the table of outcomes below) o phosphate (‘phosphate’ in the table of outcomes below))</td>
<td>English</td>
<td>Systematic reviews and randomised controlled trials (RCTs) Comparative observational studies (including cohort and case-control studies)</td>
<td>Published articles (no limitation on year of publication)</td>
</tr>
<tr>
<td>The review questions for type 1 and type 2 diabetes are identical</td>
<td>The scope also requires consideration of assessment of dehydration and the volume of fluid administration; these will be covered by separate review questions linked to the questions about clinical assessment and investigations at presentation and during management of DKA</td>
<td></td>
<td></td>
<td>Although this is an update and expansion of a review question considered in the 2004 guideline, no date limit will be applied to searches for these specific review questions to ensure that all relevant evidence is captured.</td>
</tr>
</tbody>
</table>
### Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

<table>
<thead>
<tr>
<th>Population</th>
<th>Children and young people with type 1 or type 2 diabetes (although the diabetes may not yet have been recognised, for example, if the child or young person is presenting for the first time with DKA)</th>
<th>The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years. The GDG noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention or index test</td>
<td>Any fluid management regimen for children and young people presenting with DKA</td>
<td></td>
</tr>
<tr>
<td>Comparator or reference standard</td>
<td>Any other fluid management regimen for children and young people presenting with DKA</td>
<td></td>
</tr>
<tr>
<td>Clinical outcomes</td>
<td>Physical outcomes</td>
<td>The GDG prioritised different outcomes for the different aspects of the review questions covered by this protocol (‘route’, ‘rate’, ‘fluid/sodium’, ‘glucose’, ‘potassium’, ‘bicarbonate’ and ‘phosphate’); ‘Y’ in the cells of the table indicates that an outcome was prioritised for the corresponding aspect of the questions covered by the protocol. Some outcomes (for example, mortality) are common to all aspects of the questions</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Route</th>
<th>Rate</th>
<th>Fluid/sodium</th>
<th>Glucose</th>
<th>Potassium</th>
<th>Bicarbonate</th>
<th>Phosphate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Time to resolution of dehydration</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rate of change of blood glucose concentration (this is likely to be reported in research studies, whereas resolution of hyperglycaemia (which would otherwise be of interest) might not be)</td>
<td>Y</td>
<td>Y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence of hypoglycaemia</td>
<td>Y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

| Resolution of acidosis (this is likely to be reported, especially in older studies that do not report resolution of blood ketosis, but it is likely to be of lower priority in formulating recommendations) | Y | Y | Y | Y | Y | Y |
| Resolution of blood ketosis | Y | Y | Y | Y | Y | Y |
| Serum chloride concentration (a raised concentration is linked to acidosis) | Y | Y | Y | Y | Y | Y |
| Incidence of cerebral oedema (this could cause morbidity or mortality), to include participants with symptoms or signs suggestive of cerebral oedema (for example, development of unconsciousness) provided these are reported as being related to cerebral oedema | Y | Y | Y | Y | Y | Y |
| Hypokalaemia (this is important because people with DKA die of this) | Y | Y | Y | Y | Y | Y |
| Serum sodium concentration | Y | Y | Y | Y | Y | Y |
| Serum calcium concentration | Y | Y | Y | Y | Y | Y |
| Carbon dioxide (CO2) | Y | Y | Y | Y | Y | Y |

For some aspects, the GDG prioritised 8 outcomes initially and this remained acceptable because of the sparsity of the evidence identified for inclusion.

GDG to consider changing terminology from 'hypokalaemia' to 'serum potassium concentration', etc in review questions related to DKA.
## Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

| Healthcare utilisation (for example, duration of admission, requirement for ventilation (as a proxy for severity of DKA or presence of cerebral oedema)) | Y | Y | Y | Y | Y | Y | Y |

### Health economics outcomes

These questions were not prioritised for health economic analysis

### Other criteria for inclusion/exclusion of studies

Exclude studies with <10 participants in total

Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation

Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this

### Search strategies

See separate document

A single search for evidence will be undertaken across the questions relating to fluid management in children and young people presenting with DKA

Possible search terms to include the following

For fluid composition:
- sodium chloride or sodium lactate concentration
- pH
- specific fluids such as Ringer’s solution, Hartmann’s solution, isolyte, and plasmalyte
Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

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

For route of administration:
- intravenous
- intraosseus
- oral
- not intramuscular
## E.13 Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents

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

<table>
<thead>
<tr>
<th>Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Management from diagnosis</strong></td>
</tr>
<tr>
<td>Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document.</td>
</tr>
<tr>
<td><strong>Diabetic ketoacidosis</strong></td>
</tr>
<tr>
<td>Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes.</td>
</tr>
<tr>
<td>Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children’s ward.</td>
</tr>
<tr>
<td>Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit.</td>
</tr>
<tr>
<td>Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit.</td>
</tr>
<tr>
<td>Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.</td>
</tr>
<tr>
<td><strong>Review question for update</strong></td>
</tr>
<tr>
<td>What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
</tr>
<tr>
<td>To assess the effectiveness of intravenous osmotic agents in the treatment of cerebral oedema associated with DKA in children and young people</td>
</tr>
<tr>
<td>The main intervention of interest from the GDG is the urgent administration of mannitol whilst the child is still on a general paediatric ward.</td>
</tr>
<tr>
<td>Note the setting in which agents are administered and the duration of treatment in the evidence tables.</td>
</tr>
</tbody>
</table>
### Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents

<table>
<thead>
<tr>
<th>Language</th>
<th>English</th>
</tr>
</thead>
</table>
| **Study design** | Systematic reviews and randomised controlled trials (RCTs)  
Comparative observational studies (including cohort and case-control studies) |
| | Although there may be some RCTs for this question the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies |
| **Status** | Published articles (no limitation on year of publication) |
| **Population** | Children and young people with DKA and cerebral oedema |
| | The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years |
| | The GDG noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services |
| **Intervention or index test** | Any treatment based on administration of intravenous osmotic agents |
| | For example, mannitol, hypertonic saline or a combination of the two |
| | May also be referred to as osmotic therapy or osmotherapy |
| **Comparator or reference standard** | Any other treatment based on administration of intravenous osmotic agents  
No treatment with osmotic agents |
| **Clinical outcomes** | Physical outcomes  
- Mortality  
- Persistent neurological deficit  
- Healthcare utilisation (for example, duration of admission, requirement for ventilation (as a proxy for severity of DKA or presence of cerebral oedema)) |
<p>| <strong>Health economics outcomes</strong> | This question was not prioritised for health economic analysis |
| <strong>Other criteria for inclusion/exclusion of studies</strong> | Exclude studies with &lt;10 participants in total |
| | Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation |
| | Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this |</p>
<table>
<thead>
<tr>
<th><strong>Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Search strategies</strong></td>
</tr>
<tr>
<td><strong>Review strategies</strong></td>
</tr>
<tr>
<td><strong>Equality</strong></td>
</tr>
</tbody>
</table>
**E.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin**

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

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

<table>
<thead>
<tr>
<th>Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – timing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Existing recommendation(s) in 2004 guideline</strong></td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td><strong>Review question for update</strong></td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
</tr>
<tr>
<td><strong>All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

© 2014 National Collaborating Centre for Women’s and Children’s Health
<table>
<thead>
<tr>
<th><strong>Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – timing</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>adverse consequence of starting intravenous insulin therapy too early (during intravenous infusion of fluids without glucose), whereas the optimal time to stop intravenous insulin therapy is likely to be determined by the timescale for continuing intravenous glucose infusion once ketoacidosis has been resolved. In some children and young people with DKA or ketonaemia who are not very ill it may not be necessary to use intravenous insulin therapy at all, and the question also covers this scenario. The GDG may also wish to make recommendations for the insulin regimen to be used immediately after stopping intravenous insulin therapy (taking into account the fact that the child or young person may or may not have been recognised as having type 1 or type 2 diabetes before presenting with DKA). Overall the GDG noted that the part of the question that deals with when to start intravenous insulin therapy was of greater clinical importance (as it could be associated with a risk of mortality).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Language</strong></th>
<th>English</th>
</tr>
</thead>
</table>

| **Study design** | Systematic reviews and randomised controlled trials (RCTs)  
Comparative observational studies (including cohort and case-control studies) |
<table>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Status</strong></td>
<td>Published articles (no limitation on year of publication)</td>
</tr>
</tbody>
</table>

For the part of the question about when to start intravenous insulin infusion: there may be no RCTs but some comparative observational studies. For the part of the question about when to stop intravenous insulin infusion: it is very unlikely that there will be any RCTs and evidence from observational studies will be considered. The GDG noted, therefore, that for these questions the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies. Although this is an update and expansion of a review question considered in the 2004 guideline, no date limit will be applied to searches for these specific review questions to ensure that all relevant articles are identified for.
<table>
<thead>
<tr>
<th>Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – timing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
</tr>
<tr>
<td>Children and young people with type 1 or type 2 diabetes (although the diabetes may not yet have been recognised, for example, if the child or young person is presenting for the first time with DKA)</td>
</tr>
<tr>
<td>The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years. The GDG noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services</td>
</tr>
</tbody>
</table>

| **Intervention or index test** |
| For the part of the question about when to start intravenous insulin infusion: delayed insulin (delaying the start of intravenous insulin therapy until intravenous fluid therapy is established) |
| For the part of the question about when to stop intravenous insulin infusion: outcomes should be compared according to the blood ketone concentration at which intravenous insulin is stopped |
| For the part of the question about when to start intravenous insulin infusion: the important consideration is the timing of intravenous insulin in relation to the timing of intravenous fluids |
| For the part of the question about when to stop intravenous insulin infusion: there may be evidence in terms of retrospective comparison of outcomes before and after resolution of ketosis |

| **Comparator or reference standard** |
| For the part of the question about when to start intravenous insulin infusion: immediate insulin (starting intravenous insulin therapy before or at the same time as starting intravenous fluids) |
| For the part of the question about when to stop intravenous insulin infusion: outcomes should be compared according to the blood ketone concentration at which intravenous insulin is stopped |

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

<table>
<thead>
<tr>
<th>Equality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)</td>
</tr>
</tbody>
</table>

The GDG’s view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first presentation with diabetes.

### Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – dosage

<table>
<thead>
<tr>
<th>Existing recommendation(s) in 2004 guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Management from diagnosis</td>
</tr>
<tr>
<td>Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document.</td>
</tr>
</tbody>
</table>

**Diabetic ketoacidosis**

Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes.

Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children’s ward.

Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit.

Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit.

Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose.

<table>
<thead>
<tr>
<th>Review</th>
</tr>
</thead>
<tbody>
<tr>
<td>How should the dosage of insulin be calculated for</td>
</tr>
</tbody>
</table>

The review questions for...
<table>
<thead>
<tr>
<th>Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>question for update</strong></td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
</tr>
<tr>
<td><strong>Language</strong></td>
</tr>
<tr>
<td><strong>Study design</strong></td>
</tr>
<tr>
<td><strong>Status</strong></td>
</tr>
<tr>
<td><strong>Population</strong></td>
</tr>
<tr>
<td><strong>Intervention or index</strong></td>
</tr>
<tr>
<td>Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – dosage test</td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>This question. Most studies are likely to compare 0.05 units/kg/hour with 0.1 units/kg/hour; a few might compare 0.025 units/kg/hour with 0.05 units/kg/hour or 0.1 units/kg/hour.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comparators or reference standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin dosage of 0.1 units/kg/hour</td>
</tr>
<tr>
<td>0.1 units/kg/hour, 0.05 units/kg/hour, and 0.025 units/kg/hour are the dosages likely to be used; the intended starting dosage will be important and evidence tables and GRADE profiles should reflect this.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical outcomes</td>
</tr>
<tr>
<td>Mortality</td>
</tr>
<tr>
<td>• Rate of change of blood glucose concentration (this is likely to be reported in research studies, whereas resolution of hyperglycaemia (which would otherwise be of interest) might not be)</td>
</tr>
<tr>
<td>• Incidence of hypoglycaemia</td>
</tr>
<tr>
<td>• Resolution of acidosis (this is likely to be reported, especially in older studies that do not report resolution of blood ketosis, but it is likely to be of lower priority in formulating recommendations)</td>
</tr>
<tr>
<td>• Resolution of blood ketosis</td>
</tr>
<tr>
<td>• Incidence of cerebral oedema (this could cause morbidity or mortality), to include participants with symptoms or signs suggestive of cerebral oedema (for example, development of unconsciousness) provided these are reported as being related to cerebral oedema</td>
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<tr>
<td>• Hypokalaemia (this is important because people with DKA die of this)</td>
</tr>
<tr>
<td>• Healthcare utilisation (for example, duration of admission, requirement for ventilation (as a proxy for severity of DKA or presence of cerebral oedema))</td>
</tr>
<tr>
<td>The GDG prioritised 8 outcomes initially (based on those selected for the question on when to start and stop intravenous insulin infusion in children and young people with DKA); this was found to be acceptable based on the sparsity of evidence identified for inclusion.</td>
</tr>
<tr>
<td>GDG to consider using the terminology ‘serum potassium concentration’ rather than ‘hypokalaemia’ etc</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Health economics outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>These questions were not prioritised for health economic analysis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other criteria for inclusion/exclusion of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exclude studies with &lt;10 participants in total</td>
</tr>
<tr>
<td>Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation</td>
</tr>
<tr>
<td>Additionally, subgroup analysis by age group (for example, pre-school versus primary school or...</td>
</tr>
</tbody>
</table>
### Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin – dosage

<table>
<thead>
<tr>
<th></th>
<th>secondary school) would be useful if the evidence from the included studies allows this</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Search strategies</strong></td>
<td>See separate document</td>
</tr>
<tr>
<td><strong>Review strategies</strong></td>
<td>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence</td>
</tr>
<tr>
<td><strong>Equality</strong></td>
<td>Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)</td>
</tr>
</tbody>
</table>
E.15 **Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis**

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

<table>
<thead>
<tr>
<th><strong>Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis</strong></th>
</tr>
</thead>
</table>
| **Existing recommendation(s) in 2004 guideline** | Management from diagnosis  
Children and young people who present with diabetic ketoacidosis should have their diabetic ketoacidosis treated in hospital according to the guidance outlined in this document.  
Diabetic ketoacidosis  
Children and young people with diabetic ketoacidosis should be treated according to the guidelines published by the British Society for Paediatric Endocrinology and Diabetes.  
Children and young people with diabetic ketoacidosis should be managed initially in a high-dependency unit or in a high-dependency bed on a children’s ward.  
Children and young people with deteriorating consciousness or suspected cerebral oedema and those who are not responding appropriately to treatment should be managed in a paediatric intensive care unit.  
Children with diabetic ketoacidosis who are younger than 2 years of age should be managed in a paediatric intensive care unit.  
Children and young people with a blood pH of less than 7.3 (hydrogen ion concentration of more than 50 nmol/litre), but who are clinically well (with no tachycardia, vomiting, drowsiness, abdominal pain or breathlessness) and less than 5% dehydrated, may respond appropriately to oral rehydration, frequent subcutaneous insulin injections and monitoring of blood glucose. |
| **Review question for update** | All recommendations relating to the recognition and management of diabetic ketoacidosis (DKA) are listed here for completeness  
The guidelines published by the British Society for Paediatric Endocrinology and Diabetes (BSPED) were reproduced in an appendix of the 2004 guideline.  
The 2004 guideline was specific to type 1 diabetes  
The review questions relating to DKA will be considered separately from the remaining questions by a subgroup of the GDG plus an expert adviser (a paediatric intensivist) who will advise on fluid management and clinical care during DKA. The DKA subgroup will meet and consider the evidence base and draw conclusions in parallel with development of the remainder of the guideline. The full GDG will ratify all conclusions and recommendations based on the DKA evidence. |
| **Objectives** | The review questions for type 1 and type 2 diabetes are identical  
To determine whether anticoagulant prophylaxis is effective in preventing venous thrombosis in children and young people with DKA. The GDG noted that deep vein thrombosis, visceral thrombosis, and cerebral thrombosis would all be relevant in this review question  
Children and young people with DKA who have central venous lines inserted are at greater risk of developing central venous thrombosis. Current practice is typically to provide prophylactic anticoagulation to these children and young people. The review for this question will focus on comparison of outcomes for some |
<table>
<thead>
<tr>
<th><strong>Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Language</strong></td>
</tr>
</tbody>
</table>
| **Study design** | Systematic reviews and randomised controlled trials (RCTs)  
Comparative observational studies (including cohort and case-control studies) |
| **Status** | Published articles (no limitation on year of publication) |
| **Population** | Children and young people with type 1 or type 2 diabetes (although the diabetes may not yet have been recognised, for example, if the child or young person is presenting for the first time with DKA) |
| **Intervention or index test** | Any anticoagulation prophylaxis regimen |
| **Comparator or reference standard** | No anticoagulation prophylaxis regimen |
| **Clinical outcomes** | Physical outcomes  
• Mortality  
• Incidence of venous thrombosis (of any type, including deep vein thrombosis, visceral) |

Form of prophylactic anticoagulation compared with no anticoagulation

Although there may be some RCTs for this question the systematic search for evidence should encompass observational studies from the outset and the review itself will cover RCTs and observational studies.

As this is a new question which was not considered in the original 2004 guideline, no date limit will be applied to searches for these review questions to ensure that all relevant articles are identified for both type 1 and 2 diabetes.

The guideline scope defines children and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years.

The GDG noted that the management of DKA in adults is likely to be different to that in children and young people, and this may be an important area to consider in relation to transition from paediatric to adult services.

The following terminology may be useful in relation to specifying search terms relevant to anticoagulation regimens:
- aspirin
- dalteparin
- dicoumarol
- fragmin
- heparin
- low-dose heparin
- synthetic warfarins (these newer products are not licensed for use in children and young people but any relevant evidence can still be considered as part of the review)
- warfarin

The review will not compare different anticoagulation regimens with one another.
**Type 1 and type 2 diabetes – diabetic ketoacidosis –anticoagulant prophylaxis**

<table>
<thead>
<tr>
<th>Health economics outcomes</th>
<th>These questions were not prioritised for health economic analysis</th>
<th>If any evidence is identified in relation to healthcare utilisation the decision not to prioritise this question for health economic analysis might be revisited (but the GDG does not expect there to be much evidence at all)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other criteria for inclusion/exclusion of studies</td>
<td>Exclude studies with &lt;10 participants in total</td>
<td>Subgroup analysis by type of diabetes (type 1 or type 2) should be presented if possible, as should subgroup analysis by previously recognised diabetes or first presentation. Additionally, subgroup analysis by age group (for example, pre-school versus primary school or secondary school) would be useful if the evidence from the included studies allows this.</td>
</tr>
<tr>
<td>Search strategies</td>
<td>See separate document</td>
<td>A single search for evidence will be undertaken for both type 1 and type 2 diabetes</td>
</tr>
<tr>
<td>Review strategies</td>
<td>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012). A list of excluded studies will be provided following weeding. Evidence tables and an evidence profile will be used to summarise the evidence.</td>
<td>The GDG’s view was that DKA would be more prevalent in certain ethnic minorities and people with lower socio-economic status, especially in the case of children or young people with DKA at the first presentation with diabetes.</td>
</tr>
<tr>
<td>Equality</td>
<td>Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)</td>
<td></td>
</tr>
</tbody>
</table>
**E.16 Type 1 diabetes – retinopathy**

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

<table>
<thead>
<tr>
<th><strong>Type 1 diabetes – retinopathy</strong></th>
<th><strong>Existing recommendation(s) in 2004 guideline</strong></th>
<th><strong>Review question for update</strong></th>
<th><strong>Objectives</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Children and young people with type 1 diabetes should be offered screening for:</td>
<td>What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 1 diabetes?</td>
<td>To determine when retinopathy screening should start following diagnosis of type 1 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter, and taking account of the severity (grade) of retinopathy, including the clinical importance of any background retinopathy.</td>
</tr>
<tr>
<td></td>
<td>• coeliac disease at diagnosis</td>
<td></td>
<td>Note that background retinopathy can revert to normal, giving rise to intermittent retinopathy. The GDG’s recommendations should take into account the practicalities of starting screening based on duration of diabetes rather than age (because screening for retinopathy requires referral to an ophthalmologist and ophthalmology services may not have access to information about duration of diabetes).</td>
</tr>
<tr>
<td></td>
<td>• thyroid disease at diagnosis and annually thereafter until transfer to adult services</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• retinopathy annually from the age of 12 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• microalbuminuria annually from the age of 12 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• blood pressure annually from the age of 12 years.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Only those aspects relating to retinopathy and nephropathy in the 2004 recommendation about screening for complications in children and young people with type 1 diabetes are being updated</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>The reason for updating this recommendation is to reconsider the time at which to test (age/duration of diabetes), not how to test.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Language</strong></td>
<td>English</td>
<td><strong>Useful background reading in</strong></td>
<td><strong>Notes</strong></td>
</tr>
<tr>
<td><strong>Study design</strong></td>
<td>Cohort studies or consecutive case series</td>
<td><a href="http://www.guidelines.gov/content.aspx?id=13502">http://www.guidelines.gov/content.aspx?id=13502</a></td>
<td>Note that background retinopathy can revert to normal, giving rise to intermittent retinopathy. The GDG’s recommendations should take into account the practicalities of starting screening based on duration of diabetes rather than age (because screening for retinopathy requires referral to an ophthalmologist and ophthalmology services may not have access to information about duration of diabetes).</td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td>Published articles (no limitation on year of publication)</td>
<td><strong>Cross-sectional studies which report prevalence and longitudinal studies which report incidence will be considered</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>Children and young people with type 1 diabetes</td>
<td></td>
<td>The guideline scope defines children and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are presented on an age group which extends into people aged &gt;18 years, these will be included only if the mean age in the group is ≤ 18 years.</td>
</tr>
</tbody>
</table>
### Type 1 diabetes – retinopathy

| Intervention or index test | Universal retinopathy screening using digital retinal photography | Digital retinal photography is the method currently recommended in the NHS Diabetic Eye Screening Programme |

| Comparator or reference standard | Prevalence or incidence at different time intervals after diagnosis and/or at different ages | Exclude studies which consider only fluorescein angiography or ophthalmoscopy |

| Clinical outcomes | Prevalence of retinopathy at different timepoints after diagnosis (this might include data obtained via ‘survival analysis’ methods) Incidence of retinopathy over time When available, severity (grade) of retinopathy will be reported based on the NHS Diabetic Eye Screening Programme (see, for example, [http://medweb.bham.ac.uk/easdec/gradingretinopathy.htm](http://medweb.bham.ac.uk/easdec/gradingretinopathy.htm)) | • Look at finding the earliest time at which retinopathy becomes sufficiently common/severe to warrant screening • The GDG may need to consider not just the existence of retinopathy but also the severity (grade) of retinopathy • Current practice is to refer children and young people with diabetes to an ophthalmologist only if they have sight-threatening diabetic retinopathy, and this is unlikely in people younger than 12 years; as noted above, background retinopathy can revert to normal • It might be worth identifying retinopathy that will not lead to referral to an ophthalmologist if this would support provision of education about risks associated with retinopathy • Subgroup analysis based on age may be relevant |

| Health economic outcomes | This question was not identified as a priority for health economic analysis |

| Other criteria for exclusions | Exclude studies that do not: • report prevalence of retinopathy at a |
### Type 1 diabetes – retinopathy

| inclusion/exclusion of studies | particular timepoint after diagnosis  
|--------------------------------|--------------------------------------
|                                | • have a systematic approach to screening, as opposed to selective patient screening based on individual concerns |

| Search strategies | See separate document |

| Review strategies | Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)  
|                   | A list of excluded studies will be provided following weeding  
|                   | Evidence tables and an evidence profile will be used to summarise the evidence |

| Equality | Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012) |

|                              | The practicalities of offering screening for retinopathy will vary according to the child or young person’s age and whether or not they have learning difficulties (because digital retinal photography requires the person to sit still and stare at a fixed point) |
E.17 **Type 1 diabetes – nephropathy**

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

<table>
<thead>
<tr>
<th>Type 1 diabetes – nephropathy</th>
</tr>
</thead>
</table>
| **Existing recommendation(s) in 2004 guideline** | Children and young people with type 1 diabetes should be offered screening for:  
- coeliac disease at diagnosis  
- thyroid disease at diagnosis and annually thereafter until transfer to adult services  
- retinopathy annually from the age of 12 years  
- microalbuminuria annually from the age of 12 years  
- blood pressure annually from the age of 12 years. |
| **Review question for update** | What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes? |
| **Objectives** | To determine when nephropathy screening should start following diagnosis of type 1 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter, and taking account of issues such as the clinical importance of intermittent microalbuminuria. |
| **Language** | English |
| **Study design** | Cohort studies or consecutive case series |
| **Status** | Published articles (no limitation on year of publication) |

Only those aspects relating to retinopathy and nephropathy in the 2004 recommendation about screening for complications in children and young people with type 1 diabetes are being updated.

The existing recommendation about screening for microalbuminuria relates to testing based on urine albumin:creatinine ratio. The reason for updating this recommendation is to reconsider the time at which to test (age/duration of diabetes) not how to test.

If the GDG intends to recommend screening for microalbuminuria (as a marker of nephropathy) from an age lower than 12 years then the possibility of revising the recommendation about when to start monitoring blood pressure should be raised with NICE (because hypertension is also associated with nephropathy).

### Type 1 diabetes – nephropathy

| Intervention or index test | Screening for microalbuminuria (however measured, and including using measurement through urine albumin:creatinine ratio (ACR)) | The guidelines relating to type 1 diabetes in adults and type 2 diabetes in adults include specific recommendations on:  
  - repeated measurement of ACR over a 4-month period to establish a diagnosis of microalbuminuria  
  - measuring serum creatinine at the same time, and  
  - in type 2 diabetes, estimating the glomerular filtration rate (GFR) at the same time (using the method-abbreviated modification of diet in renal disease four-variable equation)  

Usual practice is to measure only microalbuminuria in children and young people with type 1 diabetes (serum creatinine concentration is measured only if the microalbuminuria measurement is abnormal because this provides evidence of renal damage from microalbuminuria or hypertension); an abnormal urine ACR is the first feature of nephropathy, whereas abnormal serum creatinine concentration is a later feature that is not relevant in children and young people with type 1 diabetes because

and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are presented on an age group which extends into people aged >18 years, these will be included only if the mean age in the group is ≤ 18 years or if more than 50% of group participants are aged ≤ 18 years.

Studies will be included only if they provide data on prevalence for specific groups of children or young people (stratified by age or duration of diabetes).

Only include data on incidence if exact figures (for example, incidence per hundred person years) are described in the text, and not if data are solely presented as survival curve analysis.
### Type 1 diabetes – nephropathy

- They are unlikely to have nephropathy at diagnosis.
- Urine ACR is the practice for screening of microalbuminuria in the UK. For studies which report on albumin excretion rate (AER) rather than ACR for the confirmation of microalbuminuria, convert to ACR measurements using separate conversion equations for males and females (Schultz et al. 1999).

Reference is:

- Using ACR > 2.5mg/mmol for males and ACR > 3.5 mg/mmol for females (at least 2 of 3 consecutive collections over a period of 3-4 months) which are the standards for confirming microalbuminuria in UK adults. Exclude studies where the ACR measurement falls below 2.5 mg/mmol or 3.5mg/mmol for males and females, respectively.

### Comparators or reference standard

| Prevalence or incidence at different time intervals after diagnosis and/or at different ages |

### Clinical outcomes

| Prevalence of microalbuminuria (however measured, and including using measurement through urine albumin:creatinine ratio) |

| Incidence of microalbuminuria over time |

| Evidence tables should document cut-offs and definitions of microalbuminuria used in included studies |

| NCC-WCH to discuss with GDG to determine which studies should be included if necessary |

Note that the 2004 guideline on type 1 diabetes in adults, and the 2008 guideline on type 2 diabetes in adults use repeated tests of ACR >2.5mg/mmol for men, and >3.5mg/mmol for women (in at least 2 of 3 consecutive collections over a period of 3-4 months) to confirm microalbuminuria.

It will be important to consider the severity of microalbuminuria and...
<table>
<thead>
<tr>
<th><strong>Type 1 diabetes – nephropathy</strong></th>
<th>how should this be reported (for example, thresholds for ‘severe microalbuminuria’, etc)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Health economic outcomes</strong></td>
<td>This question was not identified as a priority for health economic analysis</td>
</tr>
</tbody>
</table>
| **Other criteria for inclusion/exclusion of studies** | Exclude studies that do not:  
  - report prevalence of microalbuminuria  
  - have a systematic approach to screening, as opposed to selective patient screening based on individual concerns |
| **Search strategies**            | See separate document                                                            |
|                                  | NCC-WCH to consider using a single search to cover both review questions relating to monitoring for nephropathy (type 1 diabetes and type 2 diabetes)  
  The search terms microalbuminuria and diabetes should identify relevant studies |
| **Review strategies**            | Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)  
  A list of excluded studies will be provided following weeding  
  Evidence tables and an evidence profile will be used to summarise the evidence |
| **Equality**                     | Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012) |

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### Type 2 diabetes – education

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

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

The above terms were listed in the corresponding protocol for children and young people with type 1 diabetes; for type 2 diabetes the search also needs to be broad enough to encompass relevant education about:

• exercise
• physical activity
• lifestyle
• weight loss or management programmes

This review should cover:
all settings (diabetes clinics, schools, etc), while recognising that recommendations will be limited to the clinical practice context
all forms of delivery of education (for example, one-to-one, brief, face-to-face, and remote (telemedicine, including text messaging))

Names of studies that might be relevant (not to be used as search terms):
DESMOND X-PERT

<table>
<thead>
<tr>
<th>Comparators or reference standard</th>
<th>Alternative models of education</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual care</td>
<td>Usual care in this context usually includes unstructured, informal education, provision of information leaflets or multimedia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Outcomes</th>
<th>Physical outcomes</th>
<th>The priority outcomes selected by the GDG are different to those for</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Glycaemic control</td>
<td></td>
</tr>
</tbody>
</table>
### Type 2 diabetes – education

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c</td>
<td>HbA1c (minimum follow-up 6 months after completion of primary intervention)</td>
</tr>
<tr>
<td>Adherence</td>
<td>Adherence to education intervention</td>
</tr>
<tr>
<td>Changes in BMI</td>
<td>Changes in body mass index (BMI) standard deviation score (SDS)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Achievement and maintenance of weight loss during the programme</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Change in level of physical activity (for example, hours of exercise per week; minimum follow-up 6 months after completion of primary intervention)</td>
</tr>
</tbody>
</table>

**Psychosocial outcomes**

- Health-related quality of life
- Children and young people’s and families’ satisfaction with intervention (education intervention)

### The review questions on behavioural interventions because psychosocial outcomes are more relevant there

The GDG identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and change in level of physical activity, and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required.

- HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)
- BMI SDS MID is 0.5 for weight-loss interventions and 0 for all other interventions

Note that incidence of severe hypoglycaemic episodes is not a relevant outcome in children and young people with type 2 diabetes because their diabetes is not likely to be treated with insulin or any other pharmaceutical agent that would case hypoglycaemia. Also diabetic ketoacidosis (DKA) may be a problem at initial presentation but it is unlikely to occur subsequently.

Adherence to diabetes management, including self-management was not prioritised as an outcome for this question. The GDG agreed that this was a lower priority than adherence to the educational intervention itself because insulin is not always used in the treatment of type 2 diabetes.

No long-term complications needed to be prioritised as outcomes because HbA1c will determine these.

### Health economic outcomes

- This question was not prioritised for health economic analysis

### Other criteria for

- None

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

### Review questions:
- What is the effectiveness of behavioural interventions to promote engagement with clinical services in children and young people with type 2 diabetes?
- What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 2 diabetes?

### Type 2 diabetes – behavioural interventions

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

<table>
<thead>
<tr>
<th>Language</th>
<th>English</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study design</td>
<td>Systematic reviews and randomised controlled trials (RCTs) only</td>
</tr>
<tr>
<td>Status</td>
<td>Published articles (no limitation on year of publication)</td>
</tr>
<tr>
<td>Population</td>
<td>Children and young people with type 2 diabetes</td>
</tr>
<tr>
<td>Intervention or index test</td>
<td>Behavioural interventions specific to the management of type 2 diabetes in children and young people (this could involve interventions aimed at families and healthcare professionals as well as those aimed at the child or young person)</td>
</tr>
</tbody>
</table>

- Peer support (and peer-led interventions): these can be delivered one-to-one or in groups. The intervention typically involves people of similar age to the person receiving peer support
- Family therapy (include only validated therapies such as BFST – expert adviser to advise in relation to search results)
- CBT
- Motivational interviewing
- Counseling
- Mentoring
- Peer support (and peer-led interventions)

Use the terms specific to the prioritised behavioural interventions when conducting the searches for this question

Useful reference (systematic review) for educational and behavioural interventions is AHQR 2008 (Evidence report 166 http://www.ahrq.gov/clinic/tp/diabedt.p.htm)

The following search terms from the AHQR 2008 systematic review were considered by the GDG and expert adviser as part of the prioritisation of behavioural interventions for this question but they were not selected for the reasons given and they should not be used as search terms for this question:

- Adherence (an outcome not an intervention)
- Behavioural therapy (poorly defined so not a priority)
- Biofeedback (more relevant to the question relating to education programmes)
- Cognitive therapy (not a priority because it focuses on awareness)
### Type 2 diabetes – behavioural interventions

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavioural interventions</td>
<td>of behaviour but not changing behaviour</td>
</tr>
<tr>
<td>• Conjoint therapy (refers to any two therapies joined together)</td>
<td></td>
</tr>
<tr>
<td>• Educational therapy (will be addresses in the education question)</td>
<td></td>
</tr>
<tr>
<td>• Psychological interventions (not specific)</td>
<td></td>
</tr>
<tr>
<td>• Psychological therapy (not specific)</td>
<td></td>
</tr>
<tr>
<td>• Solution-focused therapy (not specific – refers to any therapy that focuses on solutions rather than problems; several of the prioritised interventions are solution-focused)</td>
<td></td>
</tr>
<tr>
<td>• Therapy (not specific)</td>
<td></td>
</tr>
</tbody>
</table>

This review should cover:

- all settings (diabetes clinics, schools, etc), while recognising that recommendations will be limited to the clinical practice context
- all forms of delivery of the prioritised behavioural interventions (for example, one-to-one, brief, face-to-face, and remote (telemedicine))

Names of studies that might be relevant (not to be used as search terms):

- DESMOND
- X-PERT

### Comparator or reference standard

An alternative behavioural intervention listed above
An alternative and well defined behavioural intervention not listed above (expert adviser to advise on what is well defined in relation to search results)
Any other intervention aimed at changing a specific behaviour, a range of behaviours, or psychosocial adjustment to diabetes self-management
Usual care (this will be the most common comparator)

### Usual care in this context usually includes education, no therapy, provision of information leaflets or multimedia (DVDs, CDs, websites, apps)

### Clinical outcomes

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>For the question about engagement with clinical services</td>
<td></td>
</tr>
<tr>
<td>Physical outcomes</td>
<td></td>
</tr>
<tr>
<td>• Adherence to diabetes management (the scope requires this; to include self-management)</td>
<td></td>
</tr>
<tr>
<td>Psychosocial outcomes</td>
<td></td>
</tr>
<tr>
<td>• Children and young people’s and families’</td>
<td></td>
</tr>
</tbody>
</table>

The GDG identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and change in level of physical activity, and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required.
### Type 2 diabetes – behavioural interventions

<table>
<thead>
<tr>
<th>Satisfaction with intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk-taking behaviours (such as smoking)</td>
</tr>
<tr>
<td>Engagement with clinical services (for example, attendance at clinic appointments)</td>
</tr>
<tr>
<td>For the general question about improving outcomes</td>
</tr>
<tr>
<td>Physical outcomes</td>
</tr>
<tr>
<td>Glycaemic control</td>
</tr>
<tr>
<td>HbA1c (minimum follow-up 6 months after completion of primary intervention)</td>
</tr>
<tr>
<td>Adverse events (for example, diabetes-related hospital admission or self-harm)</td>
</tr>
<tr>
<td>Changes in body mass index (BMI) standard deviation score (SDS)</td>
</tr>
<tr>
<td>Achievement and maintenance of weight loss during the programme (NCC-WCH to seek clarification from GDG about whether weight-loss outcomes are relevant after searches have been completed)</td>
</tr>
<tr>
<td>Change in level of physical activity (for example, hours of exercise per week; minimum follow-up 6 months after completion of primary intervention)</td>
</tr>
<tr>
<td>Psychosocial outcomes</td>
</tr>
<tr>
<td>Health-related quality of life (this outcome might capture bullying about weight)</td>
</tr>
<tr>
<td>Depression or anxiety</td>
</tr>
</tbody>
</table>

The GDG agreed that change in body mass index (BMI) standard deviation score (SDS) would be more important than DKA than in the corresponding question for type 1 diabetes

HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)

BMI SDS MID is 0.5 for weight-loss interventions and 0 for all other interventions

No long-term complications needed to be prioritised as outcomes because HbA1c will determine these

<table>
<thead>
<tr>
<th>Health economic outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>This question was not prioritised for health economic analysis</td>
</tr>
</tbody>
</table>

The GDG might wish to evaluate the cost effectiveness of behavioural interventions for type 2 diabetes – see notes on protocol for weight loss in type 2 diabetes

<table>
<thead>
<tr>
<th>Other criteria for inclusion/exclusion of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
</tr>
</tbody>
</table>

Evidence tables should document who delivered the intervention(s) and the frequency of contact with healthcare or other relevant professionals to deliver the intervention(s)

<table>
<thead>
<tr>
<th>Search strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>See separate document</td>
</tr>
</tbody>
</table>

A single search will be used to cover both questions

<table>
<thead>
<tr>
<th>Review strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</td>
</tr>
<tr>
<td>A list of excluded studies will be provided following weeding</td>
</tr>
<tr>
<td>Evidence tables and an evidence profile will be used to summarise the evidence</td>
</tr>
</tbody>
</table>

NCC-WCH technical team to search the PsycINFO bibliographic database for this review question (in addition to the standard bibliographic databases)
### Type 2 diabetes – behavioural interventions

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

## E.20 Type 2 diabetes – dietary advice

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

<table>
<thead>
<tr>
<th><strong>Type 2 diabetes – dietary advice</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Existing recommendation(s) in 2004 guideline</strong></td>
<td>None</td>
</tr>
<tr>
<td><strong>Review question for update</strong></td>
<td>What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>To identify the dietetic advice to be given to children and young people with type 2 diabetes to optimise glycaemic control. The question includes evaluation of the effectiveness of different forms of dietetic advice in terms of achieving outcomes relating to glycaemic control</td>
</tr>
<tr>
<td><strong>Language</strong></td>
<td>English</td>
</tr>
<tr>
<td><strong>Study design</strong></td>
<td>Systematic reviews and randomised controlled trials (RCTs) only</td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td>Published articles (no limitation on year of publication)</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>Children and young people with type 2 diabetes</td>
</tr>
<tr>
<td><strong>Intervention or index test</strong></td>
<td>Dietetic advice intended to optimise glycaemic control</td>
</tr>
<tr>
<td><strong>Comparator or reference standard</strong></td>
<td>Usual care</td>
</tr>
</tbody>
</table>

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

| increased risk of this type of diabetes according to ethnicity and socioeconomic status) |
**E.21 Type 2 diabetes – weight loss**

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

<table>
<thead>
<tr>
<th><strong>Type 2 diabetes – weight loss</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Existing recommendation(s) in 2004 guideline</strong></td>
</tr>
<tr>
<td><strong>Review question for update</strong></td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
</tr>
<tr>
<td><strong>Language</strong></td>
</tr>
<tr>
<td><strong>Study design</strong></td>
</tr>
<tr>
<td><strong>Status</strong></td>
</tr>
<tr>
<td><strong>Population</strong></td>
</tr>
</tbody>
</table>

The NICE clinical guideline on obesity (http://guidance.nice.org.uk/CG43) includes the following recommendations:

- Bariatric surgery is recommended as a treatment option for people with obesity if all of the following criteria are fulfilled:
  - they have a body mass index (BMI) of 40 kg/m2 or more, or between 35 kg/m2 and 40 kg/m2 and other significant disease (for example, type 2 diabetes or high blood pressure) that could be improved if they lost weight [other bullets in this recommendation omitted for brevity]

- Surgical intervention is not generally recommended in children or young people.

- Bariatric surgery may be considered for young people only in exceptional circumstances, and if they have achieved or nearly achieved physiological maturity.

It is not expected that there will be RCTs that fully answer this question (in terms of the association between weight loss and glycaemic control) and so no restriction in study design will be applied to this question.

This is a completely new topic for the update so no date limit will be applied to searches.

The guideline scope defines children and young people with type 2 diabetes.
<table>
<thead>
<tr>
<th><strong>Type 2 diabetes – weight loss</strong></th>
<th><strong>Intervention or index test</strong></th>
<th><strong>Comparator or reference standard</strong></th>
<th><strong>Clinical outcomes</strong></th>
<th><strong>Health economic outcomes</strong></th>
</tr>
</thead>
</table>
| diabetes who are overweight or obese | RCTs: Weight loss interventions specific to the management of type 2 diabetes in children and young people. Note that the guideline scope relates specifically to children and young people with diabetes, and so studies that focus on prevention of type 2 diabetes should be excluded | RCTs: An alternative weight loss intervention or usual care | Physical outcomes  
- Glycaemic control  
  - HbA1c (minimum follow-up 6 months)  
  - Adherence to diabetes management, including self-management  
  - Changes in body mass index (BMI) standard deviation score (SDS)  
  - Remission of diabetes (normal HbA1c and no treatment for diabetes, for example at 1 year after starting the weight loss intervention)  
- Time to treatment failure (when insulin is required to manage diabetes; the physiological basis for this is that initial management should postpone the need for insulin, but insulin will be needed eventually as insulin resistance changes and secretion of insulin by the pancreas stops) | This question was not prioritised for health economic analysis |
<p>| and young people as those younger than 18 years. The initial approach will be to include studies only if they report results for people younger than 18 years | The specified interventions assume that RCTs are available but as noted above the review will include consideration of observational studies from the outset so that any association between weight loss and glycaemic control can be evaluated | Observational studies: Weight change in relation to glycaemic control | Usual care could include informal, general advice or programmes relating to weight loss | This question was proposed as the top priority for health economic analysis among the questions relating to type 2 diabetes, but the |
| Evidence tables should document any pharmacological treatment (for example, metformin or insulin) in the intervention and comparison groups | | | Weight change or a comparable measure such as change in body mass index (BMI) standard deviation score (SDS) | |</p>
<table>
<thead>
<tr>
<th>Type 2 diabetes – weight loss</th>
<th>NCC-WCH will refer to the guidelines on obesity (update) and type 2 diabetes in adults rather than undertaking any modelling for this guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other criteria for inclusion/exclusion of studies</td>
<td>None</td>
</tr>
<tr>
<td>Search strategies</td>
<td>See separate document</td>
</tr>
</tbody>
</table>
| Review strategies | Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)  
A list of excluded studies will be provided following weeding  
Evidence tables and an evidence profile will be used to summarise the evidence |
| Equality | Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)  
Ethnicity, languages other than English, and literacy may all be important considerations for this question. These issues are specific to children and young people with type 2 diabetes (because of the increased risk of this type of diabetes according to ethnicity and socioeconomic status) |
## E.22 Type 2 diabetes – metformin

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

<table>
<thead>
<tr>
<th><strong>Type 2 diabetes – metformin</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Existing recommendation(s) in 2004 guideline</strong></td>
</tr>
<tr>
<td><strong>Review question for update</strong></td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
</tr>
<tr>
<td><strong>Language</strong></td>
</tr>
<tr>
<td><strong>Study design</strong></td>
</tr>
<tr>
<td><strong>Status</strong></td>
</tr>
<tr>
<td><strong>Population</strong></td>
</tr>
<tr>
<td><strong>Intervention or index test</strong></td>
</tr>
</tbody>
</table>
| **Comparator or reference standard** | • Usual care  
• Placebo | Usual care in this instance includes lifestyle advice, education, etc |
| **Clinical outcomes** | • Haemoglobin A1c (HbA1c)  
• Number needing rescue medication  
• Number of dropouts  
• Number with any adverse events, including diabetic ketoacidosis (DKA)  
• Changes in fasting plasma glucose (FPG)  
• Changes in body mass index (BMI) standard deviation score (SDS)  
• Patient satisfaction with the intervention |
| **Health economic outcomes** | This question was not prioritised for health economic analysis  
Most of the outcomes above, but should not necessarily be limited to seven and could be extended to include generic measures of health-related quality of life |
<p>| <strong>Other criteria for inclusion/exclusion of studies</strong> | None |</p>
<table>
<thead>
<tr>
<th><strong>Type 2 diabetes – metformin</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Search strategies</strong></td>
<td>See separate document</td>
</tr>
<tr>
<td><strong>Review strategies</strong></td>
<td>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence</td>
</tr>
<tr>
<td><strong>Equality</strong></td>
<td>Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)</td>
</tr>
<tr>
<td></td>
<td>Ethnicity, languages other than English, and literacy may all be important considerations for this question. These issues are specific to children and young people with type 2 diabetes (because of the increased risk of this type of diabetes according to ethnicity and socioeconomic status)</td>
</tr>
</tbody>
</table>
### E.23 Type 2 diabetes – HbA1c targets

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

<table>
<thead>
<tr>
<th>Type 2 diabetes – HbA1c targets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Existing recommendation(s) in 2004 guideline</strong></td>
</tr>
<tr>
<td><strong>Review question for update</strong></td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
</tr>
<tr>
<td><strong>Language</strong></td>
</tr>
<tr>
<td><strong>Study design</strong></td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td><strong>Status</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Population</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
</tr>
</tbody>
</table>
## Type 2 diabetes – HbA1c targets

<table>
<thead>
<tr>
<th>Comparator or reference standard</th>
<th>Comparisons to be made between outcomes according to target values for HbA1c and/or HbA1c values achieved (recorded)</th>
<th>Development or worsening of long-term complications are the most important outcomes for this question</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical outcomes</strong></td>
<td></td>
<td>The GDG identified a minimum follow-up period of 6 months after completion of the primary intervention for HbA1c and 4 months for other outcomes. Include further follow-up if reported, for example, if a top-up intervention is required</td>
</tr>
<tr>
<td><strong>Glycaemic control</strong></td>
<td>Development or worsening of long-term complications</td>
<td>HbA1c minimally important difference (MID) is 0.5 percentage points (5.5 mmol/mol)</td>
</tr>
<tr>
<td></td>
<td>o Hypertension (important in children and young people with type 2 diabetes because they often have it at diagnosis and/or are obese)</td>
<td>Severe hypoglycaemic episodes defined according to either of the following criteria.</td>
</tr>
<tr>
<td></td>
<td>o Retinopathy (important in children and young people with type 2 diabetes because they often have it at diagnosis and/or are obese)</td>
<td>- International Society for Pediatric and Adolescent Diabetes (ISPAD) 2009 – the mental state of the child or young person is altered and they cannot assist in their care, they are semiconscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose)</td>
</tr>
<tr>
<td></td>
<td>o Nephropathy (important in children and young people with type 2 diabetes because they often have it at diagnosis and/or are obese)</td>
<td>- ISPAD 2000 grade 2 or 3 – the child or young person cannot respond to hypoglycaemia and needs help from another person, but oral treatment is successful (grade 2) or they are semi-conscious or unconscious, or in coma (with or without convulsions) and may need parenteral treatment (glucagon or intravenous glucose)</td>
</tr>
<tr>
<td></td>
<td>Changes in body mass index (BMI) standard deviation score (SDS)</td>
<td>BMI SDS minimally important difference is 0.5 for weight-loss interventions and 0 for all other interventions</td>
</tr>
<tr>
<td><strong>Psychosocial outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Health-related quality of life</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Children and young people’s and families’ satisfaction with intervention (the impact of blood sampling would be reflected here)</td>
<td></td>
</tr>
<tr>
<td><strong>Health economic outcomes</strong></td>
<td>This question was not prioritised for health economic analysis</td>
<td></td>
</tr>
<tr>
<td><strong>Other criteria for inclusion/exclusion of studies</strong></td>
<td>None</td>
<td></td>
</tr>
<tr>
<td><strong>Search strategies</strong></td>
<td>See separate document</td>
<td></td>
</tr>
<tr>
<td>Type 2 diabetes – HbA1c targets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Review strategies</strong></td>
<td>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012) A list of excluded studies will be provided following weeding Evidence tables and an evidence profile will be used to summarise the evidence</td>
<td></td>
</tr>
<tr>
<td><strong>Equality</strong></td>
<td>Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)</td>
<td></td>
</tr>
</tbody>
</table>
### Type 2 diabetes – hypertension

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

<table>
<thead>
<tr>
<th>Type 2 diabetes – hypertension</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Existing recommendation(s) in 2004 guideline</strong></td>
<td>None</td>
</tr>
<tr>
<td><strong>Review question for update</strong></td>
<td>What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?</td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
<td>To determine when monitoring for hypertension should start following diagnosis of type 2 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter</td>
</tr>
<tr>
<td></td>
<td>This review will need to consider how to identify hypertension, in terms of:</td>
</tr>
<tr>
<td></td>
<td>• which parameters to measure (systolic and/or diastolic blood pressure)</td>
</tr>
<tr>
<td></td>
<td>• which thresholds to use for parameters of interest (for example, ( \geq 95\text{th} ) or ( \geq 98\text{th} ) centile for sex, age and height), and</td>
</tr>
<tr>
<td></td>
<td>• how many measurements to use (for example, measure once and if above the chosen threshold measure again at same clinic visit; if still elevated measure a third time at same visit; and accept the lowest value recorded).</td>
</tr>
<tr>
<td></td>
<td>GDG to note that in children and young people in whom clinic blood pressure measurements suggest hypertension, confirmation will be necessary using ambulatory 24-hour monitoring or home blood pressure monitoring, for example, as described in the NICE guideline on hypertension in adults (CG127). The guideline comments on the choice and maintenance of devices used to measure blood pressure. The GDG may wish to consider cuff size to be used when measuring blood pressure in children and young people with type 2 diabetes</td>
</tr>
<tr>
<td></td>
<td>The National Screening Committee 2010 review may provide useful information for reference</td>
</tr>
</tbody>
</table>

| **Language** | English |
| **Study design** | Cohort studies or consecutive case series |
| **Status** | Published articles (no limitation on year of publication) |

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<table>
<thead>
<tr>
<th>Type 2 diabetes – hypertension</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>Children and young people with type 2 diabetes</td>
</tr>
<tr>
<td><strong>Intervention or index test</strong></td>
<td>Screening for hypertension</td>
</tr>
<tr>
<td><strong>Comparator or reference standard</strong></td>
<td>Prevalence or incidence at different time intervals after diagnosis and/or at different ages</td>
</tr>
<tr>
<td><strong>Clinical outcomes</strong></td>
<td>Prevalence of hypertension at different timepoints after diagnosis Incidence of hypertension over time</td>
</tr>
<tr>
<td><strong>Health economic outcomes</strong></td>
<td>This question was not identified as a priority for health economic analysis</td>
</tr>
<tr>
<td><strong>Other criteria for inclusion/exclusion of studies</strong></td>
<td>Exclude studies that do not: • report prevalence of hypertension at a particular timepoint after diagnosis • have a systematic approach to screening, as opposed to selective patient screening based on individual concerns</td>
</tr>
<tr>
<td><strong>Search strategies</strong></td>
<td>See separate document</td>
</tr>
<tr>
<td><strong>Review</strong></td>
<td>Evidence will be assessed for quality</td>
</tr>
<tr>
<td><strong>Type 2 diabetes – hypertension</strong></td>
<td></td>
</tr>
<tr>
<td>-----------------------------------</td>
<td></td>
</tr>
<tr>
<td><strong>strategies</strong></td>
<td></td>
</tr>
<tr>
<td>According to the process described in the NICE guidelines manual (November 2012)</td>
<td></td>
</tr>
<tr>
<td>A list of excluded studies will be provided following weeding</td>
<td></td>
</tr>
<tr>
<td>Evidence tables and an evidence profile will be used to summarise the evidence</td>
<td></td>
</tr>
<tr>
<td><strong>Equality</strong></td>
<td></td>
</tr>
<tr>
<td>Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)</td>
<td></td>
</tr>
<tr>
<td>Type 2 diabetes is associated with obesity and so the GDG may wish to consider the appropriate cuff size to use when measuring blood pressure in children and young people with type 2 diabetes</td>
<td></td>
</tr>
</tbody>
</table>
## Type 2 diabetes – dyslipidaemia

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

<table>
<thead>
<tr>
<th>Type 2 diabetes – dyslipidaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Existing recommendation(s) in 2004 guideline</strong></td>
</tr>
<tr>
<td><strong>Review question for update</strong></td>
</tr>
</tbody>
</table>
| **Objectives** | To determine when monitoring for dyslipidaemia should start following diagnosis of type 2 diabetes and how frequently it should be repeated. The review will need to consider the clinical utility of monitoring based on prevalence at diagnosis and intervals thereafter | This review will need to consider how to identify dyslipidaemia, in terms of which serum lipids to measure, for example:  
- total cholesterol  
- high-density lipoprotein (HDL) cholesterol  
- low-density lipoprotein (LDL) cholesterol  
- triglycerides  

The ratio of HDL:total cholesterol is also of interest |
| **Language** | English |
| **Study design** | Cohort studies or consecutive case series | Cross-sectional studies which report prevalence and longitudinal studies which report incidence will be considered |
| **Status** | Published articles (no limitation on year of publication) | This is a completely new topic for the update so no date limit will be applied to searches |
| **Population** | Children and young people with type 2 diabetes | The guideline scope defines children and young people as those younger than 18 years. For the review questions related to monitoring for complications, studies which include people aged over 18 years will be considered, but only if data for people under 18 years can be analysed separately. If data are presented on an age group which extends into people aged >18 years, these will be included only if the mean age in the group is ≤ 18 years or if more than 50% of group participants are aged ≤ 18 years. Studies will be included only if they provide data on prevalence for |
### Type 2 diabetes – dyslipidaemia

<table>
<thead>
<tr>
<th>Intervention or index test</th>
<th>Measurement of any of the following serum lipids:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• total cholesterol</td>
</tr>
<tr>
<td></td>
<td>• HDL cholesterol</td>
</tr>
<tr>
<td></td>
<td>• LDL cholesterol</td>
</tr>
<tr>
<td></td>
<td>• triglycerides</td>
</tr>
<tr>
<td></td>
<td>The ratio of HDL:total cholesterol is also of interest</td>
</tr>
</tbody>
</table>

- The terms in the bullet list to the left, plus lipoprotein (US synonym for cholesterol) should be used as search terms
- Evidence tables should document whether the evidence identified for inclusion relates to fasting or non-fasting measurements (both are of interest)

<table>
<thead>
<tr>
<th>Comparator or reference standard</th>
<th>Prevalence or incidence at different time intervals after diagnosis and/or at different ages</th>
</tr>
</thead>
</table>

### Clinical outcomes

<table>
<thead>
<tr>
<th>Prevalence of dyslipidaemia at different timepoints after diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of dyslipidaemia over time</td>
</tr>
</tbody>
</table>

- Look at finding the earliest time at which dyslipidaemia becomes sufficiently common to warrant screening
- Subgroup analysis based on age may be relevant

### Health economic outcomes

- This question was not identified as a priority for health economic analysis

### Other criteria for inclusion/exclusion of studies

- Exclude studies that do not:
  - report prevalence of dyslipidaemia at a particular timepoint after diagnosis
  - have a systematic approach to screening, as opposed to selective patient screening based on individual concerns

### Search strategies

- See separate document

### Review strategies

- Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)
- A list of excluded studies will be provided following weeding
- Evidence tables and an evidence profile will be used to summarise the evidence

### Equality

- Equalities issues with be assessed according to processes described in NICE guidelines manual (November 2012)
E.26  **Type 2 diabetes – retinopathy**  
**Review question:** What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?

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

<table>
<thead>
<tr>
<th>Intervention or index test</th>
<th>Universal retinopathy screening using digital retinal photography</th>
<th>Digital retinal photography is the method currently recommended in the NHS Diabetic Eye Screening Programme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparator or reference standard</td>
<td>Prevalence or incidence at different time intervals after diagnosis and/or at different ages</td>
<td></td>
</tr>
</tbody>
</table>
| Clinical outcomes | Prevalence of retinopathy at different timepoints after diagnosis (this might include data obtained via ‘survival analysis’ methods)  
Incidence of retinopathy over time  
When available, severity (grade) of retinopathy will be reported based on the NHS Diabetic Eye Screening Programme (see, for example, http://medweb.bham.ac.uk/easdec/gradingretinopathy.htm) | • Look at finding the earliest time at which retinopathy becomes sufficiently common/severe to warrant screening  
• The GDG may need to consider not just the existence of retinopathy but also the severity (grade) of retinopathy  
• Current practice is to refer children and young people with diabetes to an ophthalmologist only if they have sight-threatening diabetic retinopathy, and this is unlikely in people younger than 12 years; |
### Type 2 diabetes – retinopathy

<table>
<thead>
<tr>
<th></th>
<th>as noted above, background retinopathy can revert to normal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• It might be worth identifying retinopathy that will not lead to referral to an ophthalmologist if this would support provision of education about risks associated with retinopathy</td>
</tr>
<tr>
<td></td>
<td>• Subgroup analysis based on age may be relevant</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Health economic outcomes</strong></th>
<th>This question was not identified as a priority for health economic analysis</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th><strong>Other criteria for inclusion/exclusion of studies</strong></th>
<th>Exclude studies that do not:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• report prevalence of retinopathy at a particular timepoint after diagnosis</td>
</tr>
<tr>
<td></td>
<td>• have a systematic approach to screening, as opposed to selective patient screening based on individual concerns</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Search strategies</strong></th>
<th>See separate document</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th><strong>Review strategies</strong></th>
<th>Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A list of excluded studies will be provided following weeding</td>
</tr>
<tr>
<td></td>
<td>Evidence tables and an evidence profile will be used to summarise the evidence</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Equality</strong></th>
<th>Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)</th>
</tr>
</thead>
</table>

| | The practicalities of offering screening for retinopathy will vary according to the child or young person’s age and whether or not they have learning difficulties (because digital retinal photography requires the person to sit still and stare at a fixed point); learning difficulties are more often associated with type 2 diabetes than with type 1 diabetes |

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### E.27 Type 2 diabetes – nephropathy

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

<table>
<thead>
<tr>
<th>Type 2 diabetes – nephropathy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Existing recommendation(s) in 2004 guideline</strong></td>
</tr>
<tr>
<td><strong>Objectives</strong></td>
</tr>
<tr>
<td><strong>Language</strong></td>
</tr>
<tr>
<td><strong>Study design</strong></td>
</tr>
<tr>
<td><strong>Status</strong></td>
</tr>
<tr>
<td><strong>Population</strong></td>
</tr>
<tr>
<td>\</td>
</tr>
</tbody>
</table>
### Type 2 diabetes – nephropathy

<table>
<thead>
<tr>
<th>Intervention or index test</th>
<th>The guidelines relating to type 1 diabetes in adults and type 2 diabetes in adults include specific recommendations on:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• repeated measurement of ACR over a 4-month period to establish a diagnosis of microalbuminuria</td>
</tr>
<tr>
<td></td>
<td>• measuring serum creatinine at the same time, and</td>
</tr>
<tr>
<td></td>
<td>• in type 2 diabetes, estimating the glomerular filtration rate (GFR) at the same time (using the method-abbreviated modification of diet in renal disease four-variable equation)</td>
</tr>
</tbody>
</table>

An abnormal urine ACR is the first feature of nephropathy, whereas abnormal serum creatinine concentration is a later feature; both may be relevant in children and young people with type 2 diabetes because they may have nephropathy at diagnosis (because the diabetes can go undetected for longer in the case of type 2 diabetes); children and young people with type 2 diabetes are also likely to have hypertension at diagnosis and/or to be obese, and both of these are independent risk factors for impaired renal function.

Urine ACR is the practice for screening of microalbuminuria in the UK. For studies which report on albumin excretion rate (AER) rather than ACR for the confirmation of microalbuminuria, convert to ACR measurements using separate conversion equations for males and females (Schultz et al. 1999).

Reference is:
Schultz, C.J., et al. 1999. Microalbuminuria prevalence varies with age, sex, and puberty in children with type 1 diabetes followed from diagnosis in a
## Type 2 diabetes – nephropathy

<table>
<thead>
<tr>
<th>Comparator or reference standard</th>
<th>Prevalence or incidence at different time intervals after diagnosis and/or at different ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical outcomes</td>
<td>Prevalence of microalbuminuria (however measured, and including using measurement through urine albumin:creatinine ratio (ACR))</td>
</tr>
<tr>
<td></td>
<td>Incidence of microalbuminuria over time</td>
</tr>
<tr>
<td></td>
<td>Prevalence of elevated serum creatinine (and/or reduced estimated GFR) using serum creatinine concentration</td>
</tr>
<tr>
<td></td>
<td>Evidence tables should document cut-offs and definitions of microalbuminuria used in included studies</td>
</tr>
<tr>
<td></td>
<td>NCC-WCH to discuss with GDG to determine which studies should be included if necessary</td>
</tr>
<tr>
<td></td>
<td>Note that the 2004 guideline on type 1 diabetes in adults, and the 2008 guideline on type 2 diabetes in adults use repeated tests of ACR &gt;2.5mg/mmol for men, and &gt;3.5mg/mmol for women (in at least 2 of 3 consecutive collections over a period of 3-4 months) to confirm microalbuminuria</td>
</tr>
<tr>
<td></td>
<td>It will be important to consider the severity of microalbuminuria and how should this be reported (for example, thresholds for ‘severe microalbuminuria’, etc)</td>
</tr>
</tbody>
</table>

| Health economic outcomes | This question was not identified as a priority for health economic analysis |

<table>
<thead>
<tr>
<th>Other criteria for inclusion/exclusion of studies</th>
<th>Exclude studies that do not</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>report either prevalence of microalbuminuria or prevalence of elevated serum creatinine at a particular time-point after diagnosis</td>
</tr>
<tr>
<td></td>
<td>have a systematic approach to screening as opposed to selective patient screening based on individual concerns</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Search strategies</th>
<th>See separate document</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NCC-WCH to consider using a single search to cover both review questions relating to monitoring for nephropathy (type ...</td>
</tr>
</tbody>
</table>
**Type 2 diabetes – nephropathy**

<table>
<thead>
<tr>
<th>1 diabetes and type 2 diabetes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The search terms microalbuminuria and diabetes should identify relevant studies</td>
</tr>
</tbody>
</table>

### Review strategies

Evidence will be assessed for quality according to the process described in the NICE guidelines manual (November 2012)

A list of excluded studies will be provided following weeding

Evidence tables and an evidence profile will be used to summarise the evidence

### Equality

Equalities issues will be assessed according to processes described in NICE guidelines manual (November 2012)

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**Appendix F: Search strategies**

**F.1 Diagnosis**

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

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

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

# Searches

1. Diabetes mellitus, type 1/
2. Diabetic ketoacidosis/
3. ((diabet* or DM) adj4 (type 1 or type1 or type l 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.
Search strategies

23 or/15-22
24 23 not (randomized controlled trial/ or random*.ti,ab.)
25 animals/ not humans/
26 exp Animals, Laboratory/
27 exp Animal Experimentation/
28 exp Models, Animal/
29 exp Rodentia/
30 (rat or rats or mouse or mice).ti.
31 or/24-30
32 14 not 31
33 limit 32 to english language
34 C-peptide/
35 *Autoantibodies/
36 Glutamate decarboxylase/
37 Insulinoma/
38 Glucose-6-phosphatase/
39 C peptide*.ti,ab.
40 ((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod* or autoantibod*)).ti,ab.
41 zinc transporter 8.ti,ab.
42 (islet adj5 (phosphatase or catalytic)).ti,ab.
43 (IGRP* or ICA* or IA-2* or IA2* or ZnT8* or GAD*).ti,ab.
44 or/34-43
45 33 and 44
46 (diagnos* or screen* or test*).ti,ab,hw.
47 exp "sensitivity and specificity"/
48 ROC Curve/
49 Area Under Curve/
50 Proportional Hazards Models/
51 (ROC or AUC or (area and curve)).ti,ab.
52 (sensitivity or specificity).ti,ab.
53 gold standard.ab.
54 (predictive value* or PPV or NPV).ti,ab.
55 likelihood ratio*.ti,ab.
56 or/46-55
57 45 and 56
58 randomized controlled trial.pt.
59 controlled clinical trial.pt.
60 random#.ed.ab.
61 placebo.ab.
62 randomly.ab.
63 Clinical Trials as topic.sh.
64 trial*.ti.
65 or/58-64
66 Meta-Analysis/
67 Meta-Analysis as Topic/
68 (meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
69 ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
70 (reference list* or bibliography* or hand search* or manual search* or relevant journals).ab.
71 (search strategy or search criteria or systematic search or study selection or data extraction).ab.
72 (search* adj4 literature).ab.
Diagnosis and management of type 1 diabetes in children and young people

**Search strategies**

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

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

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

Search strategies

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

### Search strategies

<table>
<thead>
<tr>
<th>Search Strategy</th>
<th>Term(s)</th>
</tr>
</thead>
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<tr>
<td><strong>81</strong> C-peptide/</td>
<td></td>
</tr>
<tr>
<td><strong>82</strong> <em>Autoantibodies/</em></td>
<td></td>
</tr>
<tr>
<td><strong>83</strong> Glutamate decarboxylase/</td>
<td></td>
</tr>
<tr>
<td><strong>84</strong> Insulinoma/</td>
<td></td>
</tr>
<tr>
<td><strong>85</strong> Glucose-6-phosphatase/</td>
<td></td>
</tr>
<tr>
<td><strong>86</strong> C peptide*.ti,ab.</td>
<td></td>
</tr>
<tr>
<td><strong>87</strong> (islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod* or autoantibod*).ti,.ab.</td>
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<tr>
<td><strong>88</strong> zinc transporter 8.ti,ab.</td>
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<td><strong>89</strong> (islet adj5 (phosphatase or catalytic)).ti,ab.</td>
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<td><strong>90</strong> (IGRP* or ICA* or IA-2* or IA2* or ZnT8* or GAD*).ti,ab.</td>
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<td><strong>91</strong> or/81-90</td>
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<td><strong>92</strong> 80 and 91</td>
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<tr>
<td><strong>93</strong> (diagnos* or screen* or test*).ti,ab,hw.</td>
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<tr>
<td><strong>94</strong> exp &quot;sensitivity and specificity&quot;/</td>
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<tr>
<td><strong>95</strong> ROC Curve/</td>
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<td><strong>96</strong> Area Under Curve/</td>
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<tr>
<td><strong>97</strong> Proportional Hazards Models/</td>
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<tr>
<td><strong>98</strong> (ROC or AUC or area and curve)).ti,ab.</td>
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<td><strong>99</strong> (sensitivity or specificity).ti,ab.</td>
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<tr>
<td><strong>100</strong> gold standard.ab</td>
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<td><strong>101</strong> (predictive value* or PPV or NPV).ti,ab.</td>
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<td><strong>102</strong> likelihood ratio*.ti,ab.</td>
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<td><strong>103</strong> or/93-102</td>
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<td><strong>104</strong> 92 and 103</td>
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<td><strong>106</strong> controlled clinical trial.pt.</td>
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<td><strong>108</strong> placebo.ab.</td>
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<td><strong>111</strong> trial*.ti</td>
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<td><strong>112</strong> or/105-111</td>
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<td><strong>113</strong> Meta-Analysis/</td>
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<td><strong>114</strong> Meta-Analysis as Topic/</td>
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<td><strong>115</strong> (meta analy* or metanal* or metaanaly* or meta regression).ti,ab.</td>
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<td><strong>116</strong> ((systematic* or evidence*) adj2 (review* or overview*).ti,ab.</td>
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<td><strong>117</strong> (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.</td>
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<td><strong>118</strong> (search strategy or search criteria or systematic search or study selection or data extraction).ab.</td>
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<td><strong>119</strong> (search* adj4 literature).ab.</td>
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<td><strong>120</strong> (medline or pubmed or cochrane or embase or psychlit or psyclin or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.</td>
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<td><strong>121</strong> cochrane,jw.</td>
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<td><strong>123</strong> or/113-122</td>
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<td><strong>124</strong> Epidemiologic studies/</td>
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<td><strong>125</strong> exp case control studies/</td>
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<td><strong>126</strong> exp cohort studies/</td>
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<td><strong>127</strong> Cross-sectional studies/</td>
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<td><strong>128</strong> case control.ti,ab.</td>
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<td><strong>129</strong> ((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*). adj (study or studies)).ti,ab.</td>
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</table>
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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

<table>
<thead>
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<td>#2</td>
<td>MeSH descriptor: [Diabetic Ketoacidosis] this term only</td>
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<td>#3</td>
<td>(diabet* or DM) near/4 (&quot;type 1&quot; or type1 or &quot;type I&quot; or &quot;type one&quot;):ti,ab</td>
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<tr>
<td>#4</td>
<td>(diabet* near/2 (autoimmun* or &quot;auto immun&quot;):ti,ab</td>
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<td>#5</td>
<td>(diabet* near/2 (brittle or labile)):ti,ab</td>
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<tr>
<td>#6</td>
<td>(diabet* near/2 (&quot;sudden onset&quot; or juvenile or child&quot;):ti,ab</td>
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<tr>
<td>#7</td>
<td>(diabet* near/3 (keto* or acido* or gastropare&quot;):ti,ab</td>
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<tr>
<td>#8</td>
<td>(dm1 or iddm or t1d* or dka or LADA):ti,ab</td>
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<tr>
<td>#9</td>
<td>(diabet* near/2 (insulin next depend&quot;):ti,ab</td>
</tr>
<tr>
<td>#10</td>
<td>#9 and not &quot;non insulin dependent&quot;</td>
</tr>
<tr>
<td>#11</td>
<td>diabetes mellitus:ti</td>
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<td>#12</td>
<td>#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #10 or #11</td>
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<tr>
<td>#13</td>
<td>(pregnan* or gestation&quot;):ti</td>
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<td>#14</td>
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<td>MeSH descriptor: [Autoantibodies] this term only</td>
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<td>MeSH descriptor: [Insulinoma] this term only</td>
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<td>#19</td>
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<td>#21</td>
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<td>#22</td>
<td>(&quot;zinc transporter 8&quot;):ti,ab</td>
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<td>#23</td>
<td>(islet* and (phosphatase or catalytic)):ti,ab</td>
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<td>#24</td>
<td>(IGRP* or ICA* or &quot;IA-2&quot; or IA2* or ZnT8* or GAD*):ti,ab</td>
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<td>#25</td>
<td>#15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24</td>
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<tr>
<td>#26</td>
<td>#14 and #25</td>
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<td>#27</td>
<td>MeSH descriptor: [Diagnosis] explode all trees</td>
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<td>#28</td>
<td>(diagnos* or screen* or test&quot;):ti,ab</td>
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<tr>
<td>#29</td>
<td>MeSH descriptor: [Sensitivity and Specificity] explode all trees</td>
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<td>#30</td>
<td>MeSH descriptor: [Area Under Curve] this term only</td>
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<td>#31</td>
<td>MeSH descriptor: [Proportional Hazards Models] this term only</td>
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<tr>
<td>#32</td>
<td>(ROC or AUC) or (area and curve):ti,ab</td>
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<tr>
<td>#33</td>
<td>(sensitivity or specificity):ti,ab</td>
</tr>
<tr>
<td>#34</td>
<td>gold standard:ab</td>
</tr>
<tr>
<td>#35</td>
<td>(&quot;predictive value&quot; or PPV or NPV):ti,ab</td>
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<tr>
<td>#36</td>
<td>likelihood ratio:ti,ab</td>
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<tr>
<td>#37</td>
<td>#27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36</td>
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<td>#38</td>
<td>#26 and #37</td>
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Database(s): Embase

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<td>Insulin dependent diabetes mellitus/</td>
</tr>
<tr>
<td>2</td>
<td>Juvenile diabetes mellitus/</td>
</tr>
<tr>
<td>3</td>
<td>Diabetic ketoacidosis/</td>
</tr>
<tr>
<td>4</td>
<td>(diabet* or DM) adj4 (type 1 or type1 or type I or type one&quot;):ti,ab</td>
</tr>
<tr>
<td>5</td>
<td>(diabet* adj2 (autoimmun* or auto immun&quot;):ti,ab</td>
</tr>
<tr>
<td>6</td>
<td>(LADA or MODY):ti,ab</td>
</tr>
<tr>
<td>7</td>
<td>(diabet* adj2 (brittle or labile)):ti,ab.</td>
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</tbody>
</table>
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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 (2003$ or 2004$ or 2005$ or 2006$ or 2007$ or 2008$ or 2009$ or 2010$ or 2011$ or 2012$ or 2013$).em.
33 31 and 32
34 C peptide/
35 Glutamate decarboxylase 65 antibody/
36 Insulinoma/
37 *Autoantibody/
38 Glucose 6 phosphatase/
39 ((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod* or autoantibod*)).ti,ab.
40 zinc transporter 8.ti,ab.
41 (islet adj5 (phosphatase or catalytic)).ti,ab.
42 (IGRP* or ICA* or IA-2* or IA2* or ZnT8* or GAD*).ti,ab.
43 or/34-42
44 33 and 43
45 (diagnos* or screen* or test*).ti,ab,hw.
46 exp "sensitivity and specificity"/
47 Receiver operating characteristic/
48 Area under the curve/
49 Proportional hazards model/
50 (ROC or AUC or (area and curve)).ti,ab.
51 (sensitivity or specificity).ti,ab.
52 gold standard.ab.
53 (predictive value* or PPV or NPV).ti,ab.
54 likelihood ratio*.ti,ab.
55 or/45-54
56 44 and 55
57 random*.ti,ab.
58 factorial*.ti,ab.
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

Database(s): Embase

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

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

Search strategies

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

64 note.pt.
65 editorial.pt.
66 case report/ or case study/
67 (letter or comment*).ti.
68 or/63-67
69 68 not (randomized controlled trial/ or random*.ti,ab.)
70 animal/ not human/
71 nonhuman/
72 exp Animal Experiment/
73 exp Experimental Animal/
74 animal model/
75 exp Rodent/
76 (rat or rats or mouse or mice).ti.
77 or/69-76
78 62 not 77
79 ("201406" or "201407" or "201408" or "201409" or 20141* or 20142* or 20143*).em.
80 78 and 79
81 C peptide/
82 Glutamate decarboxylase 65 antibody/
83 Insulinoma/
84 *Autoantibody/
85 Glucose 6 phosphatase/
86 ((islet cell or decarboxylase or glutamic or insulinoma) and (antibod* or anti bod* or autoantibod*)),ti,ab.
87 zinc transporter 8.ti,ab.
88 (islet adj5 (phosphatase or catalytic)).ti,ab.
89 (IGRP* or ICA* or IA-2* or IA2* or ZnT8* or GAD*).ti,ab.
90 or/81-89
91 80 and 90
92 (diagnos* or screen* or test*).ti,ab,hw.
93 exp "sensitivity and specificity"/
94 Receiver operating characteristic/
95 Area under the curve/
96 Proportional hazards model/
97 (ROC or AUC or (area and curve)).ti,ab.
98 (sensitivity or specificity).ti,ab.
99 gold standard.ab.
100 (predictive value* or PPV or NPV).ti,ab.
101 likelihood ratio*.ti,ab.
102 or/92-101
103 91 and 102
104 random*.ti,ab.
105 factorial*.ti,ab.
106 (crossover* or cross over*).ti,ab.
107 ((doubt* or singl*) adj blind*).ti,ab.
108 (assign* or allocat* or volunteer* or placebo*).ti,ab.
109 crossover procedure/
110 single blind procedure/
111 randomized controlled trial/
112 double blind procedure/
113 or/104-112
114 Meta-Analysis/
115 Meta-Analysis as Topic/
F.2 Type 1 diabetes – education

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

Ovid MEDLINE(R)

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

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

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

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

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

Cochrane Central Register of Controlled Trials

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

Search strategies

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

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

Health Technology Assessment

# Searches
1. ADOLESCENT/ or MINORS/
2. (adolescent$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3. exp CHILD/
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

Embase

# Searches
1 CLINICAL TRIAL/ or "CLINICAL TRIAL (TOPIC)/"
2 (clinic$ adj5 trial$).ti,ab,sh.
3 SINGLE BLIND PROCEDURE/
4 DOUBLE BLIND PROCEDURE/
5 RANDOM ALLOCATION/
6 CROSSOVER PROCEDURE/
7 PLACEBO/
8 placebo$.ti,ab,sh.
9 random$.ti,ab,sh.
10 RANDOMIZED CONTROLLED TRIAL/ or "RANDOMIZED CONTROLLED TRIAL (TOPIC)/"
11 ((single or double or triple or treble) adj (blind$ or mask$)).ti,ab,sh.
12 randomi?ed control$ trial$.tw.
13 /or/1-12
META ANALYSIS/
((meta adj analy$) or metaanalys$ or meta-analy$.).ti,ab.sh.
(systematic$ adj5 (review$ or overview$)).ti,sh,ab.
(methodologic$ adj5 (review$ or overview$)).ti,ab.sh.
or/14-17
review.pt.
(medline or medlars or embase).ab.
(scisearch or science citation index).ab.
(psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
((hand or manual$) adj2 search$).tw.
(electronic database$ or bibliographic database$ or computer?ed database$ or online database$).tw.
(pooling or pooled or mantel haenszel).tw.
(peto or dersimonian or "der simonian" or fixed effect).tw.
or/20-26
and/19,27
or/18,28
(book or conference paper or editorial or letter or note or proceeding or short survey).pt.
13 not 30
29 not 30
or/31-32
exp ADOLESCENT/
(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
exp CHILD/
(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
exp INFANT/
(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
exp PEDIATRICS/ or exp PUBERTY/
(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
or/34-41
INSULIN DEPENDENT DIABETES MELLITUS/
(diabe$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
(IDDM or T1D or TID or DM1 or DMI).ti,ab.
or/43-45
JUVENILE DIABETES MELLITUS/
and/42,46
or/47-48
PATIENT EDUCATION/
DIABETES EDUCATION/
DIABETES EDUCATOR/
EDUCATION PROGRAM/
PROBLEM SOLVING/
((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).ti,ab.
(problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
((patient? or parent? or parental or child$ or adolescent$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
((patient? or parent? or parental or child$ or adolescent$ or young or youth? or family$ or families) adj3 information).ti,ab.
((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or...
cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.

((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.

((diabet$ or insulin$ or glyc?emi$ or hypogl?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.

((diabet$ or insulin$ or glyc?emi$ or hypogl?emi$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.

or/50-62

and/49,63

and/33,64

conference abstract.pt.

letter.pt. or LETTER/

note.pt.

toeditorial.pt.

CASE REPORT/ or CASE STUDY/

(letter or comment* or abstracts).ti.

or/66-71

RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.

72 not 73

ANIMAL/ not HUMAN/

NONHUMAN/

exp ANIMAL EXPERIMENT/

exp EXPERIMENTAL ANIMAL/

exp ANIMAL MODEL/

exp RODENT/

(rat or rats or mouse or mice).ti.

or/74-81

65 not 82

limit 83 to english language

PsycINFO

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

Search strategies

### CINAHL with Full Text

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

S24 TI ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat** or self-
monitor* or "self monitor** or self-manag* or "self manag** or self-efficacy or "self efficacy" or cope or coping) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) OR AB ((self-help or "self help" or self-care or "self care" or self-regulat* or "self regulat** or self-monitor* or "self monitor** or self-manag* or "self manag** or self-efficacy or "self efficacy" or cope or coping) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) Search modes - Boolean/Phrase

S23 TI ((patient# or parent# or parental or child* or adolescent* or young or youth# or family* or families) N3 information) OR AB ((patient# or parent# or parental or child* or adolescent* or young or youth# or family* or families) N3 information) Search modes - Boolean/Phrase

S22 TI ((patient# or parent# or parental or child* or adolescent* or young or youth# or family* or families) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) OR AB ((patient# or parent# or parental or child* or adolescent* or young or youth# or family* or families) N6 (educat* or train* or teach* or knowledge or aware* or skill* or advi#e or instruct* or learn* or program# or programme or programmes)) Search modes - Boolean/Phrase

S21 TI (problem-solving or "problem solving" or problem-based or "problem based") OR AB (problem-solving or "problem solving" or problem-based or "problem based") Search modes - Boolean/Phrase

S20 TI ((educat* or training) N6 (intervention* or program# or programme or programmes)) OR AB ((educat* or training) N6 (intervention* or program# or programme or programmes)) Search modes - Boolean/Phrase

S19 MW "ED" Search modes - Boolean/Phrase

S18 (MH "Patient Education") OR (MH "Diabetes Education") Search modes - Boolean/Phrase

S17 TI (("type one" or "type 1" or "insulin depend"* or juvenile or child* or early* or labile or brittle or "sudden onset" or "auto immun*" or "autoimmun*" or "auto-immun*")) OR AB ("type one" or "type 1" or "insulin depend"* or juvenile or child* or early* or labile or brittle or "sudden onset" or "auto immun*" or "autoimmun*" or "auto-immun*")) Search modes - Boolean/Phrase

S16 S12 AND S15 Search modes - Boolean/Phrase

S15 S13 OR S14 Search modes - Boolean/Phrase

S14 TI (diabet* N5 ("type one" or "type 1" or "insulin depend"* or juvenile or child* or early* or labile or brittle or "sudden onset" or "auto immun*" or "autoimmun*" or "auto-immun*")) OR AB (diabet* N5 ("type one" or "type 1" or "insulin depend"* or juvenile or child* or early* or labile or brittle or "sudden onset" or "auto immun*" or "autoimmun*" or "auto-immun*")) Search modes - Boolean/Phrase

S13 (MH "Diabetes Mellitus, Type 1+") Search modes - Boolean/Phrase

S12 S7 OR S8 OR S9 OR S10 OR S11 Search modes - Boolean/Phrase

S11 TI (pediatric* or paediatric* or pubert* or prepubert* or pubescen* or prepubescen* or pre-pubescen* or pre-pubescent*) OR AB (pediatric* or paediatric* or pubert* or prepubert* or pubescen* or prepubescent* or pre-pubescent* or pre-pubert* or pubescen* or prepubescent* or pre-pubescent*) Search modes - Boolean/Phrase

S10 TI (infan* or neonat* or newborn* or baby or babies) OR AB (infan* or neonat* or newborn* or baby or babies) OR SO (infan* or neonat* or newborn* or baby or babies) Search modes - Boolean/Phrase

S9 TI (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR AB (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR SO (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) Search modes - Boolean/Phrase

S8 TI (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR AB (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR SO (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) Search modes - Boolean/Phrase

S7 (MH "Infant, Newborn") OR (MH "Infant") OR (MH "Child, Preschool") OR (MH "Child") OR (MH "Adolescence") Search modes - Boolean/Phrase

S6 S1 OR S2 OR S3 OR S4 OR S5 Search modes - Boolean/Phrase
F.3 Type 1 diabetes – behavioural interventions

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

Ovid MEDLINE(R)

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

Search strategies

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

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

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

Search strategies

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

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

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

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

Embase 1974 to 2014 Week 13

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

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

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PsycINFO 1967 to March Week 4 2014

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

Search strategies

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

CINAHL with Full Text

# Query Limiters/Expanders
S33 S6 AND S31 Limiters - English Language; Exclude MEDLINE records
S32 Search modes - Boolean/Phrase
S31 S6 AND S30 Search modes - Boolean/Phrase
S30 S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 Search modes - Boolean/Phrase
S29 TI ((peer or social$ or "self help" or self-help) N3 (group$ or support$)) OR AB ((peer or social$ or "self help" or self-help) N3 (group$ or support$)) Search modes - Boolean/Phrase
S28 TI (motivation$ or counsel#ing or mentor$) OR AB (motivation$ or counsel#ing or mentor$) Search modes - Boolean/Phrase
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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F.4  Type 1 diabetes – multiple daily injections

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

Ovid MEDLINE(R)

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

Search strategies

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

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

Cochrane Central Register of Controlled Trials

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

Search strategies

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

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

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

Health Technology Assessment

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

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

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

Search strategies

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

F.5 Type 1 diabetes – HbA1c targets

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

Ovid MEDLINE(R)

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

14 random$.tw,sh.
15 or/7-14
16 or/6-15
17 META ANALYSIS/
18 META ANALYSIS AS TOPIC/
19 meta analysis.pt.
20 (metaanaly$ or meta-analy$ or (meta adj analy$)).tw,sh.
21 (systematic$ adj5 (review$ or overview$)).tw,sh.
22 (methodologic$ adj5 (review$ or overview$)).tw,sh.
23 or/17-22
24 review$.pt.
25 (medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psychlit or "web of science" or "science citation" or scisearch).tw.
26 (hand or manual$) adj2 search$.tw.
27 (electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw,sh.
28 (pooling or pooled or mantel haenszel).tw,sh.
29 (peto or dersimonian or der simonian or fixed effect).tw,sh.
30 or/25-29
31 and/24,30
32 exp CASE-CONTROL STUDIES/
33 (case$ adj2 control$).tw.
34 exp COHORT STUDIES/
35 cohort$.tw.
36 or/32-35
37 letter.pt.
38 or/16,23,31,36
39 comparative study.pt.
40 or/38-39
41 ADOLESCENT/ or MINORS/
42 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
43 exp CHILD/
44 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
45 exp INFANT/
46 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
47 exp PEDIATRICS/ or exp PUBERTY/
48 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescent$).ti,ab,jw.
49 or/41-48
50 exp DIABETES MELLITUS, TYPE 1/
51 (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
52 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
53 or/50-52
54 HEMOGLOBIN A, GLY COSYLATED/
56 (glycated adj3 h?emoglobin?).ti,ab.
57 (glyco?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).ti,ab.
58 "hemoglobin A1c protein, human".nm.
59 or/54-58
60 REFERENCE STANDARDS/ or REFERENCE VALUES/
61 (reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?).ti,ab.
<table>
<thead>
<tr>
<th></th>
<th>Search strategies</th>
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</thead>
<tbody>
<tr>
<td>62</td>
<td>(F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$).ti,ab.</td>
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<tr>
<td>63</td>
<td>((normogly?emi$ or euglyc?emi$ or glyc?emi$) adj3 (value$ or target$ or rang$ or level$ or threshold$)).ti,ab.</td>
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<tr>
<td>64</td>
<td>or/60-63</td>
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<tr>
<td>65</td>
<td>and/49,53,59,64</td>
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<td>66</td>
<td>and/40,65</td>
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<td>67</td>
<td>LETTER/</td>
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<td>69</td>
<td>NEWS/</td>
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<td>70</td>
<td>exp HISTORICAL ARTICLE/</td>
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<td>71</td>
<td>ANECDOTES AS TOPIC/</td>
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<tr>
<td>72</td>
<td>COMMENT/</td>
</tr>
<tr>
<td>73</td>
<td>CASE REPORT/</td>
</tr>
<tr>
<td>74</td>
<td>(letter or comment* or abstracts).ti.</td>
</tr>
<tr>
<td>75</td>
<td>or/67-74</td>
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<tr>
<td>76</td>
<td>RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.</td>
</tr>
<tr>
<td>77</td>
<td>75 not 76</td>
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<td>78</td>
<td>ANIMALS/ not HUMANS/</td>
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<tr>
<td>79</td>
<td>exp ANIMALS, LABORATORY/</td>
</tr>
<tr>
<td>80</td>
<td>exp ANIMAL EXPERIMENTATION/</td>
</tr>
<tr>
<td>81</td>
<td>exp MODELS, ANIMAL/</td>
</tr>
<tr>
<td>82</td>
<td>exp RODENTIA/</td>
</tr>
<tr>
<td>83</td>
<td>(rat or rats or mouse or mice).ti.</td>
</tr>
<tr>
<td>84</td>
<td>or/77-83</td>
</tr>
<tr>
<td>85</td>
<td>66 not 84</td>
</tr>
<tr>
<td>86</td>
<td>limit 85 to english language</td>
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**Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations**

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

**Cochrane Central Register of Controlled Trials**

| # | Searches |
Search strategies

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

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

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

Search strategies

Health Technology Assessment

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

Embase

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

12 random?ed control$ trial$.tw.
13 or/1-12
14 META ANALYSIS/
15 ((meta adj analy$) or metaanalys$ or meta-analy$).tw.sh.
16 (systematic$ adj5 (review$ or overview$)).tw.sh.
17 (methodologic$ adj5 (review$ or overview$)).tw.sh.
18 or/14-17
19 review.pt.
20 (medline or medlars or embase).ab.
21 (scisearch or science citation index).ab.
22 (psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
23 ((hand or manual$) adj2 search$).tw.
24 (electronic database$ or bibliographic database$ or computeri?ed database$ or online database$).tw.
25 (pooling or pooled or mantel haenszel).tw.
26 (peto or dersimonian or "der simonian" or fixed effect).tw.
27 or/20-26
28 and/19,27
29 exp CASE CONTROL STUDY/
30 RETROSPECTIVE STUDY/
31 (case$ adj2 control$).tw.
32 COHORT ANALYSIS/
33 LONGITUDINAL STUDY/
34 FOLLOW UP/
35 PROSPECTIVE STUDY/
36 cohort$.tw.
37 or/29-36
38 or/13,18,28,37
39 (book or conference paper or editorial or letter or note or proceeding or short survey).pt.
40 38 not 39
41 COMPARATIVE STUDY/
42 (compar$ adj3 stud$).tw.
43 or/41-42
44 or/40,43
45 exp ADOLESCENT/
46 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
47 exp CHILD/
48 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
49 exp INFANT/
50 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
51 exp PEDIATRICS/ or exp PUBERTY/
52 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
53 or/45-52
54 INSULIN DEPENDENT DIABETES MELLITUS/
55 (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
56 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
57 JUVENILE DIABETES MELLITUS/
58 or/54-57
59 HEMOGLOBIN A1c/
60 (glyco?emoglobin? or HbA1c or HbA1c or Hb a1c or Hb A1c or Hb A1c).ti,ab.
Type 1 diabetes blood glucose targets

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

Ovid MEDLINE(R)

# Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen$ or teen$ or youth$ or young or juvenile? or min$ or highschool$).ti,ab,jw.
3 exp CHILD/
4 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?!).ti,ab,jw.
5 exp INFANT/
6 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/
11 (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immu$ or auto?immu$)).ti,ab.
(IDDM or T1D or TID or DM1 or DMI).ti,ab.
or/10-12
BLOOD GLUCOSE/
BLOOD GLUCOSE SELF-MONITORING/
((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
(F#G or P#G or R#G or BG or HMBG or SMBG or BGM).ti,ab.
(glyc?emi$ adj3 (norm$ or near?norm$)).ti,ab.
or/14-19
REFERENCE STANDARDS/ or REFERENCE VALUES/
GOALS/
((reference? or normal$ or standard?) adj3 (value$ or rang$ or level$ or threshold?)).ti,ab.
target$.ti.
target$.ab. /freq=2
((tight$ or intens$ or aggressive$ or strict$ or rigid$ or liberal$ or conventional$ or regular or usual or routin$ or standard?) adj3 (control$ or target$ or goal$ or rang$ or therap$ or regime$ or treatment? or interven$ or manag$ or monitor$)).ti,ab.
or/21-26
and/20,27
("American Diabetic Association" or ADA or "Australasian Pediatric Endocrine Group" or APEG or "International Society for Pediatric and Adolescent Diabetes" or ISPAD) adj3 (value$ or target$ or goal$ or rang$ or level$ or threshold?).ti,ab.
(glyc?emi$ adj3 control$ adj3 (target$ or goal$)).ti,ab.
or/28-30
TIME FACTORS/
((time or timing or prandial or preprandial or postprandial) adj3 (monitor$ or test$ or measur$ or value$ or target$ or goal$ or rang$ or level$ or threshold?)).ti,ab.
or/32-33
and/20,34
or/31,35
and/9,13,36
limit 37 to english language
LETTER/
EDITORIAL/
NEWS/
exp HISTORICAL ARTICLE/
ANECDOTES AS TOPIC/
COMMENT/
CASE REPORT/
(letter or comment* or abstracts).ti.
or/39-46
RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
not 48
ANIMALS/ not HUMANS/
exp ANIMALS, LABORATORY/
exp ANIMAL EXPERIMENTATION/
exp MODELS, ANIMAL/
exp RODENTIA/
(rat or rats or mouse or mice).ti.
or/49-55
38 not 56
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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

Cochrane Central Register of Controlled Trials

# Searches
1 ADOLESCENT/ or MINORS/
2 (adolescent$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab.
3 exp CHILD/
4 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?!).ti,ab.
5 exp INFANT/
6 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/
11 (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
13 or/10-12
14 BLOOD GLUCOSE/
BLOOD GLUCOSE SELF-MONITORING/
(blood or plasma) adj3 (glucose or sugar?).ti,ab.
(F#G or P#G or R#G or BG or HMBG or SMBG or BGM).ti,ab.
(glyc?emi$ adj3 (norm$ or near?norm$)).ti,ab.

or/14-19

REFERENCE STANDARDS/ or REFERENCE VALUES/
GOALS/
(reference? or normal$ or standard?) adj3 (value$ or rang$ or level$ or threshold?).ti,ab.
target$.ti.
target$.ab. /freq=2
(tight$ or intens$ or aggressive$ or strict$ or rigid$ or liberal$ or conventional$ or regular or usual or routin$ or standard?) adj3 (control$ or target$ or goal$ or rang$ or therap$ or regime$ or treatment? or interven$ or manag$ or monitor$)).ti,ab.

or/21-26

and/20,27

("American Diabetic Association" or ADA or "Australasian P?ediatric Endocrine Group" or APEG or "International Society for P?ediatric and Adolescent Diabetes" or ISPAD) adj3 (value$ or target$ or goal$ or rang$ or level$ or threshold?).ti,ab.
(glyc?emi$ adj3 control$ adj3 (target$ or goal$)).ti,ab.
or/28-30

TIME FACTORS/
(time or timing or prandial or preprandial or postprandial) adj3 (monitor$ or test$ or measur$ or value$ or target$ or goal$ or rang$ or level$ or threshold?).ti,ab.
or/32-33

and/20,34

or/31,35

and/9,13,36

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects
# Searches
(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,kw.
(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx,kw.
(infan$ or neonat$ or newborn$ or baby or babies).tw,tx,kw.
(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,kw.
or/1-4
(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw,tx,kw.
(IDDM or T1D or TID or DM1 or DMI).tw,tx.
or/6-7
(blood or plasma) adj3 (glucose or sugar?).tw,tx,kw.
(F#G or P#G or R#G or BG or HMBG or SMBG or BGM).tw,tx.
(glyc?emi$ adj3 (norm$ or near?norm$)).tw,tx.
or/9-12

or/13

(REFERENCE STANDARDS or REFERENCE VALUES).kw.
GOALS.kw.
(reference? or normal$ or standard?) adj3 (value$ or rang$ or level$ or threshold?).tw,tx.
target$.tw,tx,kw.
(tight$ or intens$ or aggressive$ or strict$ or rigid$ or liberal$ or conventional$ or regular or usual or routin$ or standard?) adj3 (control$ or target$ or goal$ or rang$ or therap$ or regime$ or treatment? or interven$ or manag$ or monitor$)).tw,tx.
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

Health Technology Assessment

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

Embase
# Searches
1 exp ADOLESCENT/
2 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3 exp CHILD/
4 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergarten$ or boy? or girl?).ti,ab,jx.
5 exp NEWBORN/
6 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9 or/1-8
10 INSULIN DEPENDENT DIABETES MELLITUS/
11 (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
13 or/10-12
14 JUVENILE DIABETES MELLITUS/
15 and/9,13
16 or/14-15
17 GLUCOSE BLOOD LEVEL/
18 BLOOD GLUCOSE MONITORING/
19 GLYCEMIC CONTROL/
20 ((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
21 (F#G or P#G or R#G or BG or HMBG or SMBG or BGM).ti,ab.
22 (normoglyc?emi$ or euglyc?emi$).ti,ab.
23 (glyc?emi$ adj3 (norm$ or near?norm$)).ti,ab.
24 or/17-23
25 STANDARD/
26 REFERENCE VALUE/ or NORMAL VALUE/
27 MOTIVATION/
28 ((reference? or normal$ or standard?) adj3 (value$ or rang$ or level$ or threshold?)).ti,ab.
29 target$.ti.
30 target$.ab. /freq=2
31 ((tight$ or intens$ or aggressive$ or strict$ or rigid$ or liberal$ or conventional$ or regular or usual or routine$ or standard?) adj3 (control$ or target$ or goal$ or rang$ or therap$ or therapy? or treatment? or interven$ or manag$ or monitor$)).ti,ab.
32 or/25-31
33 and/24,32
34 ("American Diabetic Association" or ADA or "Australasian P?ediatric Endocrine Group" or APEG or "International Society for P?ediatric and Adolescent Diabetes" or ISPAD) adj3 (value$ or target$ or goal$ or rang$ or level$ or threshold?)).ti,ab.
35 (glyc?emi$ adj3 control$ adj3 (target$ or goal$)).ti,ab.
36 or/33-35
37 TIME/
38 ((time or timing or prandial or preprandial or postprandial) adj3 (monitor$ or test$ or measur$ or value$ or target$ or goal$ or rang$ or level$ or threshold?)).ti,ab.
39 or/37-38
40 and/24,39
41 or/36,40
42 and/16,41
43 limit 42 to english language
44 conference abstract.pt.
45 letter.pt. or LETTER/
46 note.pt.
47 editorial.pt.
48 CASE REPORT/ or CASE STUDY/
49 (letter or comment* or abstracts).ti.
50 or/44-49
51 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
52 50 not 51
53 ANIMAL/ not HUMAN/
54 NONHUMAN/
55 exp ANIMAL EXPERIMENT/
56 exp EXPERIMENTAL ANIMAL/
57 ANIMAL MODEL/
58 exp RODENT/
59 (rat or rats or mouse or mice).ti.
60 or/52-59
61 43 not 60

F.7 Type 1 diabetes – blood glucose monitoring

Review questions:

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

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

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

**MEDLINE(R)**

<table>
<thead>
<tr>
<th>#</th>
<th>Searches</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ADOLESCENT/ or MINORS/</td>
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<tr>
<td>2</td>
<td>(adolescen$ or teen$ or youth$ or young or juvenile? or minos or highschool$).ti,ab,jw.</td>
</tr>
<tr>
<td>3</td>
<td>exp CHILD/</td>
</tr>
<tr>
<td>4</td>
<td>(child$ or schoolchild$ or &quot;school age&quot; or &quot;school aged&quot; or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.</td>
</tr>
<tr>
<td>5</td>
<td>exp INFANT/</td>
</tr>
<tr>
<td>6</td>
<td>(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.</td>
</tr>
<tr>
<td>7</td>
<td>exp PEDIATRICS/ or exp PUBERTY/</td>
</tr>
<tr>
<td>8</td>
<td>(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.</td>
</tr>
<tr>
<td>9</td>
<td>or/1-8</td>
</tr>
<tr>
<td>10</td>
<td>exp DIABETES MELLITUS, TYPE 1/</td>
</tr>
</tbody>
</table>
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

© 2014 National Collaborating Centre for Women's and Children's Health

(Adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.

(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.

(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.

(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.

(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.

(IDDM or T1D or T1D or DM1 or DMI).ti,ab.

or/10-12

and/9,13

BLOOD GLUCOSE SELF-MONITORING/

(glucose or blood sugar$ or insulin$) adj3 (meter$ or monitor$ or sensor$ or capillary)).ti,ab.

(HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucosemeter$ or (glucose adj meter$)).ti,ab.

(finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.

or/15-18

and/14,19

limit 20 to english language

LETTER/

EDITORIAL/

NEWS/

exp HISTORICAL ARTICLE/

ANECDOTES AS TOPIC/

COMMENT/

CASE REPORT/

(letter or comment* or abstracts).ti.

or/22-29

RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.

30 not 31

ANIMALS/ not HUMANS/

exp ANIMALS, LABORATORY/

exp ANIMAL EXPERIMENTATION/

exp MODELS, ANIMAL/

exp RODENTIA/

(rat or rats or mouse or mice).ti.

39 or/32-38

21 not 39

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

# Searches

1 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.

2 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.

3 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.

4 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.

or/1-4

6 (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.

7 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.

or/6-7

and/5,8

10 (glucose or blood sugar$ or insulin$) adj3 (meter$ or monitor$ or sensor$ or capillary)).ti,ab.

11 (HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucosemeter$ or (glucose adj meter$)).ti,ab.

12 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.

or/10-12

and/9,13

limit 14 to english language
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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

Health Technology Assessment
# Searches
1 ADOLESCENT/ or MINORS/
2 (adolescent$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
exp CHILD/
  (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.

exp INFANT/
  (infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.

exp PEDIATRICS/ or exp PUBERTY/
  (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx,rw.

or/1-8

exp DIABETES MELLITUS, TYPE 1/
  (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw.
  (IDDM or T1D or TID or DM1 or DMI).tw.

or/10-12

and/9,13

BLOOD GLUCOSE SELF-MONITORING/
  ((glucose or blood sugar$ or insulin) adj3 (meter$ or monitor$ or sensor$ or capillary)).tw.
  (HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucometer$ or (glucose adj meter$)).tw.
  (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").tw.

or/15-18

and/14,19

**Embase**

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

2 exp CHILD/
  (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.

3 exp INFANT/
  (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.

4 exp PEDIATRICS/ or exp PUBERTY/
  (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.

5 or/1-8

6 INSULIN DEPENDENT DIABETES MELLITUS/
  (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
  (IDDM or T1D or TID or DM1 or DMI).ti,ab.

7 or/10-12

8 JUVENILE DIABETES MELLITUS/
  and/9,13

9 or/14-15

10 BLOOD GLUCOSE MONITORING/
  ((glucose or blood sugar$ or insulin) adj3 (meter$ or monitor$ or sensor$ or capillary)).ti,ab.
  (HBGM or SMBG or BGM or CGM or CGMS or glucometer or glucometer$ or (glucose adj meter$)).ti,ab.

11 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.

12 or/17-20

13 and/16,21

14 limit 22 to english language
15 conference abstract.pt.
16 letter.pt. or LETTER/
17 note.pt.
F.8 Type 1 diabetes – blood ketone monitoring

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

Ovid MEDLINE(R)

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

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

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

Cochrane Central Register of Controlled Trials

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

Cochrane Database of Systematic Reviews, EBM Reviews - Database of Abstracts of Reviews of Effects
# Searches
1. (adolescent$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,kw.
2. (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or
kindergarten$ or boy? or girl?).tw,tx,kw.
3. (infant$ or neonate$ or newborn$ or baby or babies).tw,tx,kw.
4. (pediatric$ or prepubertal$ or pubescent$ or prepubescence$).tw,tx,kw.
5. or/1-4
6. (diabetes adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or
child$ or early$ or labile or brittle or sudden onset or auto immun$ or autoimmun$)).tw,tx,kw.
7. (IDDM or T1D or T1D or DM1 or DM1).tw,tx.
8. (ketosis or ketoacid$ or ketotic or ketonuria$ or ketonemia$ or hyperketonemia$ or
ketogenesis).tw,tx,kw.
9. (DK or DKA).tw,tx.
10. or/6-9
11. or/10-11

Embase
# Searches
1. exp ADOLESCENT/
2. (adolescent$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3. exp CHILD/
4. (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or
kindergarten$ or boy? or girl?).ti,ab,jx.
5. exp INFANT/
6. (infant$ or neonate$ or newborn$ or baby or babies).ti,ab,jx.
7. exp PEDIATRICS/ or exp PUBERTY/
8. (pediatric$ or prepubertal$ or pubescent$ or prepubescence$).ti,ab,jx,ec.
9. or/1-8
10. exp INSULIN DEPENDENT DIABETES MELLITUS/
11. (diabetes adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or
child$ or early$ or labile or brittle or sudden onset or auto immun$ or autoimmun$)).ti,ab.
12. (IDDM or T1D or T1D or DM1 or DM1).ti,ab.
13. exp KETOACIDOSIS/ or exp DIABETIC KETOACIDOSIS/
14. exp KETONURIA/
15. (ketosis or ketoacid$ or ketotic or ketonuria$ or ketonemia$ or hyperketonemia$ or
ketogenesis).ti,ab.
16. (DK or DKA).ti,ab.
17. or/10-16
18. and/9,17
F.9 Type 1 diabetes – dietary advice

Review questions:

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

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

Ovid MEDLINE(R)

# Searches

1. ADOLESCENT/ or MINORS/
2. (adolescen$ or teen$ or youth$ or young or juvenile? or min$ or highschool$).ti,ab,jw.
3. exp CHILD/
4. (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5. exp INFANT/
6. (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7. exp PEDIATRICS/ or exp PUBERTY/
8. (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9. or/1-8
10. exp DIABETES MELLITUS, TYPE 1/
11 (diabetes adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or early or labile or brittle or sudden onset or auto immune or autoimmunity)).ti,ab.
12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
13 or/10-12
14 GLYCEMIC INDEX/
15 DIETARY CARBOHYDRATES/
16 (glycemic adj3 (index or indice or load)).ti,ab.
17 ((carbohydrate? or CHO) adj3 (count$ or quant$ or exchange or diet or intake)).ti,ab.
18 (CHOx or GI).ti,ab.
19 or/14-18
20 and/9,13,19
21 limit 20 to english language
22 LETTER/
23 EDITORIAL/
24 NEWS/
25 exp HISTORICAL ARTICLE/
26 ANECDOTES AS TOPIC/
27 COMMENT/
28 CASE REPORT/
29 (letter or comment* or abstracts).ti.
30 or/22-29
31 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
32 30 not 31
33 ANIMALS/ not HUMANS/
34 exp ANIMALS, LABORATORY/
35 exp ANIMAL EXPERIMENTATION/
36 exp MODELS, ANIMAL/
37 exp RODENTIA/
38 (rat or rats or mouse or mice).ti.
39 or/32-38
40 21 not 39

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations
# Searches
1 (adolescent$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergarten$ or boy? or girl?).ti,ab,jw.
3 (infant$ or neonate$ or newborn$ or baby or babies).ti,ab,jw.
4 (pediatric$ or pubert$ or prepubert$ or pubescence$ or prepubescence$).ti,ab,jw.
5 or/1-4
6 (diabetes adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or early or labile or brittle or sudden onset or auto immune or autoimmunity)).ti,ab.
7 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
8 or/6-7
9 glycemic adj3 (index or indice or load)).ti,ab.
10 ((carbohydrate? or CHO) adj3 (count$ or quant$ or exchange or diet or intake)).ti,ab.
11 (CHOx or GI).ti,ab.
12 or/9-11
13 and/5,8,12
14 limit 13 to english language

Cochrane Central Register of Controlled Trials
# Searches
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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

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

Health Technology Assessment

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

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245
Search strategies

# Embase

## Searches

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

## Embase

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

#### Search strategies

<table>
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<td>exp ANIMAL EXPERIMENT/</td>
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<tr>
<td>exp EXPERIMENTAL ANIMAL/</td>
<td></td>
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<tr>
<td>ANIMAL MODEL/</td>
<td></td>
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<td>exp RODENT/</td>
<td></td>
</tr>
<tr>
<td>(rat or rats or mouse or mice).ti.</td>
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<tr>
<td>or/34-41</td>
<td></td>
</tr>
<tr>
<td>25 not 42</td>
<td></td>
</tr>
</tbody>
</table>

#### PsycINFO

**Searches**

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

#### CINAHL with Full Text

**Searches**

1. S6 AND S9 AND S20  Limiters - English Language; Exclude MEDLINE records
2. S16 OR S19  Search modes - Boolean/Phrase
3. S17 AND S18  Search modes - Boolean/Phrase
4. TI (count* or quant* or exchang* or diet* or intake) or AB (count* or quant* or exchang* or diet* or intake)  Search modes - Boolean/Phrase
5. TI (carbohydrate* or CHO) or AB (carbohydrate* or CHO)  Search modes - Boolean/Phrase
6. S10 OR S11 OR S12 OR S13 OR S14 OR S15  Search modes - Boolean/Phrase
7. S15  Search modes - Boolean/Phrase
8. S14  Search modes - Boolean/Phrase
9. S13  Search modes - Boolean/Phrase
10. S12  Search modes - Boolean/Phrase
11. (MH "Dietary Carbohydrates+")  Search modes - Boolean/Phrase
12. (MH "Glycemic Load") OR (MH "Glycemic Index")  Search modes - Boolean/Phrase

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

Search strategies

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

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

Ovid MEDLINE(R)

# Searches
1 ADOLESCENT/ or MINORS/
2 (adolescent$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).ti,ab,jw.
3 exp CHILD/
4 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergarten$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infant$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre-pubescen$) or (pediatric$ or paediatric$ or puberty$ or pre-puberty$ or pubescence$ or prepubescence$ or prepubescence$)
9 or/1-8
10 DIABETIC KETOACIDOSIS/
11 (DK or DKA).ti,ab.
12 or/10-11
13 exp KETOSIS/
14 (ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
15 or/13-14
exp DIABETES MELLITUS/
diabet$.mp.
or/16-17
and/15,18
9 and (12 or 19)
POLYDIPSIA/
DRINKING BEHAVIOR/
THIRST/
(polydypsia$ or dehydrat$ or ((excess$ or frequen$) adj3 (thrist$ or fluid intake or drink$))).ti,ab.
or/21-24
POLYURIA/
(polyuri$ or ((excess$ or frequen$) adj3 (urinat$ or urine))).ti,ab.
or/26-27
WEIGHT LOSS/
(weight adj3 (loss or lost or reduc$)).ti,ab.
or/29-30
DEHYDRATION/
(dehydrat$ or rehydrat$ or re hydrat$ or hydration status).ti,ab.
or/32-33
NAUSEA/ or VOMITING/
(nausea or emesis or vomit$).ti,ab.
or/35-36
ABDOMINAL PAIN/ or ABDOMEN, ACUTE/
((abdominal adj3 pain$) or acute abdomen).ti,ab.
or/38-39
DYSPNEA/
TACHYPNEA/
HYPERVENTILATION/
(respirat$ adj (distress or rate)).ti,ab.
(breath$ adj3 (difficult$ or pattern$ or abnormal$ or dysfunction$ or labo?r$ or deep$ or shallow$ or rapid$ or short$ or effort$)).ti,ab.
gasping or kussmaul or dyspnea or tachypnea or breathless$ or hyperventilat$).ti,ab.
or/41-46
CONSCIOUSNESS DISORDERS/ or exp CONFUSION/
(conscious$ or confus$ or deliri$ or mental state$).ti,ab.
or/48-49
"SIGNS AND SYMPTOMS"/
(sign? or symptom? or indicat$ or presentation).ti,ab.
((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest$ or aspect$)).ti,ab.
or/51-53
or/25,28,31,34,37,40,47,50,54
exp HYPERGLYCEMIA/
hyperglyc?emi$.ti,ab.
((high or elevat$ or excess$ or abnormal$ or above or extreme$) adj3 (blood glucose or blood sugar$))).ti,ab.
BLOOD GLUCOSE/an
(BGM or glucometer or glucosemeter$ or (glucose adj meter$)).ti,ab.
(finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
or/56-61
exp KETOSIS/
(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuria or hyperketonuria or keton?emi$ or hyperketon?emi$ or ketogenesis).ti,ab.

KETONES/

3-HYDROXYBUTYRIC ACID/

HYDROXYBUTYRATES/

or/65-67

URINALYSIS/

BLOOD CHEMICAL ANALYSIS/

or/69-70

and/68,71

KETONES/an, bl, ur [Analysis, Blood, Urine]

3-HYDROXYBUTYRIC ACID/an, bl, ur [Analysis, Blood, Urine]

HYDROXYBUTYRATES/an, bl, ur [Analysis, Blood, Urine]

((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or ”3 hydroxybutyr$” or ”3-hydroxybutyr$” or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or ”3 OHB” or ”3-OHB” or 3OHb or ”3 HB” or ”3-HB” or 3HB)).ti,ab.

((urine or urinary) adj3 (dipstick or dip test)).ti,ab.

or/63-64,72-77

ACIDOSIS/

(acidosis or (blood? adj3 acid$) or acid?emi$).ti,ab.

HYDROGEN-ION CONCENTRATION/

ACID-BASE EQUILIBRIUM/

ACID-BASE IMBALANCE/

BICARBONATES/

ELECTROLYTES/

or/81-85

BLOOD GAS ANALYSIS/

BLOOD CHEMICAL ANALYSIS/

or/87-88

and/86,89

HYDROGEN-ION CONCENTRATION/an, bl, ur [Analysis, Blood, Urine]

ACID-BASE EQUILIBRIUM/an, bl [Analysis, Blood]

ACID-BASE IMBALANCE/bl, ur [Blood, Urine]

BICARBONATES/an, bl, ur [Analysis, Blood, Urine]

ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]

((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate$ or electrolyte$)).ti,ab.

(blood gas or ABG or blood test$).ti,ab.

or/79-80,90-97

(biochemical adj3 (variable? or measur$ or marker? or parameter? or abnormal$)).ti,ab.

or/62,78,98-99

or/55,100

exp "SENSITIVITY AND SPECIFICITY"

exp BLOOD CHEMICAL ANALYSIS/

URINALYSIS/

(detect$ or diagnos$ or predict$ or sensitiv$ or accuracy or test$).mp.

or/102-105

and/20,101,106

limit 107 to english language

LETTER/

EDITORIAL/

NEWS/
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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

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

Search strategies

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

Cochrane Central Register of Controlled Trials

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

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

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

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

# Searches
1 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).kw,tw.tx,jw.rw.
2 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).kw,tw.tx,jw.rw.
3 (infan$ or neonat$ or newborn$ or baby or babies).kw,tw.tx,jw.rw.
4 (p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescen$ or prepubescen$ or pre pubescen$).kw,tw.tx,jw.rw.
5 or/1-4
6 (diabetic ketoacidosis or DK or DKA).kw,tw.tx.
7 (ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).kw,tw.tx.
8 diabet$.kw,tw.tx.
9 and/7-8
10 5 and (6 or 9)
11 POLYDIPSIA.kw.
12 DRINKING BEHAVIOR.kw.
13 THIRST.kw.
14 (polyd#$psi$ or dehydrat$ or ((excess$ or frequen$) adj3 (thirst$ or fluid intake or drink$))).tw,tx.
15 or/11-14
16 POLYURIA.kw.
17 (polyuri$ or ((excess$ or frequen$) adj3 (urinat$ or urine))).tw,tx.
18 or/16-17
19 WEIGHT LOSS.kw.
20 (weight adj3 (loss or lost or reduc$)).tw,tx.
21 or/19-20
22 DEHYDRATION.kw.
23 (dehydrat$ or rehydrat$ or re hydrat$ or hydration status).tw,tx.
24 or/22-23
25 (NAUSEA or VOMITING).kw.
26 (nausea or emesis or vomit$).tw,tx.
27 or/25-26
28 (ABDOMINAL PAIN or ABDOMEN, ACUTE).kw.
29 ((abdom#$n$ adj3 pain$) or acute abdomen).tw,tx.
30 or/28-29
31 DYSPNEA.kw.
32 TACHYPNEA.kw.
33 HYPERVENTILATION.kw.
34 (respirat$ adj (distress or rate)).tw,tx.
35 (breath$ adj3 (difficult$ or pattern$ or abnormal$ or dysfunction$ or labo?r$ or deep$ or shallow$ or rapid$ or short$ or effort$)).tw,tx.
36 (gasp$ing or kussmaul or dyspnea or tachypnea or breathless$ or hyperventilat$).tw,tx.
37 or/31-36
38 (CONSCIOUSNESS DISORDERS or CONFUSION or DELIRIUM).kw.
39 (conscious$ or confus$ or deliri$ or mental state$).tw,tx.
40 or/38-39
41 "SIGNS AND SYMPTOMS":kw.
42 (sign? or symptom? or indicat$ or presentation).tw,tx.
43 ((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest$ or aspect?!)).tw,tx.
44 or/41-43
45 or/15,18,21,24,27,30,37,40,44
46 (HYPERGLYCEMIA or GLUCOSE INTOLERANCE).kw.
47 hyperglyc?emi$.tw,tx.
48 ((high or elevat$ or excess$ or abnormal$ or above or extreme$) adj3 (blood glucose or blood sugar?!)).tw,tx.
49 (BGM or glucometer or glucometer$ or (glucose adj meter$)).tw,tx.
50 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").tw,tx.
51 or/46-50
52 (KETOSIS or DIABETIC KETOACIDOSIS).kw.
53 (ketosis or ketoacid$ or keto acid$ or ketotic or ketonuria or hyperketonuria or keton?emi$ or hyperketon?emi$ or ketogenesis).tw,tx.
54 KETONES.kw.
55 3-HYDROXYBUTYRIC ACID.kw.
56 HYDROXYBUTYRATES.kw.
57 or/54-56
58 URINALYSIS.kw.
Diagnosis and management of type 1 diabetes in children and young people

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

Health Technology Assessment

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

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13 exp KETOSIS/
14 (ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).tw.
15 or/13-14
16 exp DIABETES MELLITUS/
17 diabet$.mp.
18 or/16-17
19 and/15,18
20 9 and (12 or 19)
21 POLYDIPSIA/
22 DRINKING BEHAVIOR/
23 THIRST/
24 (polyd#psi$ or dehydrat$ or ((excess$ or frequen$) adj3 (thirst$ or fluid intake or drink$))).tw.
25 or/21-24
26 POLYURIA/
27 (polyuri$ or ((excess$ or frequen$) adj3 (urinat$ or urine))).tw.
28 or/26-27
29 WEIGHT LOSS/
30 (weight adj3 (loss or lost or reduc$)).tw.
31 or/29-30
32 DEHYDRATION/
33 (dehydrat$ or rehydrat$ or re hydrat$ or hydration status).tw.
34 or/32-33
35 NAUSEA/ or VOMITING/
36 (nausea or emesis or vomit$).tw.
37 or/35-36
38 ABDOMINAL PAIN/ or ABDOMEN, ACUTE/
39 ((abdom#n$ adj3 pain$) or acute abdomen).tw.
40 or/38-39
41 DYSPNEA/
42 TACHYPNEA/
43 HYPERVENTILATION/
44 (respirat$ adj (distress or rate)).tw.
45 (breath$ adj3 (difficult$ or pattern$ or abnormal$ or dysfunction$ or labo?r$ or deep$ or shallow$ or rapid$ or short$ or effort$)).tw.
46 (gasping or kussmaul or dyspnea or tachypnea or breathless$ or hyperventilat$).tw.
47 or/41-46
48 CONSCIOUSNESS DISORDERS/ or exp CONFUSION/
49 (conscious$ or confus$ or deliri$ or mental state$).tw.
50 or/48-49
51 "SIGNS AND SYMPTOMS"/
52 (sign? or symptom? or indicat$ or presentation).tw.
53 ((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest$ or aspect$)).tw.
54 or/51-53
55 or/25,28,31,34,37,40,47,50,54
56 exp HYPERGLYCEMIA/
57 hyperglyc?emi$.tw.
58 ((high or elevat$ or excess$ or abnormal$ or above or extreme$) adj3 (blood glucose or blood sugar$)).tw.
59 BLOOD GLUCOSE/an
60 (BGM or glucometer or glucosemeter$ or (glucose adj meter$)).tw.
61 (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").tw.
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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<td>exp KETOSIS/</td>
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<td>64</td>
<td>(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuria or hyperketonuria or keton?emi$ or hyperketon?emi$ or ketogenesis).tw.</td>
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<tr>
<td>65</td>
<td>KETONES/</td>
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<td>3-HYDROXYBUTYRIC ACID/</td>
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<td>or/65-67</td>
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<td>and/68,71</td>
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<td>73</td>
<td>KETONES/an, bl, ur [Analysis, Blood, Urine]</td>
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<td>3-HYDROXYBUTYRIC ACID/an, bl, ur [Analysis, Blood, Urine]</td>
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<td>HYDROXYBUTYRATES/an, bl, ur [Analysis, Blood, Urine]</td>
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<td>76</td>
<td>((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or beta hydroxybutyr$ or &quot;3 hydroxybutyr$&quot; or &quot;3-hydroxybutyr$&quot; or 3-hydroxybutyr$ or 3 hydroxybutyr$ or OHB or beta OHB or beta OHB or Beta OHB or Beta OHB or BOHB or &quot;3 OHB&quot; or &quot;3-OHB&quot; or 3 OHB or &quot;3 HB&quot; or &quot;3-HB&quot; or &quot;3 HB&quot; or &quot;3 HB&quot;)).tw.</td>
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<td>77</td>
<td>((urine or urinary) adj3 (dipstick or dip test)).tw.</td>
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<td>78</td>
<td>or/63-64,72-77</td>
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<td>ACIDOSIS/</td>
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<tr>
<td>80</td>
<td>(acidosis or (blood? adj3 acid$) or acid?emi$).tw.</td>
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<tr>
<td>81</td>
<td>HYDROGEN-ION CONCENTRATION/</td>
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<td>ACID-BASE EQUILIBRIUM/</td>
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<td>and/86,89</td>
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<td>91</td>
<td>HYDROGEN-ION CONCENTRATION/an, bl, ur [Analysis, Blood, Urine]</td>
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<td>ACID-BASE EQUILIBRIUM/an, bl [Analysis, Blood]</td>
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<td>ACID-BASE IMBALANCE/bl, ur [Blood, Urine]</td>
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<td>BICARBONATES/an, bl, ur [Analysis, Blood, Urine]</td>
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<td>ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]</td>
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<td>96</td>
<td>((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate$ or electrolyte$)).tw.</td>
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<td>97</td>
<td>(blood gas or ABG or blood test$).tw.</td>
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<td>98</td>
<td>or/79-80,90-97</td>
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<td>99</td>
<td>(biochemical adj3 (variable? or measur$ or marker? or parameter? or abnormal$)).tw.</td>
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<td>or/62,78,98-99</td>
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<td>101</td>
<td>55 or 100</td>
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<td>102</td>
<td>20 and 101</td>
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<td>103</td>
<td>exp &quot;SENSITIVITY AND SPECIFICITY&quot;/</td>
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<td>104</td>
<td>exp BLOOD CHEMICAL ANALYSIS/</td>
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<td>105</td>
<td>URINALYSIS/</td>
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<td>106</td>
<td>(detect$ or diagno$ or predict$ or sensitiv$ or accuracy or test$).mp.</td>
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<td>107</td>
<td>or/103-106</td>
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**Embase**

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

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259
Search strategies

48  (conscious$ or confus$ or delir$ or mental state$).ti,ab.
49  or/46-48
50  PHYSICAL DISEASE BY BODY FUNCTION/
51  (sign? or symptom? or indicat$ or presentation).ti,ab.
52  ((clinical or physical or presenting) adj3 (feature? or finding? or factor? or manifest$ or aspect$)).ti,ab.
53  or/50-52
54  or/25,28,31,34,37,40,45,49,53
55  HYPERGLYCEMIA/
56  hyperglycemi$.ti,ab.
57  ((high or elevat$ or excess$ or abnormal$ or above or extreme$) adj3 (blood glucose or blood sugar$)).ti,ab.
58  GLUCOSE BLOOD LEVEL/
59  BLOOD GLUCOSE MONITORING/
60  BLOOD GLUCOSE METER/
61  (BGM or glucometer or glucometer$ or (glucose adj meter$)).ti,ab.
62  (finger prick or finger-prick or fingerstick or finger-stick or "finger stick").ti,ab.
63  or/55-62
64  KETOACIDOSIS/
65  KETONEMIA/
66  KETONURIA/
67  (ketosis or ketoacid$ or keto acid$ or ketotic or ketonuria or hyperketonuria or keton?emi$ or hyperketon?emi$ or ketogenesis).ti,ab.
68  KETONE/
69  KETONE BODY/
70  3-HYDROXYBUTYRIC ACID/
71  HYDROXYBUTYRIC ACID/
72  or/68-71
73  URINALYSIS/ or BLOOD ANALYSIS/ or BLOOD CHEMISTRY/
74  and/72-73
75  KETONE/an [Drug Analysis]
76  KETONE BODY/an [Drug Analysis]
77  3-HYDROXYBUTYRIC ACID/an [Drug Analysis]
78  HYDROXYBUTYRIC ACID/an [Drug Analysis]
79  ((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 30HB or "3 HB" or "3-HB" or "3HB").ti,ab.
80  (urine or urinary) adj3 (dipstick or dip test)).ti,ab.
81  or/64-67,74-80
82  ACIDOSIS/
83  (acidosis or (blood? adj3 acid$) or acid?emi$).ti,ab.
84  ACID BASE BALANCE/
85  BLOOD pH/
86  BICARBONATE/
87  ELECTROLYTE/
88  or/84-87
89  BLOOD ANALYSIS/ or BLOOD CHEMISTRY/ or BLOOD GAS ANALYSIS/
90  and/88-89
91  BICARBONATE BLOOD LEVEL/
92  exp ELECTROLYTE BLOOD LEVEL/
93  ACID BASE BALANCE/an [Drug Analysis]
94  BICARBONATE/an [Drug Analysis]
Search strategies

- ELECTROLYTE/an [Drug Analysis]
- ((capillary$ or blood$ or plasma or serum or urine or urinary) adj3 (acid base or pH or bicarbonate$ or electrolyte$)).ti,ab.
- (blood gas or ABG or blood test$).ti,ab.
- or/82-83,90-97
- (biochemical adj3 (variable? or measur$ or marker? or parameter? or abnormal$)).ti,ab.
- or/63,81,98-99
- or/54,100
- "SENSITIVITY AND SPECIFICITY"
- DIAGNOSTIC ACCURACY/
- DIAGNOSTIC TEST/
- DIAGNOSTIC VALUE/
- PREDICTIVE VALUE/
- (detect$ or diagnos$ or predict$ or sensitiv$ or specificity).tw.
- or/102-107
- and/21,101,108
- limit 109 to english language
- conference abstract.pt.
- letter.pt. or LETTER/
- note.pt.
- editorial.pt.
- CASE REPORT/ or CASE STUDY/
- (letter or comment* or abstracts).ti.
- or/111-116
- RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
- 117 not 118
- ANIMAL/ not HUMAN/
- NONHUMAN/
- exp ANIMAL EXPERIMENT/
- exp EXPERIMENTAL ANIMAL/
- ANIMAL MODEL/
- exp RODENT/
- (rat or rats or mouse or mice).ti.
- or/119-126
- 110 not 127
F.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions:

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

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

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

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

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

Ovid MEDLINE(R)

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

or/13-14

exp DIABETES MELLITUS/
diabet$.mp.

or/16-17

and/15,18

9 and (12 or 19)

exp VITAL SIGNS/

exp SYMPTOM ASSESSMENT/

exp AIRWAY MANAGEMENT/

exp INTUBATION/

exp NEUROLOGIC EXAMINATION/

exp BLOOD PRESSURE DETERMINATION/

exp CONFUSION/

CONSCIOUSNESS DISORDERS/

GLASGOW COMA SCALE/

((clinical or physical or physiolog$ or neurologic$) adj3 (observ$ or indication? or indicator? or investigat$ or assess$ or status or sign? or symptom? or characteristic? or monitor$)).ti.

freq=2

((clinical or physical or physiolog$ or neurologic$) adj3 (observ$ or indication? or indicator? or investigat$ or assess$ or status or sign? or symptom? or characteristic? or monitor$)).ab.

(vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$ or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental stat$ or reflex$ or pupil).ti.

freq=2

(vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$ or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental stat$ or reflex$ or pupil).ab.

or/21-33

and/20,34

exp BODY WEIGHT CHANGES/

(body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).ti.

freq=2

(body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).ab.

or/36-38

and/20,39

DEHYDRATION/

(dehydrat$ or hydration status or rehydrate$ or re hydrat$).ti,ab.

WATER-ELECTROLYTE BALANCE/

WATER-ELECTROLYTE IMBALANCE/

exp FLUID THERAPY/

((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?!)).ti.

((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?!)).ab. /freq=2

(volume adj3 expan$).ti,ab.

OLIGURIA/

((urine or urinary) adj3 (reduc$ or decreas$ or drop$ or fall$ or produc$ or output$)).ti,ab.

REGIONAL BLOOD FLOW/ and (FINGERS/bs or CAPILLARIES/ph)

capillary refill$.ti,ab.

SKIN/
(skin turgor or skin color or pinch test).ti,ab.
EYE/
sunken eye?.ti,ab.
exp LOWER EXTREMITY/
exp UPPER EXTREMITY/
(cold adj3 (extremity or limb? or hand? or finger? or foot or feet or toe?)).ti,ab.
MOUTH MUCOSA/
(mucosa or mucous membrane?).ti,ab.
or/41-61
and/20,62
ELECTROCARDIOGRAPHY/
(electrocardio$ or ECG).ti,ab.
or/64-65
and/20,66
or/35,40,63,67
CLINICAL LABORATORY TECHNIQUES/
BLOOD GAS ANALYSIS/
URINALYSIS/
(laboratory adj3 (parameter? or value? or observes or indication? or indicator? or investigat$ or assess$ or evaluat$ or analy$ or test? or monitor$)).ti.
(laboratory adj3 (parameter? or value? or observes or indication? or indicator? or investigat$ or assess$ or evaluat$ or analy$ or test? or monitor$)).ab. /freq=2
((capillary or blood or plasma or serum or urinary) adj3 (parameter? or value? or observes or indication? or indicator? or investigat$ or assess$ or evaluat$ or analy$ or test? or monitor$)).ti.
((capillary or blood or plasma or serum or urinary) adj3 (parameter? or value? or observes or indication? or indicator? or investigat$ or assess$ or evaluat$ or analy$ or test? or monitor$)).ab. /freq=2
or/69-75
and/20,76
BLOOD GLUCOSE/an [Analysis]
GLUCOSE TOLERANCE TEST/
(OGTT or FPG or fasting plasma glucose).ti,ab.
((monitor$ or measure$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (glucose or blood sugar$)).ti.
((monitor$ or measure$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (glucose or blood sugar$)).ab. /freq=2
or/78-82
and/20,83
KETONES/an, bl, ur [Analysis, Blood, Urine]
exp KETONE BODIES/an, bl, ur [Analysis, Blood, Urine]
((capillary or blood or plasma or serum or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or beta hydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or B OHB or BOHB or "3 OHB" or "3-OHB" or "3 HB" or "3-HB" or 3HB)).ti,ab.
((monitor$ or measure$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or beta hydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or B OHB or BOHB or "3 OHB" or "3-OHB" or "3 HB" or "3-HB" or 3HB)).ti,ab.
or/85-88
and/20,83
POINT-OF-CARE SYSTEMS/
(near patient or bedside or bed side or point of care).ti,ab.
or/89-91
and/20,92
PLASMA/ and OSMOLAR CONCENTRATION/
((plasma or serum or blood) adj3 (osmola$ or tonicity)).ti,ab.

HYDROGEN-ION CONCENTRATION/

ACID-BASE EQUILIBRIUM/

ACID-BASE IMBALANCE/

BICARBONATES/an, bl, ur [Analysis, Blood, Urine]

ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]

SODIUM/an, bl, ur [Analysis, Blood, Urine]

POTASSIUM/an, bl, ur [Analysis, Blood, Urine]

exp CHLORIDES/an, bl, ur [Analysis, Blood, Urine]

UREA/an, bl, ur [Analysis, Blood, Urine]

((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte$ or sodium or potassium or chloride? or bicarbonate$ or urea)).ti,ab.

((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (acid base or pH or bicarbonate$ or electrolyte$ or urea)).ti,ab.

(blood gas or ABG).ti,ab.

or/94-107
and/20,108
or/77,84,93,109
or/68,110

*HYPOVOLEMIA/

*HYPOGLYCEMIA/

*HYPOKALEMIA/

*HYPONATREMIA/

*ACIDOSIS/


*(hypovol?emi$ or olig?emi$ or hypoglyc?emi$ or hypokal?emi$ or hyponatr?emi$).ab. /freq=2

*BRAIN EDEMA/

((cerebral or brain) adj3 (oedema? or edema?)).ti.

((cerebral or brain) adj3 (oedema? or edema?)).ab. /freq=2

*VENOUS THROMBOSIS/

(DVT or deep vein thrombo$).ti.

(DVT or deep vein thrombo$).ab. /freq=2

exp *RESPIRATORY ASPIRATION/

exp *PNEUMONIA, ASPIRATION/

aspiration.ti. or aspiration.ab. /freq=2

or/112-129

exp "SENSITIVITY AND SPECIFICITY"/

(pre test or pretest or post test or posttest) adj probability).ti,ab.

(predictive value$ or PPV or NPV).ti,ab.

likelihood ratio$.ti,ab.

LIKELIHOOD FUNCTIONS/

(ROC curve$ or AUC).ti,ab.

(detect$ or diagnos$ or predict$ or accuracy or test$).ti,ab.

di.xs.

or/131-138
and/20,130,139
or/111,140

LETTER/

EDITORIAL/
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

# Searches
1 (adolescent or teen or youth or young or juvenile or minors or high school or high school$).ti,ab,jw.
2 (child or schoolchild or "school age" or "school aged" or preschool or pre school or toddler or kid or kindergar or boy or girl?).ti,ab,jw.
3 (infant or neonate or newborn or baby or babies).ti,ab,jw.
4 (pediatric or pubertal or prepubertal or prepubeal or pubescence or prepubescence).ti,ab,jw.
5 or/1-4
6 (diabetic ketoacidosis or DK or DKA).ti,ab.
7 (ketosis or ketoacidosis or keto acidosis or ketotic or ketonuria or ketonemia or hyperketonemia or ketogenesis).ti,ab.
8 diabet$.mp.
9 and/7-8
10 5 and (6 or 9)
11 ((clinical or physical or physiologic or neurologic) adj3 (observation or indication or indicator or investigation or assessment or status of sign or symptom or characteristic or monitor)).ti.
12 ((clinical or physical or physiologic or neurologic) adj3 (observation or indication or indicator or investigation or assessment or status of sign or symptom or characteristic or monitor)).ab.
13 /freq=2
14 (vital sign or pulse or heart rate or blood pressure or circulation or respiratory or breathing or airway or nasogastric tube or nasogastric intubation or NG tube or temperature or consciousness or glasgow coma or GCS or alertness or confusion or confused or delirium or delirious or mental status or reflex or pupil).ti.
15 (body weight or (weight adj3 (gain or increase or raise or raising or rising or lose or lost or loss or decrease or drop or fall or change or fluctuation)).ti.
16 (body weight or (weight adj3 (gain or increase or raise or raising or rising or lose or lost or loss or decrease or drop or fall or change or fluctuation))).ab. /freq=2
17 (dehydration or hydration status or rehydrate or re hydration).ti,ab.
18 ((fluid or solution or electrolyte or hydrate or rehydrate or re hydration) adj3 (volume or balance or imbalance)).ti.
(((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?)).ab. /freq=2

(volume adj3 expa$n).ti,ab.

((urine or urinary) adj3 (reduc$ or decreas$ or drop$ or fall$ or produc$ or output$)).ti,ab.

capillary refill$.ti,ab.

(skin turgor or skin colo?r or pinch test).ti,ab.

sunken eye?.ti,ab.

(cold adj3 (extremit$ or limb? or hand? or finger? or foot or feet or toe?)).ti,ab.

(mucosa or mucous membrane?).ti,ab.

(electrocardio$ or ECG).ti,ab.

or/11-27

and/10,28

(laboratory adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analy$ or test? or monitor$)).ti.

(laboratory adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analy$ or test? or monitor$)).ab. /freq=2

((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analy$ or test? or monitor$)).ti.

((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analy$ or test? or monitor$)).ab. /freq=2

((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3- hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.

((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillan$ or status or level? or check$) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3- hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.

((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillan$ or status or level? or check$) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr$" or "3- hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.

(near patient or bedside or bed side or point of care).ti,ab.

((plasma or serum or blood) adj3 (osmola$ or tonicity)).ti,ab.

((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte$ or sodium or potassium or chloride? or bicarbonate$ or urea$)).ti,ab.

((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillan$ or status or level? or check$) adj5 (acid base or pH or bicarbonate$ or electrolyte$ or urea$)).ti,ab.

(blood gas or ABG).ti,ab.

or/30-43

and/10,44

or/29,45


(hypovol?emi$ or olig?emi$ or hypoglyc?emi$ or hypokal?emi$ or hyponatr?emi$).ab. /freq=2

(acidosis or (blood? adj3 acid$) or acid?emi$).ti.

(acidosis or (blood? adj3 acid$) or acid?emi$).ab. /freq=2

((cerebral or brain) adj3 (oedema? or edema?)).ti.

((cerebral or brain) adj3 (oedema? or edema?)).ab. /freq=2

(DVT or deep vein thrombo$).ti.

(DVT or deep vein thrombo$).ab. /freq=2
Cochrane Central Register of Controlled Trials

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

33 (vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$ or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental status or reflex$ or pupil).ab. /freq=2

34 or/21-33
35 and/20,34
36 exp BODY WEIGHT CHANGES/
37 (body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).ti.
38 (body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).ab. /freq=2
39 or/36-38
40 and/20,39
41 DEHYDRATION/
42 (dehydrat$ or hydration status or rehydrate$ or re hydrat$).ti,ab.

43 WATER-ELECTROLYTE BALANCE/
44 WATER-ELECTROLYTE IMBALANCE/
45 exp FLUID THERAPY/
46 ((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance$)).ti.
47 ((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance$)).ab. /freq=2
48 (volume adj3 expan$).ti,ab.
49 OLIGURIA/
50 ((urine or urinary) adj3 (reduc$ or decreas$ or drop$ or fall$ or produc$ or output$)).ti,ab.
51 REGIONAL BLOOD FLOW/ and (FINGERS/bs or CAPILLARIES/ph)
52 capillary refill$.ti,ab.
53 SKIN/
54 (skin turgor or skin colo?r or pinch test).ti,ab.
55 EYE/
56 sunken eye?.ti,ab.
57 exp LOWER EXTREMITY/
58 exp UPPER EXTREMITY/
59 (cold adj3 (extremit$ or limb? or hand? or finger? or foot or feet or toe$)).ti,ab.
60 MOUTH MUCOSA/
61 (mucosa or mucous membrane?).ti,ab.
62 or/41-61
63 and/20,62
64 ELECTROCARDIOGRAPHY/
65 (electrocardio$ or ECG).ti,ab.
66 or/64-65
67 and/20,66
68 or/35,40,63,67
69 CLINICAL LABORATORY TECHNIQUES/
70 BLOOD GAS ANALYSIS/
71 URINALYSIS/
72 (laboratory adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analy$ or test? or monitor$)).ti.
73 (laboratory adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analy$ or test? or monitor$)).ab. /freq=2
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

74 ((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ti.
75 ((capillar$ or blood$ or plasma or serum or urine or urinary) adj3 (parameter? or value? or observ$ or indication? or indicator? or investigat$ or assess$ or evaluat$ or analys$ or test? or monitor$)).ab. /freq=2
76 or/69-75
77 and/20,76
78 BLOOD GLUCOSE/an [Analysis]
79 GLUCOSE TOLERANCE TEST/
80 (OGTT or FPG or fasting plasma glucose).ti,ab.
81 ((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveil lance or status or level? or check$) adj5 (glucose or blood sugar$)).ti.
82 ((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveil lance or status or level? or check$) adj5 (glucose or blood sugar$)).ab. /freq=2
83 or/78-82
84 and/20,83
85 KETONES/an, bl, ur [Analysis, Blood, Urine]
86 exp KETONE BODIES/an, bl, ur [Analysis, Blood, Urine]
87 ((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or beta hydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
88 ((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveil lance or status or level? or check$) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or beta hydroxybutyr$ or "3 hydroxybutyr$" or "3-hydroxybutyr$" or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).ti,ab.
89 or/85-88
90 POINT-OF-CARE SYSTEMS/
91 (near patient or bedside or bed side or point of care).ti,ab.
92 or/89-91
93 and/20,92
94 PLASMA/ and OSMOLAR CONCENTRATION/
95 ((plasma or serum or blood) adj3 (osmola$ or tonicity)).ti,ab.
96 HYDROGEN-ION CONCENTRATION/
97 ACID-BASE EQUILIBRIUM/
98 ACID-BASE IMBALANCE/
99 BICARBONATES/an, bl, ur [Analysis, Blood, Urine]
100 ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]
101 SODIUM/an, bl, ur [Analysis, Blood, Urine]
102 POTASSIUM/an, bl, ur [Analysis, Blood, Urine]
103 exp CHLORIDES/an, bl, ur [Analysis, Blood, Urine]
104 UREA/an, bl, ur [Analysis, Blood, Urine]
105 ((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte$ or sodium or potassium or chloride? or bicarbonate$ or urea$)).ti,ab.
106 ((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveil lance or status or level? or check$) adj5 (acid base or pH or bicarbonate$ or electrolyte$ or urea$)).ti,ab.
107 (blood gas or ABG).ti,ab.
108 or/94-107
109 and/20,108
110 or/77,84,93,109
111 or/68,110
112 *HYPOVOLEMIA/
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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

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

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

Search strategies

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

61 ((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (glucose or blood sugar$)).tw,tx.

62 or/58-61

63 and/10,62

64 KETONES.kw.

65 (KETONE BODIES or 3-HYDROXYBUTYRIC ACID or HYDROXYBUTYRATES or ACETOACETATES or ACETONE).kw.

66 ((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or beta hydroxybutyr. or "3-hydroxybutyr$" or "3-hydroxybutyr.$" or 3hydroxybutyr.$ or OHB or beta OHB or betaOH or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw,tx.

67 ((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr" or "3-hydroxybutyr$" or 3hydroxybutyr.$ or OHB or beta OHB or betaOH or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw,tx.

68 or/64-67

69 POINT-OF-CARE SYSTEMS.kw.

70 (near patient or bedside or bed side or point of care).tw,tx.

71 or/68-70

72 and/10,71

73 (PLASMA and OSMOLAR CONCENTRATION).kw.

74 ((plasma or serum or blood) adj3 (osmolal$ or tonicity)).tw,tx.

75 HYDROGEN-ION CONCENTRATION.kw.

76 ACID-BASE EQUILIBRIUM.kw.

77 ACID-BASE IMBALANCE.kw.

78 BICARBONATES.kw.

79 ELECTROLYTES.kw.

80 SODIUM.kw.

81 POTASSIUM.kw.

82 (CHLORIDES or SODIUM CHLORIDE or POTASSIUM CHLORIDE).kw.

83 UREA.kw.

84 ((capillar$ or blood$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte$ or sodium or potassium or chloride? or bicarbonate$ or urea)).tw,tx.

85 ((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (acid base or pH or bicarbonate$ or electrolyte$ or urea)).tw,tx.

86 (blood gas or ABG).tw,tx.

87 or/73-86

88 and/10,87

89 or/57,63,72,88

90 or/50,89

91 HYPOVOLEMIA.kw.

92 HYPOGLYCEMIA.kw.

93 HYPOKALEMIA.kw.

94 HYPONATREMIA.kw.


96 ACIDOSIS.kw.

97 (acidosis or (blood? adj3 acid$) or acid?emi$).tw,tx.

98 BRAIN EDEMA.kw.

99 ((cerebral or brain) adj3 (oedema? or edema?)).tw,tx.

100 VENOUS THROMBOSIS.kw.

101 (DVT or deep vein thrombo$).tw,tx.

102 aspiration.tw,kw,tx.
Search strategies

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Health Technology Assessment

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

and/20,32
exp BODY WEIGHT CHANGES/
(body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).tw.
or/34-35
and/20,36
DEHYDRATION/
(dehydrat$ or hydration status or rehydrate$ or re hydrat$).tw.

WATER-ELECTROLYTE BALANCE/
WATER-ELECTROLYTE IMBALANCE/
exp FLUID THERAPY/
((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?!)).tw.

or/38-39
and/20,38
ELECTROCARDIOGRAPHY/
(electrocardio$ or ECG).tw.
or/60-61

and/20,62
or/33,37,59,63
and/20,70
BLOOD GLUCOSE/an [Analysis]
GLUCOSE TOLERANCE TEST/
(OGTT or FPG or fasting plasma glucose).tw.
or/72-75
and/20,76
KETONES/an, bl, ur [Analysis, Blood, Urine]
exp KETONE BODIES/an, bl, ur [Analysis, Blood, Urine]
Search strategies

((capillary$ or blood$ or plasma or serum or urine or urinary) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr"$ or "3-hydroxybutyr"$ or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw.

((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (ketone? or hydroxy butyr$ or hydroxybutyr$ or beta hydroxybutyr$ or betahydroxybutyr$ or "3 hydroxybutyr"$ or "3-hydroxybutyr"$ or 3hydroxybutyr$ or OHB or beta OHB or betaOHB or B OHB or BOHB or "3 OHB" or "3-OHB" or 3OHB or "3 HB" or "3-HB" or 3HB)).tw.

or/78-81

POINT-OF-CARE SYSTEMS/

(near patient or bedside or bed side or point of care).tw.

or/82-84

and/20,85

PLASMA/ and OSMOLAR CONCENTRATION/

((plasma or serum or blood) adj3 (osmola$ or tonicity)).tw.

HYDROGEN-ION CONCENTRATION/

ACID-BASE EQUILIBRIUM/

ACID-BASE IMBALANCE/

BICARBONATES/an, bl, ur [Analysis, Blood, Urine]

ELECTROLYTES/an, bl, ur [Analysis, Blood, Urine]

SODIUM/an, bl, ur [Analysis, Blood, Urine]

POTASSIUM/an, bl, ur [Analysis, Blood, Urine]

exp CHLORIDES/an, bl, ur [Analysis, Blood, Urine]

UREA/an, bl, ur [Analysis, Blood, Urine]

((capillary$ or blood$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte$ or sodium or potassium or chloride? or bicarbonate$ or urea)).tw.

((monitor$ or measur$ or test$ or screen$ or determin$ or assess$ or evaluat$ or surveillance or status or level? or check$) adj5 (acid base or pH or bicarbonate$ or electrolyte$ or urea)).tw.

(blood gas or ABG).tw.

or/87-100

and/20,101

or/71,77,86,102

or/64,103

*HYPOVOLEMIA/

*HYPOGLYCEMIA/

*HYPOKALEMIA/

*HYPONATREMIA/


*ACIDOSIS/

(acidosis or (blood? adj3 acid$) or acid?emi$).tw.

*BRAIN EDEMA/

((cerebral or brain) adj3 (oedema? or edema?)).tw.

*VENOUS THROMBOSIS/

(DVT or deep vein thrombo$).tw.

exp *RESPIRATORY ASPIRATION/

exp *PNEUMONIA, ASPIRATION/

aspiration.tw.

or/105-118

exp "SENSITIVITY AND SPECIFICITY"/

((pre test or pretest or post test or posttest) adj probability).tw.

(predictive value$ or PPV or NPV).tw.

likelihood ratio$.tw.
Search strategies

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

**Embase**

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

Search strategies

40 BREATHING RATE/
41 RESPIRATION CONTROL/
42 exp RESPIRATORY TRACT INTUBATION/
43 STOMACH INTUBATION/
44 CONSCIOUSNESS LEVEL/
45 CONSCIOUSNESS DISORDER/
46 exp CONFUSION/
47 exp DELIRIUM/
48 NEUROLOGIC EXAMINATION/
49 GLASGOW COMA SCALE/
50 ((clinical or physical or physiologic$ or neurologic$) adj3 (observ$ or indication? or indicator? or investigat$ or assess$ or status or sign? or symptom? or characteristic? or monitor$)).ti.
51 ((clinical or physical or physiologic$ or neurologic$) adj3 (observ$ or indication? or indicator? or investigat$ or assess$ or status or sign? or symptom? or characteristic? or monitor$)).ab. /freq=2
52 (vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$ or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental stat$ or reflex$ or pupil).ti.
53 (vital sign? or pulse? or heart rate? or blood pressure? or circulation? or respirat$ or breathing or airway or nasogastric tube or nasogastric intubat$ or NG tube or temperature or conscious$ or glasgow coma or GCS or alert$ or confusion or confused or delirium or delirious or mental stat$ or reflex$ or pupil).ab. /freq=2
54 or/30-53
55 and/29,54
56 WEIGHT CHANGE/
57 WEIGHT FLUCTUATION/
58 WEIGHT GAIN/
59 WEIGHT REDUCTION/
60 (body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).ti.
61 (body weight or (weight adj3 (gain$ or increas$ or raise or raising or rising or lose or lost or loss$ or decreas$ or drop$ or fall$ or chang$ or fluctuat$))).ab. /freq=2
62 or/56-61
63 and/29,62
64 DEHYDRATION/
65 (dehydrat$ or hydration status or rehydrate$ or re hydrat$).ti,ab.
66 FLUID BALANCE/
67 ((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?)).ti.
68 ((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj3 (volume? or balance? or imbalance?)).ab. /freq=2
69 (volume adj3 expan$).ti,ab.
70 OBLIGURIA/
71 URINE OUTPUT/
72 ((urine or urinary) adj3 (reduc$ or decreas$ or drop$ or fall$ or produc$ or output$)).ti,ab.
73 CAPILLARY FLOW/
74 capillary refill$.ti,ab.
75 SKIN TURGOR/
76 (skin turgor or skin colo?r or pinch test).ti,ab.
77 EYE/
78 sunken eye?.ti,ab.
79 COLD LIMB/
80 (cold adj3 (extremi$ or limb? or hand? or finger? or foot or feet or toe?!)).ti,ab.
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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Search strategies

121 BICARBONATE BLOOD LEVEL/
122 exp ELECTROLYTE BLOOD LEVEL/
123 exp URINE LEVEL/
124 exp UREA BLOOD LEVEL/
125 ((capillary$ or blood$ or plasma or serum or urine or urinary) adj5 (acid base or pH or electrolyte$ or sodium or potassium or chloride$ or bicarbonate$ or urea)).ti,ab.
126 ((monitor$ or measure$ or test$ or screen$ or determine$ or assess$ or evaluate$ or surveillance or status or level? or check$) adj5 (acid base or pH or bicarbonate$ or electrolyte$ or urea)).ti,ab.
127 (blood gas or ABG).ti,ab.
128 or/117-127
129 and/29,128
130 or/98,106,116,129
131 or/89,130
132 exp "HYPOVOLEMIA/
133 "HYPOGLYCAEMIA/
134 "HYPOKALEMIA/
135 "HYPONATREMIA/
137 (hypovol?emi$ or olig?emi$ or hypoglyc?emi$ or hypokal?emi$ or hyponatr?emi$).ab. /freq=2
138 "ACIDOSIS/
139 (acidosis or (blood? adj3 acid$) or acid?emi$).ti.
140 (acidosis or (blood? adj3 acid$) or acid?emi$).ab. /freq=2
141 "BRAIN EDEMA/
142 ((cerebral or brain) adj3 (oedema? or edema?)).ti.
143 ((cerebral or brain) adj3 (oedema? or edema?)).ab. /freq=2
144 "DEEP VEIN THROMBOSIS/
145 (DVT or deep vein thrombo$).ti.
146 (DVT or deep vein thrombo$).ab. /freq=2
147 "PULMONARY ASPIRATION/
148 "ASPIRATION PNEUMONIA/
149 aspiration.ti. or aspiration.ab. /freq=2
150 or/132-149
151 "SENSITIVITY AND SPECIFICITY”/
152 PREDICTIVE VALUE/
153 DIAGNOSTIC VALUE/
154 DIAGNOSTIC ACCURACY/
155 ((pre test or pretest or post test or posttest) adj probability).ti,ab.
156 (predictive value$ or PPV or NPV).ti,ab.
157 likelihood ratio$.ti,ab.
158 di.fs.
159 or/151-158
160 and/29,150,159
161 or/131,160
162 conference abstract.pt.
163 letter.pt. or LETTER/
164 note.pt.
165 editorial.pt.
166 CASE REPORT/ or CASE STUDY/
167 (letter or comment* or abstracts).ti.
168 or/162-167
169 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
170 168 not 169
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

Review questions:

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

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

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

Ovid MEDLINE(R)

# Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$ or high school$).ti,ab,jw.
3 exp CHILD/
4 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or pre school$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric$ or pubert$ or prepubert$ or pre pubert$ or pubescent$ or prepubescent$ or pre pubescent$).ti,ab,jw.
9 or/1-8
10 DIABETIC KETOACIDOSIS/
11 (DK or DKA).ti,ab.
12 or/10-11
13 exp KETOSIS/
14 (ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
15 or/13-14
16 exp DIABETES MELLITUS/
17 diabet$.mp.
18 or/16-17
19 and/15,18
20 9 and (12 or 19)
21 exp FLUID THERAPY/
22 REHYDRATION SOLUTIONS/
23 WATER-ELECTROLYTE BALANCE/
WATER-ELECTROLYTE IMBALANCE/
((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj5 (manag$ or regimen? or resuscitat$ or infusion? or administrat$ or replac$ or balanc$ or imbalanc$)).ti,ab.
or/21-25
and/20,26
DRUG ADMINISTRATION ROUTES/
ADMINISTRATION, ORAL/
ADMINISTRATION, INTRAVENOUS/
INFUSIONS, INTRAVENOUS/
INFUSIONS, INTRAOSSEOUS/
exp INFUSIONS, SUBCUTANEOUS/
INFUSION PUMP/
INTUBATION, GASTROINTESTINAL/
((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (route? or intravenous$ or oral or orally or mouth or subcutan$ or hypodermocl$ or intraosse$ or intra osse$ or intraperiton$ or intra periton$ or gavage or nasogastric or naso gastric or rectal or proctocl$)).ti,ab.
or/28-37
and/20,38
TIME FACTORS/
DRUG ADMINISTRATION SCHEDULE/
((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (rate? or variable rate? or fixed rate? or volume or fast or faster or quickly or quicker or quick or rapid$ or slow or slowly or slower or gradual$ or earlier or early or later or late)).ti,ab.
or/40-42
and/20,43
SODIUM/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
exp CHLORIDES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
GLUCOSE/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
GLUCOSE SOLUTION, HYPERTONIC/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
SALINE SOLUTION, HYPERTONIC/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
exp BICARBONATES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
POTASSIUM/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
PHOSPHATES/ad, tu, th [Administration & Dosage, Therapeutic Use, Therapy]
((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (chloride? or sodium chloride? or potassium chloride? or potassium or phosphate? or orthophosphate? or ortho phosphate?)).ti,ab.
or/45-53
and/20,54
or/27,39,44,55
LETTER/
EDITORIAL/
NEWS/
exp HISTORICAL ARTICLE/
ANECDOTES AS TOPIC/
COMMENT/
CASE REPORT/
(letter or comment* or abstracts).ti.
or/57-64
Diagnosis and management of type 1 diabetes in children and young people

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

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

Cochrane Central Register of Controlled Trials

# Searches
1 ADOLESCENT/ or MINORS/
Search strategies

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

((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (chloride? or sodium chloride? or potassium chloride? or saline? or NaCl or KCl or glucose or dextrose or hydrogen carbonate? or bicarbonate? or carbonic acid or potassium or phosphate? or orthophosphate? or ortho phosphate?))).ti,ab.
or/45-53
and/20,54
or/27,39,44,55

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

# Searches

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

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

Health Technology Assessment

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

Search strategies

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

Embase

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

exp INFANT/

(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.

exp PEDIATRICS/ or exp PUBERTY/

(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.

or/1-8

INSULIN DEPENDENT DIABETES MELLITUS/

(diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.

(IDDM or T1D or TID or DM1 or DMI).ti,ab.

or/10-12

NON INSULIN DEPENDENT DIABETES MELLITUS/

(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.

(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.

(NIDDM or T2D or TIID or DM2 or DMIII).ti,ab.

or/14-17

JUVENILE DIABETES MELLITUS/

or/13,18-19

KETOACIDOSIS/

KETONURIA/

(ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.

or/21-23

and/20,24

DIABETIC KETOACIDOSIS/

(DK or DKA).ti,ab.

or/26-27

9 and (25 or 28)

FLUID THERAPY/

FLUID RESUSCITATION/

exp REHYDRATION/

exp ELECTROLYTE BALANCE/

exp ELECTROLYTE DISTURBANCE/

((fluid? or solution? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$) adj5 (manag$ or regimen? or resuscit$ or infusion? or administrat$ or replac$ or balanc$ or imbalanc$)).ti,ab.

or/30-35

and/29,36

DRUG ADMINISTRATION ROUTE/

INTRAVENOUS ADMINISTRATION/

INTRAGASTRIC DRUG ADMINISTRATION/

INTRAOSSEOUS DRUG ADMINISTRATION/

INTRAPERITONEAL DRUG ADMINISTRATION/

SUBCUTANEOUS DRUG ADMINISTRATION/

STOMACH INTUBATION/

ORAL REHYDRATION THERAPY/

ORAL REHYDRATION SOLUTION/

INFUSION SYSTEM/

INFUSION PUMP/

((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (route? or intravenous$ or oral or orally or mouth or subcutan$ or hypodermocl$ or intraosse$ or intra osse$ or intraperiton$ or intra periton$ or gavage or nasogastric or naso gastric or rectal or proctocl$)).ti,ab.
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

50 (fluid bolus or two bag or ORT).ti,ab.
51 or/38-50
52 and/29,51
53 INFUSION RATE/
54 DRUG DOSE REGIMEN/
55 DRUG ADMINISTRATION/
56 ((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (rate? or variable rate? or fixed rate? or volume or fast or faster or quickly or quicker or quick or rapid$ or slow or slowly or slower or gradual$ or earlier or early or later or late)).ti,ab.
57 or/53-56
58 and/29,57
59 INFUSION FLUID/ad, dt, ig, os, iv, po, pa, sc [Drug Administration, Drug Therapy, Intragastric Drug Administration, Intraosseous Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Subcutaneous Drug Administration]
60 SODIUM/ad, dt, ip, iv, po, pa, sc, th [Drug Administration, Drug Therapy, Intraosseous Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Subcutaneous Drug Administration, Therapy]
61 CHLORIDE/ad, dt, ip, iv, po, pa, sc, th [Drug Administration, Drug Therapy, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Subcutaneous Drug Administration]
62 SODIUM CHLORIDE/ad, dt, dl, ig, os, ip, iv, po, pa, rc, sc, th [Drug Administration, Drug Therapy, Intradermal Drug Administration, Intragastric Drug Administration, Intraosseous Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Subcutaneous Drug Administration, Therapy]
63 GLUCOSE/ad, dt, ig, os, ip, iv, po, pa, rc, sc, th [Drug Administration, Drug Therapy, Intragastric Drug Administration, Intraosseous Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Rectal Drug Administration, Subcutaneous Drug Administration, Therapy]
64 GLUCOSE INFUSION/
65 BICARBONATE/ad, dt, ig, os, ip, iv, po, pa, rc, sc, th [Drug Administration, Drug Therapy, Intragastric Drug Administration, Intraosseous Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Rectal Drug Administration, Subcutaneous Drug Administration, Therapy]
66 POTASSIUM/ad, dt, ig, os, ip, iv, po, pa, rc, sc, th [Drug Administration, Drug Therapy, Intragastric Drug Administration, Intraosseous Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Rectal Drug Administration, Subcutaneous Drug Administration, Therapy]
67 PHOSPHATE/ad, dt, ig, ip, iv, po, pa, rc, th [Drug Administration, Drug Therapy, Intragastric Drug Administration, Intraperitoneal Drug Administration, Intravenous Drug Administration, Oral Drug Administration, Parenteral Drug Administration, Subcutaneous Drug Administration, Therapy]
68 exp ELECTROLYTE BLOOD LEVEL/
69 BICARBONATE BLOOD LEVEL/
70 GLUCOSE BLOOD LEVEL/
71 PHOSPHATE BLOOD LEVEL/
72 ((fluid? or solution? or infusion? or electrolyte? or hydrat$ or rehydrat$ or re hydrat$ or resuscitat$) adj5 (chloride? or sodium chloride? or potassium chloride? or saline? or NaCl or KCl or glucose or dextrose or hydrogen carbonate? or bicarbonate? or carbonic acid? or potassium or phosphate? or orthophosphate? or ortho phosphate?)?).ti,ab.
73 or/59-72
74 and/29,73
75 or/37,52,58,74
76 conference abstract.pt.
77 letter.pt. or LETTER/
78 note.pt.
F.13  Type 1 and type 2 diabetes – diabetic ketoacidosis intravenous osmotic agents

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

Ovid MEDLINE(R)

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

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

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

<table>
<thead>
<tr>
<th>Step</th>
<th>Search Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>ICP.ti,ab.</td>
</tr>
<tr>
<td>14</td>
<td>or/11-13</td>
</tr>
<tr>
<td>15</td>
<td>osmotherap$.ti,ab.</td>
</tr>
<tr>
<td>16</td>
<td>(osmo$ adj3 (therap$ or agent? or solution? or serum or plasma or blood)).ti,ab.</td>
</tr>
<tr>
<td>17</td>
<td>(hyperton$ adj3 (saline or solution?!)).ti,ab.</td>
</tr>
<tr>
<td>18</td>
<td>(saline or sodium chloride or NaCl).ti,ab.</td>
</tr>
<tr>
<td>19</td>
<td>(mannitol or viaflo or viaflex).ti,ab.</td>
</tr>
<tr>
<td>20</td>
<td>or/15-19</td>
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<tr>
<td>21</td>
<td>and/10,14,20</td>
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<tr>
<td>22</td>
<td>limit 21 to english language</td>
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</table>

Cochrane Central Register of Controlled Trials

# Searches

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

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

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

Health Technology Assessment

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

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

Embase

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

Review questions:

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

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

Ovid MEDLINE(R)
# Searches
1 randomized controlled trial.pt.
2 controlled clinical trial.pt.
3 DOUBLE BLIND METHOD/
4 SINGLE BLIND METHOD/
5 RANDOM ALLOCATION/
SEARCH STRATEGIES

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

Search strategies

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

# Searches
1 (adolescent$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergart$ or boy? or girl?!).ti,ab,jw.
3 (infant$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

Cochrane Central Register of Controlled Trials

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

Search strategies

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

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

NHS Economic Evaluation Database

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

Search strategies

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

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

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300
Search strategies

39 (book or conference paper or editorial or letter or note or proceeding or short survey).pt.
40 38 not 39
41 exp ADOLESCENT/
42 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
43 exp CHILD/
44 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
45 exp INFANT/
46 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
47 exp PEDIATRICS/ or exp PUBERTY/
48 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
49 or/41-48
50 KETOACIDOSIS/ or DIABETIC KETOACIDOSIS/
51 KETONURIA/
52 (ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).ti,ab.
53 (DK or DKA).ti,ab.
54 or/50-53
55 exp DIABETES MELLITUS/
56 diabet$.mp.
57 or/55-56
58 and/49,54,57
59 exp INSULIN DERIVATIVE/
60 INSULIN TREATMENT/ or INSULIN INFUSION/
61 or/59-60
62 DRUG DOSE/ or DOSE CALCULATION/ or DOSAGE SCHEDULE COMPARISON/ or DRUG DOSE COMPARISON/ or DRUG DOSE ESCALATION/ or DRUG DOSE INCREASE/ or DRUG DOSE INTENSIFICATION/ or DRUG DOSE REDUCTION/ or DRUG DOSE REGIMEN/ or LOADING DRUG DOSE/ or LOW DRUG DOSE/ or MAINTENANCE DRUG DOSE/ or OPTIMAL DRUG DOSE/
63 EARLY INTERVENTION/
64 TREATMENT DURATION/
65 THERAPY DELAY/
66 or/62-65
67 and/61,66
68 exp INSULIN DERIVATIVE/do, iv [Drug Dose, Intravenous Drug Administration]
69 (insulin$ adj5 (high-dose? or high-dosage? or low-dose or low-dosage? or dose? or dosage? or bolus$ or priming or loading$)).ti,ab.
70 (insulin$ adj5 (early or earli$ or delay$ or start? or starting or stop? or stopping or time or timing$)).ti,ab.
71 or/67-70
72 and/58,71
73 and/40,72
74 conference abstract.pt.
75 letter.pt. or LETTER/
76 note.pt.
77 editorial.pt.
78 CASE REPORT/ or CASE STUDY/
79 (letter or comment* or abstracts).ti.
80 or/74-79
81 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
82 80 not 81
83 ANIMAL/ not HUMAN/
84 NONHUMAN/
F.15 Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis

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

Ovid MEDLINE(R)

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

Search strategies

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

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

(Cochrane Central Register of Controlled Trials)

# Searches
1. ADOLESCENT/ or MINORS/
2. (adolescent$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3. exp CHILD/
4. (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?!).ti,ab,jw.
5. exp INFANT/
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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

#  Searches
1  (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).kw,tw,tx,jw,rw.
2  (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).kw,tw,tx,jw,rw.
3  (infan$ or neonat$ or newborn$ or baby or babies).kw,tw,tx,jw,rw.
4  (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).kw,tw,tx,jw,rw.
5  or/1-4
6  (ketosis or ketoacid$ or keto acid$ or ketotic or ketonuri$ or keton?emi$ or hyperketon$ or ketogenesis).kw,tw,tx.
7  (DK or DKA).kw,tw,tx.
8  or/6-7
9  diabet$.kw,tw,tx.
10  and/5,8-9
11  ANTICOAGULANTS.kw.
12  FIBRINOLYTIC.kw.
13  (THROMBOL$ or HIRUDIN).kw.
14  ASPIRIN.kw.
15  DICUMAROL.kw.
Warfarin.kw.
Heparin$.kw.
(anticoagula$ or aspirin$ or dalteparin$ or nadroparin$ or enoxaparin$ or dic?umarol or fragmin$ or heparin$ or UFH or LMWH or warfarin$ or fibrinolysis).tw.tx.
or/11-18
(EMBOLI$ or THROMBO$).kw.
HEMORRHAGE.kw.
SATISFACTION.kw.
(thromboprophylaxis or thrombus or thrombi or thrombotic$ or thrombolic$ or thromboly$ or thromboemboli$ or thrombocytc$ or thombos$ or emboli$ or bleed$ or h?emorrag$ or adverse or complication? or mortalit$ or utili#ation or satisfaction or satisfied).tw.tx.
or/20-23
and/10,19,24

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

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

Search strategies

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

F.16 Type 1 and type 2 diabetes – retinopathy

Review questions:

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

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

Ovid MEDLINE(R)

# Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3 exp CHILD/
4 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/
11 (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
13 or/10-12
exp DIABETES MELLITUS, TYPE 2/
(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
or/14-17
or/13,18
DIABETIC RETINOPATHY/
(diabet$ adj3 retinopath$).ti,ab.
or/20-21
RETINAL DISEASES/
retinopath$.ti,ab.
or/23-24
DIAGNOSTIC TECHNIQUES, OPHTHALMOLOGICAL/
exp OPHTHALMOSCOPY/
FUNDUS OCULI/
RETINA/ or RETINAL VESSELS/
PHOTOGRAPHY/
and/29-30
(retina$ or fundus or ocul$ or eye?) adj3 (photograph$ or exam$)).ti,ab.
(op?thalmoscop$ or retinoscop$).ti,ab.
fundus oculi.ti,ab.
or/26-28,31-34
MASS SCREENING/
VISION SCREENING/
exp POPULATION SURVEILLANCE/
(undiagnos$ or estimate$).ti.
(screen$ or surveill$ or predict$ or detect$).ti.
or/36-40
SEVERITY OF ILLNESS INDEX/
INTERNATIONAL CLASSIFICATION OF DISEASES/
CLASSIFICATION/
(retinopath$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging$)).ti,ab.
or/42-45
exp EYE HEMORRHAGE/
h?emorrhag$.ti,ab.
exp ANEURYSM/
(microaneurysm? or micro aneurysm?).ti,ab.
"EXUDATES AND TRANSUDATES"/
exp EYE/
and/51-52
SUBRETINAL FLUID/
exudate?.ti,ab.
PAPILLEDEMA/
EDEMA/
expeYE/
and/57-58
(retina$ or optic dis?? or optic nerve?) adj (edema? or oedema??)).ti,ab.
RETINAL NEOVASCULARIZATION/
NEOVASCULARIZATION, PATHOLOGIC/ or VASCULAR MALFORMATIONS/
expeYE/ or RETINAL VESSELS/
and/63-64
exp RETINAL VESSELS/pa, pp [Pathology, Physiopathology]

67 neovascular$.ti,ab.

68 (new adj2 vessel adj2 form$).ti,ab.

69 ((venous or vascular or microvascular or fibrovascular) adj3 (abnormal$ or malform$ or loop$ or bead$ or reduplicat$ or duplicat$ or proliferat$)).ti,ab.

70 (IRMA or ((intraretinal or intra retinal) adj microvascular adj abnormal$)).ti,ab.

71 "MACULAR DEGENERATION/"

72 MACULAR EDEMA/

73 (macular adj (degenerat$ or dysfunction$)).ti,ab.

74 (maculopath$ or macular edema? or macular oedema? or CSME or CSMO).ti,ab.

75 exp OCULAR HYPERTENSION/

76 (glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi$ or pressur$))).ti,ab.

77 OPTIC NEUROPATHY, ISCHEMIC/

78 (optic adj3 (isch?emi$ or neuropat$)).ti,ab.

79 cotton wool spot?.ti,ab.

80 RETINAL DETACHMENT/

81 ((retina$ or preretina$) adj3 (detach$ or tear$ or scar$ or thick$ or lesion? or manifest$ or fibrosis$)).ti,ab.

82 VISION DISORDERS/

83 SCOTOMA/

84 VISION, LOW/

85 (scotoma? or blind spot? or floater? or musca volitante?).ti,ab.

86 ((reduc$ or impair$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish$ or low or blur$) adj3 (vision or visual or acuity)).ti,ab.

87 or/47-50,53-56,59-62,65-86

88 PREVALENCE/

89 INCIDENCE/

90 CROSS-SECTIONAL STUDIES/

91 exp MODELS, STATISTICAL/

92 LIFE TABLES/

93 exp RISK/

94 (prevalen$ or incidence? or model$ or risk$ or rate?).ti.

95 or/88-94

96 AGE FACTORS/

97 AGE DISTRIBUTION/

98 AGE OF ONSET/

99 TIME TO TREATMENT/

100 (age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.

101 (disease adj3 (duration or onset)).ti,ab.

102 or/96-101

103 DIABETIC RETINOPATHY/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]

104 22 and (35 or 41 or 46 or 95 or 102)

105 19 and 25 and (35 or 41 or 46 or 95 or 102)

106 19 and 87 and (95 or 102)

107 or/103-106

108 and/9,107

109 limit 108 to english language

110 LETTER/

111 EDITORIAL/

112 NEWS/

113 exp HISTORICAL ARTICLE/

114 ANECDOTES AS TOPIC/
COMMENT/
(letter or comment* or abstracts).ti.

or/110-116

RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.

117 not 118

ANIMALS/ not HUMANS/

ex ANIMALS, LABORATORY/

ex ANIMAL EXPERIMENTATION/

ex MODELS, ANIMAL/

ex RODENTIA/

(rat or rats or mouse or mice).ti.

or/119-125

109 not 126

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

# Searches
1 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
2 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergarten$ or boy? or girl?).ti,ab,jw.
3 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
4 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
5 or/1-4
6 (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
7 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
8 (diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
9 (diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
10 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
11 or/6-10
12 (diabet$ adj3 retinopath$).ti,ab.
13 retinopath$.ti,ab.
14 ((retina$ or fundus or ocul$ or eye?) adj3 (photograph$ or exam$)).ti,ab.
15 (op?thalmoscop$ or retinoscop$).ti,ab.
16 fundus oculi.ti,ab.
17 or/14-16
18 (undiagnos$ or estimate$).ti.
19 (screen$ or surveill$ or predict$ or detect$).ti.
20 or/18-19
21 (retinopath$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or index$ or stage$ or staging$)).ti,ab.
22 h?emorrhag$.ti,ab.
23 (microaneurysm? or micro aneurysm?).ti,ab.
24 exudate?.ti,ab.
25 (papill?edem$ or papillitis or choked dis??).ti,ab.
26 ((retina$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).ti,ab.
27 neovascular$.ti,ab.
28 (new adj2 vessel adj2 form$).ti,ab.
29 ((venous or vascular or microvascular or fibrovascular) adj3 (abnormal$ or malformed$ or loop$ or bead$ or reduplicat$ or duplicate$ or proliferat$)).ti,ab.
30 (IRMA or ((intraretinal or intra retinal) adj microvascular adj abnormal$)).ti,ab.
31 (macular adj (degenerat$ or dysfunction$)).ti,ab.
32 (maculopath$ or macular edema? or macular oedema? or CSME or CSMO).ti,ab.
33 (glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi$ or pressur$))).ti,ab.
34 (optic adj3 (isch?emi$ or neuropath$)).ti,ab.
35 cotton wool spot?.ti,ab.
36 ((retina$ or preretina$) adj3 (detach$ or tear$ or scar$ or thick$ or lesion? or manifest$ or fibrosis$)).ti,ab.
37 (scotoma? or blind spot? or floater? or musca volitante?).ti,ab.
38 ((reduc$ or impair$ or subnormal or sub-normal or sub-optimal or sub-optimal or diminish$ or low or blur$) adj3 (vision or visual or acuity)).ti,ab.
39 or/22-38
40 (prevalen$ or incidence? or model$ or risk$ or rate?).ti.
41 (age$ adj4 (factor$ or onset or diagno$ or treatment$)).ti,ab.
42 (disease adj3 (duration or onset$)).ti,ab.
43 or/41-42
44 12 and (17 or 20 or 21 or 40 or 43)
45 11 and 13 and (17 or 20 or 21 or 40 or 43)
46 11 and 39 and (40 or 43)
47 or/44-46
48 and/5,47

**Cochrane Central Register of Controlled Trials**

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

31 and/29-30
32 (retina$ or fundus or ocul$ or eye?) adj3 (photograph$ or exam$).ti,ab.
33 (opthalmoscop$ or retinoscop$).ti,ab.
34 fundus oculi.ti,ab.
35 or/26-28,31-34
36 MASS SCREENING/
37 VISION SCREENING/
38 exp POPULATION SURVEILLANCE/
39 (undiagnos$ or estimate$).ti.
40 (screen$ or surveill$ or predict$ or detect$).ti.
41 or/36-40
42 SEVERITY OF ILLNESS INDEX/
43 INTERNATIONAL CLASSIFICATION OF DISEASES/
44 CLASSIFICATION/
45 (retinopath$ adj3 (grad$ or sever$ or classif$ or index$ or indice$ or stage$ or staging)).ti,ab.
46 or/42-45
47 exp EYE HEMORRHAGE/
48 h?emorrhag$.ti,ab.
49 exp ANEURYSM/
50 (microaneurysm$ or micro aneurysm?).ti,ab.
51 "EXUDATES AND TRANSUDATES”/
52 exp EYE/
53 and/51-52
54 SUBRETINAL FLUID/
55 exudate?.ti,ab.
56 PAPILLEDEMA/
57 EDEMA/
58 exp EYE/
59 and/57-58
60 (papill?edem$ or papillitis or choked dis??).ti,ab.
61 (retina$ or optic dis?? or optic nerve?) adj (edema? or oedema?).ti,ab.
62 RETINAL NEOVASCULARIZATION/
63 NEOVASCULARIZATION, PATHOLOGIC/ or VASCULAR MALFORMATIONS/
64 exp EYE/ or RETINAL VESSELS/
65 and/63-64
66 exp RETINAL VESSELS/pa, pp [Pathology, Physiopathology]
67 neovascular$.ti,ab.
68 (new adj2 vessel adj2 form$).ti,ab.
69 (venous or vascular or microvascular or fibrovascular) adj3 (abnormal$ or malform$ or loop$ or bead$ or reduplicat$ or duplicat$ or proliferat$)).ti,ab.
70 (IRMA or ((intraretinal or intra retinal) adj microvascular adj abnormal$)).ti,ab.
71 *MACULAR DEGENERATION*/
72 MACULAR EDEMA/
73 (macular adj (degenerat$ or dysfunction$)).ti,ab.
74 (maculopath$ or macular edema? or macular oedema? or CSME or CSMO).ti,ab.
75 exp OCULAR HYPERTENSION/
76 (glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi$ or pressur$))).ti,ab.
77 OPTIC NEUROPATHY, ISCHEMIC/
78 (optic adj3 (isch?emi$ or neuropath$)).ti,ab.
79 cotton wool spot?.ti,ab.
80 RETINAL DETACHMENT/
81 (retina$ or preretina$) adj3 (detach$ or tear$ or scar$ or thick$ or lesion? or manifest$ or fibrosis$).ti,ab.
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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VISION DISORDERS/

SCOTOMA/

VISION, LOW/

(scotoma? or blind spot? or floater? or musca volitante?).ti,ab.

((reduc$ or impair$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish$ or low or blur$) adj3 (vision or visual or acuity)).ti,ab.

or/47-50,53-56,59-62,65-86

PREVALENCE/

INCIDENCE/

CROSS-SECTIONAL STUDIES/

exp MODELS, STATISTICAL/

LIFE TABLES/

exp RISK/

(prevalen$ or incidence? or model$ or risk$ or rate?).ti.

or/88-94

AGE FACTORS/

AGE DISTRIBUTION/

AGE OF ONSET/

TIME TO TREATMENT/

(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.

disease adj3 (duration or onset)).ti,ab.

or/96-101

DIABETIC RETINOPATHY/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]

22 and (35 or 41 or 46 or 95 or 102)

19 and 25 and (35 or 41 or 46 or 95 or 102)

19 and 87 and (95 or 102)

or/103-106

and/9,107

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

# Searches

1 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,kw,jw, rw.

2 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx,kw,jw, rw.

3 (infan$ or neonat$ or newborn$ or baby or babies).tw,tx,kw,jw, rw.

4 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,kw,jw, rw.

or/1-4

5 (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw,tx,kw.

6 (IDDM or T1D or T1D or DM1 or DMI).tw,tx.

7 (diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw,tx,kw.

9 (diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw,tx,kw.

10 (NIDDM or T2D or TII or DM2 or DMII).tw,tx.

11 or/6-10

12 (diabet$ adj3 retinopath$).tw,tx,kw.

13 RETINAL DISEASES.kw.

14 retinopath$.tw,tx,kw.

15 or/13-14

16 DIAGNOSTIC TECHNIQUES, OPHTHALMOLOGICAL.kw.

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Search strategies

((retina$ or fundus or ocul$ or eye?) adj3 (photograph$ or exam$)).tw,tx,kw.
(op?thalmoscop$ or retinoscop$).tw,tx,kw.
fundus oculi.tw,tx,kw.
or/16-19
SCREENING.kw.
SURVEILLANCE.kw.
(undiagnos$ or estimate$).ti.
(screen$ or surveill$ or predict$ or detect$).ti.
or/21-24
SEVERITY OF ILLNESS INDEX.kw.
DISEASE SEVERITY.kw.
DISEASE COURSE.kw.
STAGING.kw.
INTERNATIONAL CLASSIFICATION OF DISEASES.kw.
RATING SCALE.kw.
CLASSIFICATION.kw.
(retinopath$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging)).tw,tx,kw.
or/26-33
h?emorrhag$.tw,tx,kw.
ANEURYSM.kw.
(microaneurysm? or micro aneurysm?).tw,tx,kw.
SUBRETINAL FLUID.kw.
exudate?.tw,tx,kw.
(papill?edem$ or papillitis or choked dis??).tw,tx,kw.
((retina$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).tw,tx,kw.neovascular$.tw,tx,kw.
(new adj2 vessel adj2 form$).tw,tx.
(venous or vascular or microvascular or fibrovascular) adj3 (abnormal$ or malform$ or loop$ or bead$ or reduplicat$ or duplicat$ or proliferat$)).tw,tx,kw.
(IRMA or ((intraretinal or intra retinal) adj microvascular adj abnormal$)).tw,tx,kw.
(maculopath$ or macular edema? or macular oedema? or CSME or CSMO).tw,tx,kw.
glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi$ or pressur$))).tw,tx,kw.
optic adj3 (isch?emi$ or neuropath$)).tw,tx,kw.
cotton wool spot?.tw,tx.
((retina$ or preretina$) adj3 (detach$ or tear$ or scar$ or thick$ or lesion? or manifest$ or fibrosis$)).tw,tx,kw.
(VISION DISORDERS or VISUAL DISORDER).kw.
(scotoma? or blind spot? or floater? or musca volitante?).tw,tx,kw.
((reduc$ or impair$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish$ or low or blur$) adj3 (vision or visual or acuity)).tw,tx,kw.
or/35-54
PREVALENCE.kw.
INCIDENCE.kw.
CROSS-SECTIONAL STUDIES.kw.
MODELS, STATISTICAL.kw.
LIFE TABLE$.kw.
RISK.kw.
(prevalen$ or incidence? or model$ or risk$ or rate$).ti.
or/56-62
AGE.kw.
TIME TO TREATMENT.kw.
(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).tw,tx,kw.
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

Health Technology Assessment

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

Search strategies

or/36-40
SEVERITY OF ILLNESS INDEX/
INTERNATIONAL CLASSIFICATION OF DISEASES/
CLASSIFICATION/
(retinopath$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging)).tw.
or/42-45
exp EYE HEMORRHAGE/
h?emorrhag$.tw.
exp ANEURYSM/
(microaneurysm? or micro aneurysm?).tw.
"EXUDATES AND TRANSUDATES"
exp EYE/
and/51-52
SUBRETINAL FLUID/
exudate?.tw.
PAPILLEDEMA/
EDEMA/
exp EYE/
and/57-58
(papill?edem$ or papillitis or choked dis??).tw.
((retina$ or optic dis?? or optic nerve?) adj (edema? or oedema??)).tw.
RETINAL NEOVASCULARIZATION/
NEOVASCULARIZATION, PATHOLOGIC/ or VASCULAR MALFORMATIONS/
exp EYE/ or RETINAL VESSELS/
and/63-64
exp RETINAL VESSELS/pa, pp [Pathology, Physiopathology]
neovascular$.tw.
(new adj2 vessel adj2 form$).tw.
((venous or vascular or microvascular or fibrovascular) adj3 (abnormal$ or malform$ or loop$ or bead$ or reduplicat$ or duplicat$ or proliferat$)).tw.
(IRMA or ((intraretinal or intra retinal) adj microvascular adj abnormal$)).tw.
MACULAR DEGENERATION/
MACULAR EDEMA/
(macular adj (degenerat$ or dysfunction$)).tw.
(maculopath$ or macular edema? or macular oedema? or CSME or CSMO).tw.
exp OCULAR HYPERTENSION/
(glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi$ or pressur$))).tw.
OPTIC NEUROPATHY, ISCHEMIC/
(optic adj3 (isch?emi$ or neuropath$)).tw.
cotton wool spot?.tw.
RETINAL DETACHMENT/
((retina$ or preretina$) adj3 (detach$ or tear$ or scar$ or thick$ or lesion? or manifest$ or fibrosis$)).tw.
VISION DISORDERS/
SCOTOMA/
VISION, LOW/
(scotoma? or blind spot? or floater? or musca volitante?).tw.
((reduc$ or impair$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish$ or low or blur$) adj3 (vision or visual or acuity$)).tw.
or/47-50,53-56,59-62,65-86
PREVALENCE/
INCIDENCE/
CROSS-SECTIONAL STUDIES/
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

Embase

# Searches
1 exp ADOLESCENT/
2 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3 exp CHILD/
4 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5 exp INFANT/
6 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
9 or/1-8
10 exp INSULIN DEPENDENT DIABETES MELLITUS/
11 (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12 (IDDM or T1D or T1D or DM1 or DMI).ti,ab.
13 or/10-12
14 exp NON INSULIN DEPENDENT DIABETES MELLITUS/
15 (diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or T2 or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
16 (diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
17 (NIDDM or T2D or TII or DM2 or DMII).ti,ab.
18 or/14-17
19 or/13,18
20 exp JUVENILE DIABETES MELLITUS/
21 exp DIABETIC RETINOPATHY/
22 (diabet$ adj3 retinopath$).ti,ab.
23 or/21-22
24 exp RETINOPATHY/
25 exp PROLIFERATIVE RETINOPATHY/
26 retinopath$.ti,ab.
27 or/24-26
28 exp EYE PHOTOGRAPHY/
exp RETINA EXAMINATION/
OPHTHALMOSCOPY/
RETINA/ or exp RETINA BLOOD VESSEL/
PHOTOGRAPHY/
and/31-32
exp OPHTHALMIC CAMERA/
((retina$ or fundus or ocul$ or eye?) adj3 (photograph$ or exam$)).ti,ab.
(op?thalmoscop$ or retinoscop$).ti,ab.
fundus oculi.ti,ab.
or/28-30,33-37
SCREENING/
MASS SCREENING/
SCREENING TEST/
RESCREENING/
exp DISEASE SURVEILLANCE/
(undiagnos$ or estimate$).ti.
(screen$ or surveill$ or predict$ or detect$).ti.
or/39-45
SEVERITY OF ILLNESS INDEX/
DISEASE SEVERITY/
STAGING/
ex INTERNATIONAL CLASSIFICATION OF DISEASES/
RATING SCALE/
CLASSIFICATION/
DISEASE CLASSIFICATION/
(retinopath$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging)).ti,ab.
or/47-54
exp INTRAOCULAR HEMORRHAGE/
h?emorrhag$.ti,ab.
MICROANEURYSM/
(microaneurysm? or micro aneurysm?).ti,ab.
RETINA EXUDATE/
SUBRETINAL FLUID/
exudate?.ti,ab.
PAPILLEDEMA/
RETINAL EDEMA/
((papill$edem$ or papillitis or choked dis??)).ti,ab.
((retina$ or optic dis?? or optic nerve?) adj (edema? or oedema?)).ti,ab.
RETINA NEOVASCULARIZATION/
"NEOVASCULARIZATION (PATHOLOGY)/"
RETINA/ or exp RETINA BLOOD VESSEL/
and/68-69
neovascular$.ti,ab.
(new adj2 vessel adj2 form$).ti,ab.
((venous or vascular or microvascular or fibrovascular) adj3 (abnormal$ or malformed$ or loop$ or bead$ or reduplicat$ or duplicat$ or proliferat$)).ti,ab.
(IRMA or ((intraretinal or intra retinal) adj microvascular adj abnormal$)).ti,ab.
RETINA DEGENERATION/
RETINA MACULA DEGENERATION/
RETINA MACULOPATHY/
exp MACULAR EDEMA/
(macular adj (degenerat$ or dysfunction$)).ti,ab.
(maculopath$ or macular edema? or macular oedema? or CSME or CSMO).ti,ab.
exp GLAUCOMA/
(glaucoma? or ((ocular or intraocular or eye) adj3 (hypertensi$ or pressur$))).ti,ab.

exp ISCHEMIC OPTIC NEUROPATHY/
(optic adj3 (isch?emi$ or neuropath$)).ti,ab.

retina? or preretina? adj3 (detach$ or tear$ or scar$ or thick$ or lesion? or manifest$ or fibrosis$)).ti,ab.

VISUAL DISORDER/
VISUAL IMPAIRMENT/
SCOTOMA/
VITREOUS FLOATERS/
(scotoma? or blind spot? or floater? or musca volitante?).ti,ab.

((reduc$ or impair$ or subnormal or sub-normal or suboptimal or sub-optimal or diminish$ or low or blur$) adj3 (vision or visual or acuity)).ti,ab.

or/56-67,70-94
PREVALENCE/
INCIDENCE/
STATISTICAL MODEL/
LIFE TABLE/
exp RISK/
(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
or/96-101
AGE/
AGE DISTRIBUTION/
ONSET AGE/
DISEASE DURATION/
TIME TO TREATMENT/
(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
(disease adj3 (duration or onset)).ti,ab.
or/103-109
DIABETIC RETINOPATHY/di, ep, pc [Diagnosis, Epidemiology, Prevention]
23 and (38 or 46 or 55 or 102 or 110)
19 and 27 and (38 or 46 or 55 or 102 or 110)
19 and 95 and (102 or 110)
or/111-114
and/9,115
20 and 23 and (38 or 46 or 55 or 102 or 110)
20 and 27 and (38 or 46 or 55 or 102 or 110)
20 and 95 and (102 or 110)
or/116-119
limit 120 to english language
conference abstract.pt.
letter.pt. or LETTER/
ote.pt.
editorial.pt.
(letter or comment* or abstracts).ti.
or/122-126
RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
127 not 128
ANIMAL/ not HUMAN/
NONHUMAN/
F.17 Type 1 and type 2 diabetes – nephropathy

Review questions:

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

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

Ovid MEDLINE(R)

# Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3 exp CHILD/
4 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 1/
11 (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).ti,ab.
12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
13 or/10-12
14 exp DIABETES MELLITUS, TYPE 2/
15 (diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or T1 or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
16 (diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
17 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18 or/14-17
19 or/13,18
20 DIABETIC NEPHROPATHIES/
21 nephropath$.ti,ab.
22 glomerulosclerosis.ti,ab.
23 (Kimmelstie?l Wilson adj (syndrome? or disease?)).ti,ab.
24 ALBUMINURIA/
25 PROTEINURIA/
26 SERUM ALBUMIN/
27 CREATININE/ur, [Blood, Urine]
28 (albuminuri$ or microalbuminuri$ or proteinuri$).ti,ab.
29 ((albumin$ or creatinine$) adj3 (serum or sera or blood or urin$ or ratio or concentration?)).ti,ab.
exp RENAL INSUFFICIENCY, CHRONIC/
(kidney? or renal) adj3 (fail$ or insufficien$ or disease?).ti,ab.
or/20-31
SEVERITY OF ILLNESS INDEX/
DISEASE PROGRESSION/
INTERNATIONAL CLASSIFICATION OF DISEASES/
CLASSIFICATION/
or/33-36
or/20-28
and/37-38
((nephropath$ or microalbuminuria or proteinuria) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or progress$ or degree$)).ti,ab.
or/39-40
MASS SCREENING/
exp POPULATION SURVEILLANCE/
undiagnos$ or estimate$.ti.
(screen$ or surveill$ or predict$ or detect$).ti.
or/42-45
PREVALENCE/
INCIDENCE/
CROSS-SECTIONAL STUDIES/
exp MODELS, STATISTICAL/
LIFE TABLES/
exp RISK/
(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
or/47-53
AGE FACTORS/
AGE DISTRIBUTION/
AGE OF ONSET/
TIME TO TREATMENT/
(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
or/55-60
ALBUMINURIA/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
32 and (46 or 54 or 61)
or/41,62-63
and/19,64
DIABETIC NEPHROPATHIES/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
or/65
and/9,67
limit 68 to english language
LETTER/
EDITORIAL/
NEWS/
exp HISTORICAL ARTICLE/
ANECDOTES AS TOPIC/
COMMENT/
(letter or comment* or abstracts).ti.
or/70-76
RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
77 not 78
ANIMALS/ not HUMANS/
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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

Cochrane Central Register of Controlled Trials

# Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
3 exp CHILD/
4 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

Search strategies

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

# Searches
1 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,kw,jw,rm.
2 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,tx,kw,jw,rm.
3 (infan$ or neonat$ or newborn$ or baby or babies).tw,tx,kw,jw,rm.
4 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,kw,jw,rm.
5 or/1-4
6 (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or TI or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or auto?immun$)).tw,tx,kw.
7 (IDDM or T1D or TID or DM1 or DMI).tw,tx.
8 (diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw,tx,kw.
9 (diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw,tx,kw.
10 (NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
11 or/6-10
12 nephropath$.tw,tx,kw.
13 glomerulosclerosis.tw,tx.
14 (Kimmelstiel adj (syndrome? or disease?)).tw,tx.
15 (albuminuri$ or microalbuminuri$ or proteinuri$).tw,tx,kw.
16 ((albumin$ or creatinine$) adj3 (serum or sera or blood or urin$ or ratio or concentration?)).tw,tx,kw.
17 ((kidney? or renal) adj3 (fail$ or insufficien$ or disease?)).tw,tx,kw.
18 or/12-17
19 SEVERITY OF ILLNESS INDEX.kw.
20 (DISEASE PROGRESSION or DISEASE COURSE).kw.
21 INTERNATIONAL CLASSIFICATION OF DISEASES.kw.
22 RATING SCALE.kw.
23 CLASSIFICATION.kw.
24 or/19-23
25 or/12-15
26 and/24-25
27 ((nephropath$ or microalbuminuria or proteinuria) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or progress$ or degree$)).tw,tx.
28 or/26-27
29 (SCREENING or RESCREENING).kw.
30 SURVEILLANCE.kw.
31 (undiagnos$ or estimate$).ti.
32 (screen$ or surveill$ or predict$ or detect$).ti.
33 or/29-32
34 PREVALENCE.kw.
35 INCIDENCE.kw.
36 (MODELS, STATISTICAL or STATISTICAL MODEL).kw.
37 LIFE TABLE?.kw.
38 RISK.kw.
39 (prevalen$ or incidence? or model$ or risk$ or rate?).ti.
40 or/34-39
41 AGE.kw.
42 TIME TO TREATMENT.kw.
43 (age$ adj4 (factor$ or onset or diagnos$ or treatment$)).tw,tx,kw.
44 (disease adj3 (duration or onset)).tw,tx,kw.
45 or/41-44
46 18 and (33 or 40 or 45)
47 or/28,46
48 and/5,11,47

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

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

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

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Search strategies

8 (pediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab.jx,ec.
9 or/1-8
10 INSULIN DEPENDENT DIABETES MELLITUS/
11 (diabet$ adj5 ("type one" or "type 1" or "type I" or T1 or T1 or insulin depend$ or juvenile or child$ or earl$ or labile or brittle or sudden onset or auto immun$ or autoimmun$)).ti,ab.
12 (IDDM or T1D or TID or DM1 or DMI).ti,ab.
13 or/10-12
14 NON INSULIN DEPENDENT DIABETES MELLITUS/
15 (diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
16 (diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
17 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
18 or/14-17
19 or/13,18
20 and/9,19
21 JUVENILE DIABETES MELLITUS/
22 or/20-21
23 DIABETIC NEPHROPATHY/
24 nephropath$.ti,ab.
25 glomerulosclerosis.ti,ab.
26 (Kimmelstie?l Wilson adj (syndrome? or disease?)).ti,ab.
27 exp ALBUMINURIA/
28 PROTEINURIA/
29 PROTEIN URINE LEVEL/
30 SERUM ALBUMIN/
31 ALBUMIN BLOOD LEVEL/
32 CREATININE URINE LEVEL/
33 CREATININE BLOOD LEVEL/
34 (albuminuri$ or microalbuminuri$ or proteinuri$).ti,ab.
35 ((albumin$ or creatinine$) adj3 (serum or sera or blood or urin$ or ratio or concentration?)).ti,ab.
36 KIDNEY DISEASE/
37 KIDNEY FAILURE/
38 CHRONIC KIDNEY FAILURE/
39 ((kidney? or renal) adj3 (fail$ or insufficien$ or disease?)).ti,ab.
40 or/23-39
41 SEVERITY OF ILLNESS INDEX/
42 DISEASE SEVERITY/
43 DISEASE COURSE/
44 STAGING/
45 exp INTERNATIONAL CLASSIFICATION OF DISEASES/
46 RATING SCALE/
47 CLASSIFICATION/
48 DISEASE CLASSIFICATION/
49 or/41-48
50 or/23-34
51 and/49-50
52 ((nephropath$ or microalbuminuria or proteinuria) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or progress$ or degree$)).ti,ab.
53 or/51-52
54 SCREENING/
55 MASS SCREENING/
56 SCREENING TEST/
RESCREENING/
exp DISEASE SURVEILLANCE/
(undiagnos$ or estimate$).ti.
(screen$ or surveill$ or predict$ or detect$).ti.
or/54-60
PREVALENCE/
INCIDENCE/
STATISTICAL MODEL/
LIFE TABLE/
exp RISK/
(prevalen$ or incidence? or model$ or risk$ or rate?).ti.
or/62-67
AGE/
AGE DISTRIBUTION/
ONSET AGE/
DISEASE DURATION/
TIME TO TREATMENT/
(age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
(disease adj3 (duration or onset)).ti,ab.
or/69-75
MICROALBUMINURIA/di, ep, pc [Diagnosis, Epidemiology, Prevention] 40
and (61 or 68 or 76)
or/53,77-
and/22,79
DIABETIC NEPHROPATHY/di, ep, pc [Diagnosis, Epidemiology, Prevention] 80
and/9,81
or/80,82
limit 83 to english language
conference abstract.pt.
letter.pt. or LETTER/
ote.pt.
editorial.pt.
(letter or comment* or abstracts).ti.
or/85-89
RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
or/85-89
ANIMAL/ not HUMAN/
NONHUMAN/
exp ANIMAL EXPERIMENT/
exp EXPERIMENTAL ANIMAL/
ANIMAL MODEL/
exp RODENT/
(rat or rats or mouse or mice).ti.
or/92-99
84 not 100
F.18  **Type 2 diabetes – education**

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

**Database(s): Ovid MEDLINE(R)**

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

43 ADOLESCENT/ or MINORS/
(adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jw.
45 exp CHILD/
46 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
47 exp INFANT/
48 (infan$ or neonat$ or newbor$ or baby or babies).ti,ab,jw.
49 exp PEDIATRICS/ or exp PUBERTY/
50 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
52 or/43-50
53 exp DIABETES MELLITUS, TYPE 2/
55 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
56 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
58 or/52-55
59 PATIENT EDUCATION AS TOPIC/
60 PROBLEM SOLVING/
68 ed.fs.
69 ((educat$ or training) adj6 (intervention$ or programme or programmes)).ti,ab.
70 (problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
72 ((patient? or parent? or parental or child$ or adolescent$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
73 ((patient? or parent? or parental or child$ or adolescent$ or young or youth? or family$ or families) adj3 information).ti,ab.
74 ((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
75 ((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
76 ((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
77 ((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
79 or/57-67
80 and/51,56,68
81 limit 69 to english language
82 LETTER/
83 EDITORIAL/
84 NEWS/
85 exp HISTORICAL ARTICLE/
86 ANECDOTES AS TOPIC/
87 COMMENT/
88 CASE REPORT/
89 (letter or comment* or abstracts).ti.
90 or/71-78
91 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
92 not 80
93 ANIMALS/ not HUMANS/
95 exp ANIMALS, LABORATORY/
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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

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

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

Search strategies

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((self-help or "self help" or self-care or "self care" or self-regulate$ or "self regulate$" or self-monitor$ or "self monitor$" or self-manage$ or "self manage$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).tw.

((diabetes$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educate$ or train$ or teach$ or knowledge or aware$ or skill$ or advise$ or instruct$ or learn$ or program? or programme or programmes)).tw.

((diabetes$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).tw.

or/15-25

and/9,14,26

Embase

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

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exp PEDIATRICS/ or exp PUBERTY/
(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
/or/34-41
NON INSULIN DEPENDENT DIABETES MELLITUS/
(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
/or/43-46
JUVENILE DIABETES MELLITUS/
and/42,47
or/48-49
PATIENT EDUCATION/
DIABETES EDUCATION/
DIABETES EDUCATOR/
EDUCATION PROGRAM/
PROBLEM SOLVING/
((educat$ or training) adj6 (intervention$ or program? or programme or programmes)).ti,ab.
(problem-solving or "problem solving" or problem-based or "problem based").ti,ab.
((patient? or parent? or parental or child$ or adolescent$ or young or youth? or family$ or families) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
((patient? or parent? or parental or child$ or adolescent$ or young or youth? or family$ or families) adj3 information).ti,ab.
((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat$" or self-monitor$ or "self monitor$" or self-manag$ or "self manag$" or self-efficacy or "self efficacy" or cope or coping) adj3 information).ti,ab.
((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab.
((diabet$ or insulin$ or glyc?emi$ or hypoglyc?emi$ or "blood glucose" or "blood sugar") adj3 information).ti,ab.
/or/51-63
and/50,64
limit 65 to english language
conference abstract.pt.
letter.pt. or LETTER/
note.pt.
editorial.pt.
CASE REPORT/ or CASE STUDY/
(letter or comment* or abstracts).ti.
/or/67-72
RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
73 not 74
ANIMAL/ not HUMAN/
NONHUMAN/
exp ANIMAL EXPERIMENT/
exp EXPERIMENTAL ANIMAL/
ANIMAL MODEL/
exp RODENT/
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

PsycINFO

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

35 ((diabet$ or insulin$ or glycemi$ or "blood glucose" or "blood sugar") adj6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program? or programme or programmes)).ti,ab,id.

36 ((diabet$ or insulin$ or glycemi$ or "blood glucose" or "blood sugar") adj3 information).ti,ab,id.

37 or/25-36

38 and/18,24,37

39 and/11,38

40 limit 39 to english language

CINAHL with Full Text
# Query Limiters/Expanders
S36 S6 AND S34 Limiters - English Language; Exclude MEDLINE records
Search modes - Boolean/Phrase
S35 S6 AND S34 Search modes - Boolean/Phrase
S34 S21 AND S33 Search modes - Boolean/Phrase
S33 S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 Search modes - Boolean/Phrase

S32 TI ((diabet$ or insulin$ or glycemi$ or "blood glucose" or "blood sugar") N3 information) OR AB ((diabet$ or insulin$ or glycemi$ or "blood glucose" or "blood sugar") N3 information) Search modes - Boolean/Phrase

S31 TI ((diabet$ or insulin$ or glycemi$ or "blood glucose" or "blood sugar") N6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program# or programme or programmes)) OR AB ((diabet$ or insulin$ or glycemi$ or "blood glucose" or "blood sugar") N6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program# or programme or programmes)) Search modes - Boolean/Phrase

S30 TI ((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat"$ or self-monitor$ or "self monitor"$ or self-manag$ or "self manag"$ or self-efficacy or "self efficacy" or cope or coping) N3 information) OR AB ((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat"$ or self-monitor$ or "self monitor"$ or self-manag$ or "self manag"$ or self-efficacy or "self efficacy" or cope or coping) N3 information) Search modes - Boolean/Phrase

S29 TI ((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat"$ or self-monitor$ or "self monitor"$ or self-manag$ or "self manag"$ or self-efficacy or "self efficacy" or cope or coping) N6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program# or programme or programmes)) OR AB ((self-help or "self help" or self-care or "self care" or self-regulat$ or "self regulat"$ or self-monitor$ or "self monitor"$ or self-manag$ or "self manag"$ or self-efficacy or "self efficacy" or cope or coping) N6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program# or programme or programmes)) Search modes - Boolean/Phrase

S28 TI ((patient$ or parent$ or parental or child* or adolescent$ or young or youth$ or family* or families) N3 information) OR AB ((patient$ or parent$ or parental or child* or adolescent$ or young or youth$ or family* or families) N3 information) Search modes - Boolean/Phrase

S27 TI ((patient$ or parent$ or parental or child* or adolescent$ or young or youth$ or family* or families) N6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program# or programme or programmes)) OR AB ((patient$ or parent$ or parental or child* or adolescent$ or young or youth$ or family* or families) N6 (educat$ or train$ or teach$ or knowledge or aware$ or skill$ or advi?e or instruct$ or learn$ or program# or programme or programmes)) Search modes - Boolean/Phrase

S26 TI (problem-solving or "problem solving" or problem-based or "problem based") OR AB (problem-solving or "problem solving" or problem-based or "problem based") Search modes - Boolean/Phrase

S25 TI (educat$ or training) N6 (intervention$ or program# or programme or programmes)) OR AB (educat$ or training) N6 (intervention$ or program# or programme or programmes)) Search modes - Boolean/Phrase

S24 MW "ED" Search modes - Boolean/Phrase

S23 (MH "Problem Solving+") Search modes - Boolean/Phrase
S22 (MH "Patient Education") OR (MH "Diabetes Education") Search modes - Boolean/Phrase
S21 S12 AND S20 Search modes - Boolean/Phrase
S20 S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 Search modes - Boolean/Phrase
S19 AB (NIDDM or T2D or TIID or DM2 or DMII) Search modes - Boolean/Phrase
S18 TI (NIDDM or T2D or TIID or DM2 or DMII) Search modes - Boolean/Phrase
S17 AB (diabet* adj5 non insulin or non-insulin) Search modes - Boolean/Phrase
S16 TI (diabet* adj5 non insulin or non-insulin) Search modes - Boolean/Phrase
S15 AB (diabet* N5 "type two" or "type 2" or "type II" or T2 or slow or late or stable or ketosis resistant or keto resist* or non keto* or non-keto*) Search modes - Boolean/Phrase
S14 TI (diabet* N5 "type two" or "type 2" or "type II" or T2 or slow or late or stable or ketosis resistant or keto resist* or non keto* or non-keto*) Search modes - Boolean/Phrase
S13 (MH "Diabetes Mellitus, Type 2") Search modes - Boolean/Phrase
S12 S7 OR S8 OR S9 OR S10 OR S11 Search modes - Boolean/Phrase
S11 TI (pediatric* or paediatric* or pubert* or prepubert* or pubescen* or prepubescen*) OR AB (pediatric* or paediatric* or pubert* or prepubert* or pubescen* or prepubescen*) OR SO (pediatric* or paediatric* or pubert* or prepubert* or pubescen* or prepubescen*) OR SO (pediatric* or paediatric* or pubert* or prepubert* or pubescen* or prepubescen*) Search modes - Boolean/Phrase
S10 TI (infan* or neonat* or newborn* or baby or babies) OR AB (infan* or neonat* or newborn* or baby or babies) OR SO (infan* or neonat* or newborn* or baby or babies) Search modes - Boolean/Phrase
S9 TI (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR AB (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) OR SO (child* or schoolchild* or "school age" or "school aged" or preschool* or toddler* or kid# or kindergar* or boy# or girl#) Search modes - Boolean/Phrase
S8 TI (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR AB (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) OR SO (adolescen* or teen* or youth* or young or juvenile# or minors or highschool*) Search modes - Boolean/Phrase
S7 (MH "Infant, Newborn") OR (MH "Infant") OR (MH "Child, Preschool") OR (MH "Child") OR (MH "Adolescence") Search modes - Boolean/Phrase
S6 S1 OR S2 OR S3 OR S4 OR S5 Search modes - Boolean/Phrase
S5 PT systematic review Search modes - Boolean/Phrase
S4 PT review Search modes - Boolean/Phrase
S3 TX meta-analysis OR "meta analysis" Search modes - Boolean/Phrase
S2 TX random* Search modes - Boolean/Phrase
S1 (MH "Treatment Outcomes") OR (MH "Experimental Studies") Search modes - Boolean/Phrase

F.19 Type 2 diabetes – behavioural interventions

Review questions:

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

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

Ovid MEDLINE(R)
Search strategies

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

Search strategies

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

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

Cochrane Central Register of Controlled Trials

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

Search strategies

<table>
<thead>
<tr>
<th>#</th>
<th>Search</th>
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<tbody>
<tr>
<td>19</td>
<td>PSYCHOTHERAPY, GROUP/</td>
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<tr>
<td>20</td>
<td>FAMILY THERAPY/</td>
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<td>21</td>
<td>(psychotherap$ or BFST or CBT).ti,ab.</td>
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<tr>
<td>22</td>
<td>((cogniti$ or psycho$) adj5 (intervention$ or treatment$ or therap$)).ti,ab.</td>
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<tr>
<td>23</td>
<td>((behavio?r$ or motivation$) adj5 (intervention$ or treatment$ or therap$ or chang$ or modif$)).ti,ab.</td>
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<tr>
<td>24</td>
<td>((family$ or families or parent?) adj5 (intervention$ or treatment$ or therap$ or team? or teamwork$ or team-work$)).ti,ab.</td>
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<tr>
<td>25</td>
<td>COUNSELING/</td>
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<td>26</td>
<td>MOTIVATIONAL INTERVIEWING/</td>
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<td>27</td>
<td>SOCIAL SUPPORT/</td>
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<td>SELF-HELP GROUPS/</td>
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<tr>
<td>30</td>
<td>(motivation$ or counsel?ing or mentor$).ti,ab.</td>
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<tr>
<td>31</td>
<td>((peer or social$ or self help or self-help) adj3 (group? or support?)).ti,ab.</td>
</tr>
<tr>
<td>32</td>
<td>or/16-31</td>
</tr>
<tr>
<td>33</td>
<td>and/15.32</td>
</tr>
</tbody>
</table>

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

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

Health Technology Assessment

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

### PubMed

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

### Embase

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

Search strategies

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

PsycINFO

# Searches
1 adolescens$.ag.
2 (adolescens$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,id,jw.
3 (child$ or school$ or preschool$).ag.
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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

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F.20 Type 2 diabetes – dietary advice

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

Ovid MEDLINE(R)
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

exp CHILD/
(child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.

exp INFANT/
(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.

exp PEDIATRICS/ or exp PUBERTY/
(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.

or/1-8

exp DIABETES MELLITUS, TYPE 2/
(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resi st$ or non keto$ or non?keto$)).ti,ab.

(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.

(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.

or/10-13

exp DIET THERAPY/
NUTRITION THERAPY/
dh.fs.
or/15-17

exp FOOD HABITS/
exp DIET/
Dietetics/
(diet$ or nutrition$ or food or feed$).ti,ab.
or/19-22

HEMOGLOBIN A, GLYCOSYLATED/
(h?emoglobin? adj3 (glyc$ or A1?)).ti,ab.

(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA lc or Hb A1c or Hb Alc).ti,ab.

"hemoglobin A1c protein, human".nm.

BLOOD GLUCOSE/
(blood or plasma) adj3 (glucose or sugar?).ti,ab.

(glyc?emi$ adj3 (control$ or parameter$ or status$)).ti,ab.

exp HYPERGLYCEMIA/
hyperglyc?emi$.ti,ab.

REMISSION INDUCTION/
remission?.ti,ab.

((revers$ or regress$) adj5 diabet$).ti,ab.
or/24-35

and/23,36

or/18,37

and/9,14,38

limit 39 to english language

LETTER/
EDITORIAL/
NEWS/
exp HISTORICAL ARTICLE/
ANECDOTES AS TOPIC/
COMMENT/
CASE REPORT/
(exp LETTER or comment* or abstracts).ti.
or/41-48

RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.

49 not 50

ANIMALS/ not HUMANS/
exp ANIMALS, LABORATORY/
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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

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

Cochrane Central Register of Controlled Trials

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

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

# Searches

5 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39

or/15-17  
exp FOOD HABITS/  
exp DIET/  
DIETETICS/  
(diet$ or nutrition$ or food or feed$).ti,ab.  
or/19-22  
HEMOGLOBIN A, GLYCOSYLATED/  
(h?emoglobin? adj3 (glyc$ or A1?!)).ti,ab.  
(glycoh?emoglobin? or HbA1c or HbAlc or HbA 1c or HbA lc or Hb A1c or Hb Alc).ti,ab.  
[hemoglobin A1c protein, human“].nm.]  
BLOOD GLUCOSE/  
(blood or plasma).ti,ab.  
(glyc?emi? adj3 (control$ or parameter$ or status$)).ti,ab.  
exp HYPERGLYCEMIA/  
hyperglyc?emi?.ti,ab.  
REMISSION INDUCTION/  
remission?.ti,ab.  
(revers$ or regress$) adj5 diabet$.ti,ab.  
or/24-35  
and/23,36  
or/18,37  
and/9,14,38

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

Search strategies

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Health Technology Assessment

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

Embase

# Searches
1 exp ADOLESCENT/
2 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
3 exp CHILD/
4 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5 exp INFANT/
6 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7 exp PEDIATRICS/ or exp PUBERTY/
(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
or/1-8
NON INSULIN DEPENDENT DIABETES MELLITUS/
(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
(NIDDM or T2D or TIIID or DM2 or DMII).ti,ab.
or/10-13
JUVENILE DIABETES MELLITUS/
and/9,14
or/15-16
exp DIET THERAPY/
exp FEEDING BEHAVIOR/
exp DIET/ or DIETARY COMPLIANCE/
DIETETICS/
(diet$ or nutrition$ or food or feed$).ti,ab.
or/19-22
HEMOGLOBIN A1C/
GLYCOSYLATED HEMOGLOBIN/
(h?emoglobin? adj3 (glyc$ or A1$)).ti,ab.
(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA lc or Hb A1c or Hb Alc).ti,ab.
GLUCOSE BLOOD LEVEL/
((blood or plasma) adj3 (glucose or sugar$)).ti,ab.
GLYCEMIC CONTROL/
(glyc?emi$ adj3 (control$ or parameter$ or status$)).ti,ab.
HYPERGLYCEMIA/
hyperglyc?emi$.ti,ab.
REMISSION/ or DISEASE CLEARANCE/
remission?.ti,ab.
((revers$ or regress$) adj5 diabet$).ti,ab.
or/24-36
and/23,37
or/18,38
and/17,39
limit 40 to english language
conference abstract.pt.
letter.pt. or LETTER/
ote.pt.
editorial.pt.
CASE REPORT/ or CASE STUDY/
(letter or comment* or abstracts).ti.
or/42-47
RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
48 not 49
ANIMAL/ not HUMAN/
NONHUMAN/ exp ANIMAL EXPERIMENT/
exp EXPERIMENTAL ANIMAL/
ANIMAL MODEL/
exp RODENT/
(rat or rats or mouse or mice).ti.
or/50-57
41 not 58
Type 2 diabetes – weight loss

Review question: Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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

Cochrane Central Register of Controlled Trials

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

Search strategies

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

# Searches
1. (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,tx,kw.
2. (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kinder$ or boy? or girl?).tw,tx,kw.
3. (infan$ or neonat$ or newborn$ or baby or babies).tw,tx,kw.
4. (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,tx,kw.
5. or/1-4
6. (diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw,tx,kw.
7. (diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw,tx,kw.
8. (NIDDM or T2D or TIID or DM2 or DMII).tw,tx.
9. or/6-8
10. (obes$ or overweight or over weight).tw,tx,kw.
11. ((weight or BMI or body mass index) adj3 (gain$ or los# or lose? or losing or chang$ or r#se? or rising or raise? or f#ll$ or drop$ or up or down or reduc$ or increas$ or control$ or maintain$ or maintenance)).tw,tx,kw.
12. (portion? or serv?).tw,tx,kw.
13. or/11-12
15. (glycoh?emoglobin? or HbA1c or HbAlc or HbA 1c or HbA lc or Hb A1c or Hb Alc).tw,tx.
16. ((blood or plasma) adj3 (glucose or sugar?)).tw,tx,kw.
17. (glyc$emi$ adj3 (control$ or parameter$ or status$)).tw,tx,kw.
18. hyperglyc$emi$.tw,tx,kw.
19. hypoglyc$emi$.tw,tx,kw.
20. remission?.tw,tx,kw.
21. or/15-17
22. exp BODY WEIGHT CHANGES/
23. ((weight or BMI or body mass index) adj3 (gain$ or los# or lose? or losing or chang$ or r#se? or rising or raise? or f#ll$ or drop$ or up or down or reduc$ or increas$ or control$ or maintain$ or maintenance)).ti,ab.
24. or/19-23
25. SERVING SIZE/
26. PORTION SIZE/
27. ((serving? or portion?) adj3 (size? or sizing)).ti,ab.
28. or/25-29
29. HEMOGLOBIN A, GLYCOSYLATED/
30. (h?emoglobin? adj3 (glyc$ or A1?)).ti,ab.
31. (glycoh?emoglobin? or HbA1c or HbAlc or HbA 1c or HbA lc or Hb A1c or Hb Alc).ti,ab.
32. BLOOD GLUCOSE/
33. ((blood or plasma) adj3 (glucose or sugar?)).ti,ab.
34. exp HYPERGLYCEMIA/
35. hyperglyc$emi$.ti,ab.
36. exp HYPOGLYCEMIA/
37. hypoglyc$emi$.ti,ab.
38. remission?.ti,ab.
39. and/9,14,18,24,38

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Health Technology Assessment

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

Embase 1974 to 2014 April 03

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

exp INFANT/

(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.

exp PEDIATRICS/ or exp PUBERTY/

(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.

or/1-8

NON INSULIN DEPENDENT DIABETES MELLITUS/

(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.

(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.

(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.

or/10-13

JUVENILE DIABETES MELLITUS/

and/9,14

or/15-16

exp OBESITY/

(obes$ or overweight or over weight).ti,ab.

or/18-19

WEIGHT CHANGE/ or WEIGHT CONTROL/ or WEIGHT GAIN/ or WEIGHT REDUCTION/

((weight or BMI or body mass index) adj3 (gain$ or los# or lose? or losing or chang$ or r#se? or rising or raise? or r#l or drop$ or up or down or reduc$ or increas$ or control$ or maintain$ or maintenance)).ti,ab.

((serving? or portion?) adj3 (size? or sizing)).ti,ab.

or/21-23

HEMOGLOBIN A1C/

GLYCOSYLATED HEMOGLOBIN/

(h?emoglobin? adj3 (glyc$ or A1?)).ti,ab.

(glycoh?emoglobin? or HbA1c or HbAIc or HbA 1c or HbA lc or Hb A1c or Hb Alc).ti,ab.

GLUCOSE BLOOD LEVEL/

((blood or plasma) adj3 (glucose or sugar?)).ti,ab.

GLYCEMIC CONTROL/

(glyc?emi$ adj3 (control$ or parameter$ or status$)).ti,ab.

HYPERGLYCEMIA/

hyperglyc?emi$.ti,ab.

HYPOGLYCEMIA/

hypoglyc?emi$.ti,ab.

REMISSION/

remission?.ti,ab.

((revers$ or regress$) adj5 diabet$).ti,ab.

or/25-39

and/17,20,24,40

limit 41 to english language

conference abstract.pt.

letter.pt. or LETTER/

note.pt.

editorial.pt.

(letter or comment* or abstracts).ti.

or/43-47

RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.

48 not 49

ANIMAL/ not HUMAN/

NONHUMAN/
Type 2 diabetes – metformin

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

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

Search strategies

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Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations
# Searches
1 (adolescent or teen or youth or young or juvenile or minors or highschool).ti,ab.
2 (child or schoolchild or "school age" or "school aged" or preschool or toddler or kid or kindergar or boy or girl).ti,ab.
3 (infant or neonat or newborn or baby or babies).ti,ab.
4 exp PEDIATRICS/ or exp PUBERTY/.
5 exp DIAGETES MELLITUS, TYPE 2/.
6 (diabet adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur or adult or slow or late or stable or ketosis resistant or keto resist or keto?resist or non keto or non?keto)).ti,ab.
7 (diabet adj5 (non insulin or non?insulin) adj2 depend$)).ti,ab.
8 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
9 or/49-52
10 METFORMIN/.
11 (metformin or glucophage or glucient or metsol or bolamyn or metabet).ti,ab.
12 and/48,53,56
13 and/39,57
14 limit 58 to english language
15 LETTER/.
16 EDITORIAL/.
17 NEWS/.
18 exp HISTORICAL ARTICLE/.
19 ANECDOTES AS TOPIC/.
20 COMMENT/.
21 CASE REPORT/.
22 (letter or comment* or abstracts).ti.
23 or/60-67
24 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
25 68 not 69
26 ANIMALS/ not HUMANS/.
27 exp ANIMALS, LABORATORY/.
28 exp ANIMAL EXPERIMENTATION/.
29 exp MODELS, ANIMAL/.
30 exp RODENTIA/.
31 (rat or rats or mouse or mice).ti.
32 or/70-76
33 78 not 77

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

Search strategies

Cochrane Central Register of Controlled Trials

Searches

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

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

Searches

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

Health Technology Assessment

Searches
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

Embase

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

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360
Search strategies

(30) (book or conference paper or editorial or letter or note or proceeding or short survey).pt.
(31) 13 not 30
(32) 29 not 30
(33) or/31-32
(34) exp ADOLESCENT/
(35) (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
(36) exp INFANT/
(37) (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or
kindergar$ or boy? or girl??.ti,ab,jx.
(38) exp NEWBORN/
(39) (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
(40) exp PEDIATRICS/ or exp PUBERTY/
(41) (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
(42) or/34-41
(43) NON INSULIN DEPENDENT DIABETES MELLITUS/
(44) (diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late
or stable or ketosis resistant or keto resist$ or keto$resist$ or non keto$ or non?keto$)).ti,ab.
(45) (diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
(46) (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
(47) or/43-46
(48) JUVENILE DIABETES MELLITUS/
(49) and/42,47
(50) or/48-49
(51) METFORMIN/
(52) (metformin or glucophage or glucient or metsol or bolamyn or metabet).ti,ab.
(53) or/51-52
(54) and/50,53
(55) limit 54 to english language
(56) conference abstract.pt.
(57) letter.pt. or LETTER/
(58) note.pt.
(59) editorial.pt.
(60) CASE REPORT/ or CASE STUDY/
(61) (letter or comment* or abstracts).ti.
(62) or/56-61
(63) RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
(64) 62 not 63
(65) ANIMAL/ not HUMAN/
(66) NONHUMAN/
(67) exp ANIMAL EXPERIMENT/
(68) exp EXPERIMENTAL ANIMAL/
(69) ANIMAL MODEL/
(70) exp RODENT/
(71) (rat or rats or mouse or mice).ti.
(72) or/64-71
(73) 55 not 72
(74) and/33,73
F.23 Type 2 diabetes – HbA1c targets

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

Ovid MEDLINE(R)

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

exp INFANT/

(infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.

exp PEDIATRICS/ or exp PUBERTY/

(p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.

or/41-48

exp DIABETES MELLITUS, TYPE 2/

(diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.

(diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.

(NIDDM or T2D or TIID or DM2 or DMII).ti,ab.

or/50-53

and/49,54

HEMOGLOBIN A, GLYCOSYLATED/


(glycated adj3 h?emoglobin?).ti,ab.

(glycoh?emoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).ti,ab.

"hemoglobin A1c protein, human".nm.

or/56-60

and/55,61

REFERENCE STANDARDS/ or REFERENCE VALUES/

((reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?)).ti,ab.

or/63-64

((F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$)).ti,ab.

((normogly?emi$ or euglyc?emi$ or glyc?emi$) adj3 (value$ or target$ or rang$ or level$ or threshold$)).ti,ab.

or/65-67

and/62,68

and/55,69

and/55,69

LETTER/

EDITORIAL/

NEWS/

exp HISTORICAL ARTICLE/

ANECDOTES AS TOPIC/

COMMENT/

CASE REPORT/

(letter or comment* or abstracts).ti.

or/71-78

RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.

79 not 80

ANIMALS/ not HUMANS/

exp ANIMALS, LABORATORY/

exp ANIMAL EXPERIMENTATION/

exp MODELS, ANIMAL/

exp RODENTIA/

(rat or rats or mouse or mice).ti.

or/81-87

79 not 88

limit 89 to english language
Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations

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

Cochrane Central Register of Controlled Trials

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

Search strategies

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

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

Health Technology Assessment

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

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

Embase

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

Search strategies

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26 (peto or dersimonian or "der simonian" or fixed effect).tw.
27 or/20-26
28 and/19,27
29 exp CASE CONTROL STUDY/
30 RETROSPECTIVE STUDY/
31 (case$ adj2 control$).tw.
32 COHORT ANALYSIS/
33 LONGITUDINAL STUDY/
34 FOLLOW UP/
35 PROSPECTIVE STUDY/
36 cohort$.tw.
37 or/29-36
38 or/13,18,28,37
39 (book or conference paper or editorial or letter or note or proceeding or short survey).pt.
40 38 not 39
41 COMPARATIVE STUDY/
42 (compar$ adj3 stud$).tw.
43 or/41-42
44 or/40,43
45 exp ADOLESCENT/
46 (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).ti,ab,jx.
47 exp CHILD/
48 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
49 exp INFANT/
50 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
51 exp PEDIATRICS/ or exp PUBERTY/
52 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx,ec.
53 or/45-52
54 NON INSULIN DEPENDENT DIABETES MELLITUS/
55 (diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or TII or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
56 (diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
57 (NIDDM or T2D or TIID or DM2 or DMII).ti,ab.
58 or/54-57
59 JUVENILE DIABETES MELLITUS/
60 and/53,58
61 or/59-60
62 HEMOGLOBIN A1c/
63 (glyco?hemoglobin? or HbA1c or HbAlc or Hb A1c or Hb A1c).ti,ab.
64 (h?emoglobin? adj3 glycosylat$).ti,ab.
65 (glycated adj3 h?emoglobin?).ti,ab.
66 or/62-65
67 and/61,66
68 STANDARD/
69 REFERENCE VALUE/
70 ((reference? or normal$ or standard?) adj3 (value? or target$ or rang$ or level$ or threshold?)).ti,ab.
71 or/68-70
72 ((F#G or BG) adj3 (value$ or target$ or rang$ or level$ or threshold$)).ti,ab.
73 ((normogly?emisi$ or euglyc?emisi$ or glyc?emisi$) adj3 (value$ or target$ or rang$ or level$ or threshold$)).ti,ab.
74 or/71-73
Diagnosis and management of type 1 diabetes in children and young people
Search strategies

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F.24 Type 2 diabetes – hypertension

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

Ovid MEDLINE(R)

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

Sea

Search strategies

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22 ((blood or systol$ or diastol$ or arterial) adj3 pressur$).ti,ab.
23 or/20-22
24 SEVERITY OF ILLNESS INDEX/
25 DISEASE PROGRESSION/
26 INTERNATIONAL CLASSIFICATION OF DISEASES/
27 CLASSIFICATION/
28 ((hypertens$ or prehypertens$) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).ti,ab.
29 or/24-28
30 MASS SCREENING/
31 exp POPULATION SURVEILLANCE/
32 (undiagnos$ or estimate$).ti.
33 (screen$ or surveill$ or predict$ or detect$).ti.
34 or/30-33
35 PREVALENCE/
36 INCIDENCE/
37 exp COHORT STUDIES/
38 CROSS-SECTIONAL STUDIES/
39 exp MODELS, STATISTICAL/
40 LIFE TABLES/
41 exp RISK/
42 (prevalen$ or incidence? or model$ or risk$ or rate?).ti.
43 or/35-42
44 AGE FACTORS/
45 AGE DISTRIBUTION/
46 AGE OF ONSET/
47 TIME TO TREATMENT/
48 (age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
49 (disease adj3 (duration or onset)).ti,ab.
50 or/44-49
51 19 and (23 or 29 or 34 or 43 or 50)
52 *HYPERTENSION/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
53 *PREHYPERTENSION/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
54 or/51-53
55 and/9,14,54
56 *DIABETIC ANGIOPATHIES/cl, di, ep, pc [Classification, Diagnosis, Epidemiology, Prevention & Control]
57 and/9,56
58 *DIABETES MELLITUS, TYPE 2/co, ep [Complications, Epidemiology]
59 *DIABETES COMPLICATIONS/ep [Epidemiology]
60 or/58-59
61 9 and (35 or 36) and 60
62 (diabet$ adj10 (characteristic? or feature? or presentation? or complication? or comorbidit$)).ti.
63 9 and 14 and (43 or 50) and 62
64 or/55,57,61,63
65 limit 64 to english language
66 LETTER/
67 EDITORIAL/
68 NEWS/
69 exp HISTORICAL ARTICLE/
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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

Cochrane Central Register of Controlled Trials

# Searches
1 ADOLESCENT/ or MINORS/
2 (adolescent or teen or youth or young or juvenile or minors or highschool).ti,ab,jw.
Diagnosis and management of type 1 diabetes in children and young people
Search strategies

3 exp CHILD/
4 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jw.
5 exp INFANT/
6 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jw.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?pediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jw.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 2/
11 (diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or T2I or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12 (diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13 (NIDDM or T2D or TIID or DM2 or DMI1).ti,ab.
14 or/10-13
15 HYPERTENSION/
16 PREHYPERTENSION/
17 (hypertens$ or prehypertens$).ti,ab.
18 ((high or elevat$ or increas$) adj3 blood pressur$).ti,ab.
19 or/15-18
20 BLOOD PRESSURE/
21 exp BLOOD PRESSURE DETERMINATION/
22 ((blood or systol$ or diastol$ or arterial) adj3 pressur$).ti,ab.
23 or/20-22
24 SEVERITY OF ILLNESS INDEX/
25 DISEASE PROGRESSION/
26 INTERNATIONAL CLASSIFICATION OF DISEASES/
27 CLASSIFICATION/
28 ((hypertens$ or prehypertens$) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).ti,ab.
29 or/24-28
30 MASS SCREENING/
31 exp POPULATION SURVEILLANCE/
32 (undiagnos$ or estimate$).ti.
33 (screen$ or surveill$ or predict$ or detect$).ti.
34 or/30-33
35 PREVALENCE/
36 INCIDENCE/
37 exp COHORT STUDIES/
38 CROSS-SECTIONAL STUDIES/
39 exp MODELS, STATISTICAL/
40 LIFE TABLES/
41 exp RISK/
42 (prevalen$ or incidence? or model$ or risk$ or rate?).ti.
43 or/35-42
44 AGE FACTORS/
45 AGE DISTRIBUTION/
46 AGE OF ONSET/
47 TIME TO TREATMENT/
48 (age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
49 (disease adj3 (duration or onset$)).ti,ab.
50 or/44-49
51 19 and (23 or 29 or 34 or 43 or 50)
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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

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

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

Search strategies

(13 or 21 or 25 or 31 or 36) and/5,9,37 and (13 or 21 or 25 or 31 or 36) and 39 or/38,40

Health Technology Assessment

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

Search strategies

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

Embase

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

16 JUVENILE DIABETES MELLITUS/
17 or/15-16
18 HYPERTENSION/
19 DIABETIC HYPERTENSION/
20 PREHYPERTENSION/
21 (hypertens$ or prehypertens$).ti,ab.
22 ((high or elevat$ or increas$) adj3 blood pressur$).ti,ab.
23 or/18-22
24 exp BLOOD PRESSURE/
25 exp BLOOD PRESSURE MEASUREMENT/
26 ((blood or systol$ or diastol$ or arterial) adj3 pressur$).ti,ab.
27 or/24-26
28 SEVERITY OF ILLNESS INDEX/
29 DISEASE SEVERITY/
30 DISEASE COURSE/
31 STAGING/
32 exp INTERNATIONAL CLASSIFICATION OF DISEASES/
33 RATING SCALE/
34 CLASSIFICATION/
35 DISEASE CLASSIFICATION/
36 ((hypertens$ or prehypertens$) adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).ti,ab.
37 or/28-36
38 SCREENING/
39 MASS SCREENING/
40 SCREENING TEST/
41 RESCREENING/
42 exp DISEASE SURVEILLANCE/
43 (undiagnos$ or estimate$).ti.
44 (screen$ or surveill$ or predict$ or detect$).ti.
45 or/38-44
46 PREVALENCE/
47 INCIDENCE/
48 CROSS-SECTIONAL STUDY/
49 LONGITUDINAL STUDY/
50 COHORT ANALYSIS/
51 STATISTICAL MODEL/
52 LIFE TABLE/
53 exp RISK/
54 (prevalen$ or incidence? or model$ or risk$ or rate?).ti.
55 or/46-54
56 AGE/
57 AGE DISTRIBUTION/
58 ONSET AGE/
59 DISEASE DURATION/
60 TIME TO TREATMENT/
61 (age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
62 (disease adj3 (duration or onset$)).ti,ab.
63 or/56-62
64 23 and (27 or 37 or 45 or 55 or 63)
65 *HYPERTENSION/di, ep, pc [Diagnosis, Epidemiology, Prevention]
66 *PREHYPERTENSION/di, ep, pc [Diagnosis, Epidemiology, Prevention]
67 or/64-66
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

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F.25 Type 2 diabetes – dyslipidaemia

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

Ovid MEDLINE(R)

# Searches
1 ADOLESCENT/ or MINORS/
2 (adolescen$ or teen$ or youth$ or young or juvenile? or min$ or highschool$).ti,ab,jx.
3 exp CHILD/
4 (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).ti,ab,jx.
5 exp INFANT/
6 (infan$ or neonat$ or newborn$ or baby or babies).ti,ab,jx.
7 exp PEDIATRICS/ or exp PUBERTY/
8 (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).ti,ab,jx.
9 or/1-8
10 exp DIABETES MELLITUS, TYPE 2/
11 (diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or T1 or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resis$ or keto?resist$ or non keto$ or non?keto$)).ti,ab.
12 (diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).ti,ab.
13 (NIDDM or T2D or T1ID or DM2 or DMII).ti,ab.
14 or/10-13
15 exp DYSLIPIDEMIAS/
Search strategies

16  (d#slip$ or hyp??lip$ or hyp??alphalip$ or hyp??betalip$ or hyp??cholester$ or hyp??triglycerid$ or hyp??triacy?glycerol$).ti,ab.
17  or/15-16
18  LIPIDS/bl [Blood]
19  or/15-16
20  LIPOPROTEINS/bl [Analysis, Blood]
21  CHOLESTEROL/an, bl [Analysis, Blood]
22  CHOLESTEROL, HDL/an, bl [Analysis, Blood]
23  CHOLESTEROL, LDL/an, bl [Analysis, Blood]
24  LIPIDS/bl [Blood]
25  or/18-30
26  PREVALENCE/
27  or/32-39
28  MASS SCREENING/
29  exp POPULATION SURVEILLANCE/
30  exp MODELS, STATISTICAL/
31  LIFE TABLES/
32  exp RISK/
33  PREVALENCE/
34  exp COHORT STUDIES/
35  CROSS-SECTIONAL STUDIES/
36  exp MODELS, STATISTICAL/
37  LIPIDS/bl [Blood]
38  or/18-30
39  and 9, 14, 61
40  and/9, 14, 61
41  and 9, 14, 31, 63

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

Search strategies

1. (adolescent or teen or youth or young or juvenile or minors or highschool$).ti,ab,jw.
2. (child or schoolchild or "school age" or "school aged" or preschool or toddler or kid or kindergarten or boy or girl$).ti,ab,jw.
3. (infant or neonatal or newborn or baby or babies).ti,ab,jw.
4. (pediatric or pubertal or prepubertal or pubescent or prepubescent).ti,ab,jw.
5. (dialysis or hystere$ or hypere$ or hyperalphalip$ or hyper$ or beta$ or hyper$ or triglyceride$ or hyper$ or triacylglycerol$).ti,ab.
6. (cholesterol or epicholesterol or lipoprotein or lipid$).ti,ab.
7. (alphalip$ or alpha lipoprotein or HDL cholesterol$).ti,ab.
8. (betalip$ or beta lipoprotein or LDL cholesterol$).ti,ab.
9. (triglyceride or triacylglycerol$).ti,ab.
10. ((HDL or LDL) adj3 cholesterol$ adj3 ratio$).ti,ab.
11. (prevalence or incidence or model or risk or rate$).ti.
12. (undiagnos or estimate$).ti.
13. (screen or surveill$ or predict or detect$).ti.
14. (age$ adj4 (factor or onset or diagnos or treatment$)).ti,ab.
15. (disease adj3 (duration or onset$)).ti,ab.
Diagnosis and management of type 1 diabetes in children and young people

Search strategies

EBM Reviews - Cochrane Central Register of Controlled Trials

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

Search strategies

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Search strategies

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

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

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

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Search strategies

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Health Technology Assessment

# Searches
1. ADOLESCENT/ or MINORS/
2. (adolescen$ or teen$ or youth$ or young or juvenile? or minors or highschool$).tw,jx,rw.
3. exp CHILD/
4. (child$ or schoolchild$ or "school age" or "school aged" or preschool$ or toddler$ or kid? or kindergar$ or boy? or girl?).tw,jx,rw.
5. exp INFANT/
6. (infan$ or neonat$ or newborn$ or baby or babies).tw,jx,rw.
7. exp PEDIATRICS/ or exp PUBERTY/
8. (p?ediatric$ or pubert$ or prepubert$ or pubescen$ or prepubescen$).tw,jx,rw.
9. or/1-8
10. exp DIABETES MELLITUS, TYPE 2/
11. (diabet$ adj5 ("type two" or "type 2" or "type II" or T2 or T1I or matur$ or adult$ or slow or late or stable or ketosis resistant or keto resist$ or keto?resist$ or non keto$ or non?keto$)).tw.
12. (diabet$ adj5 ((non insulin or non?insulin) adj2 depend$)).tw.
13. (NIDDM or T2D or TIID or DM2 or DMIII).tw.
14. or/10-13
15. exp DYSLIPIDEMIAS/
16. ($#lip$ or hyp$??lip$ or hyp$??alphalip$ or hyp$??betalip$ or hyp$??cholester$ or hyp$??triglycerid$ or hyp$??triacy?glycerol$).tw.
17. or/15-16
18. LIPIDS/
19. CHOLESTEROL/
20. CHOLESTEROL, HDL/
21. CHOLESTEROL, LDL/

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

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

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

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

52 (undiagnos$ or estimate$).ti.
53 (screen$ or surveill$ or predict$ or detect$).ti.
54 or/47-53
55 SEVERITY OF ILLNESS INDEX/
56 DISEASE SEVERITY/
57 DISEASE COURSE/
58 STAGING/
59 exp INTERNATIONAL CLASSIFICATION OF DISEASES/
60 RATING SCALE/
61 CLASSIFICATION/
62 DISEASE CLASSIFICATION/
63 (d#slip$ adj3 (grad$ or sever$ or classif$ or index$ or indice? or stage$ or staging or defin$)).ti,ab.
64 or/55-63
65 AGE/
66 AGE DISTRIBUTION/
67 ONSET AGE/
68 DISEASE DURATION/
69 TIME TO TREATMENT/
70 (age$ adj4 (factor$ or onset or diagnos$ or treatment$)).ti,ab.
71 (disease adj3 (duration or onset)).ti,ab.
72 or/65-71
73 25 and (39 or 46 or 54 or 64 or 72)
74 exp "**DISORDERS OF CHOLESTEROL METABOLISM"/di, ep, pc [Diagnosis, Epidemiology, Prevention]
75 "**DISORDERS OF LIPID METABOLISM"/di, ep, pc [Diagnosis, Epidemiology, Prevention]
76 exp "**DISORDERS OF LIPOPROTEIN METABOLISM"/di, ep, pc [Diagnosis, Epidemiology, Prevention]
77 *DYSLIPIDEMIA/di, ep, pc [Diagnosis, Epidemiology, Prevention]
78 exp *HYPERLIPIDEMIA/di, ep, pc [Diagnosis, Epidemiology, Prevention]
79 *HYPOLIPEMIA/di, ep, pc [Diagnosis, Epidemiology, Prevention]
80 or/73-79
81 and/17,80
82 (NON INSULIN DEPENDENT DIABETES MELLITUS/ and COMORBIDITY/) or NON INSULIN DEPENDENT DIABETES MELLITUS/co [Complication]
83 and/9,39,82
84 or/81,83
85 limit 84 to english language
86 conference abstract.pt.
87 letter.pt. or LETTER/
88 note.pt.
89 editorial.pt.
90 (letter or comment* or abstracts).ti.
91 or/86-90
92 RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
93 91 not 92
94 ANIMAL/ not HUMAN/
95 NONHUMAN/
96 exp ANIMAL EXPERIMENT/
97 exp EXPERIMENTAL ANIMAL/
98 ANIMAL MODEL/
99 exp RODENT/
100 (rat or rats or mouse or mice).ti.
F.26 Health economics

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

Searches

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

Embase

Searches

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

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

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

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

Number of papers identified, 2536
Number of papers weeded out, 2216
Number of papers excluded, 298
Number of papers included, 22

G.2 Type 1 diabetes – education
Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

Number of papers identified, 1280
Number of papers weeded out, 1204
Number of papers excluded, 68
Number of papers included, 8

G.3 Type 1 diabetes – behavioural interventions
Review question: What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 1 diabetes?

Number of papers identified, 771
Number of papers weeded out, 656
Number of papers excluded, 100
Number of papers included, 15

G.4 Type 1 diabetes – multiple daily injections
Review question: What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

Number of papers identified, 3775
Number of papers weeded out, 3588
Number of papers excluded, 174
Number of papers included, 13
G.5  Type 1 diabetes – HbA1c targets

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

Number of papers identified, 293
Number of papers weeded out, 291
Number of papers excluded, 2
Number of papers included, 0

G.6  Type 1 diabetes – blood glucose targets

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

Number of papers identified, 1303
Number of papers weeded out, 1292
Number of papers excluded, 11
Number of papers included, 0

G.7  Type 1 diabetes – blood glucose monitoring

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

Number of papers identified, 2060
Number of papers weeded out, 2011
Number of papers excluded, 36
Number of papers included, 13

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

Number of papers identified, 867
Number of papers weeded out, 821
Number of papers excluded, 42
Number of papers included, 4

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

Number of papers identified, 1302
Number of papers weeded out, 1266
Number of papers excluded, 35
Number of papers included, 1
G.8 Type 1 diabetes – blood ketone monitoring

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

Number of papers identified, 435
Number of papers weeded out, 419
Number of papers excluded, 15
Number of papers included, 1

G.9 Type 1 diabetes – dietary advice

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

Number of papers identified, 729
Number of papers weeded out, 704
Number of papers excluded, 23
Number of papers included, 2

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

Number of papers identified, 712
Number of papers weeded out, 699
Number of papers excluded, 11
Number of papers included, 2

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

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

Number of papers identified, 1289
Number of papers weeded out, 1274
Number of papers excluded, 11
Number of papers included, 4

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

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

Number of papers identified, 1576
Which of the following should be performed as clinical monitoring during treatment of diabetic ketoacidosis in children and young people:
- general observations (for example, heart and respiratory rate and blood pressure)
- body weight
- hydration status
- fluid balance
- neurological observations
- electrocardiographic (ECG) monitoring?

Number of papers identified, 1576
Number of papers weeded out, 1561
Number of papers excluded, 15
Number of papers included, 0

Which of the following laboratory investigations should be performed to monitor children and young people during treatment for diabetic ketoacidosis:
- blood glucose
- blood or urine ketones
- serum urea or electrolytes
- acid/base status?

Number of papers identified, 1576
Number of papers weeded out, 1572
Number of papers excluded, 1
Number of papers included, 3

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

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

Number of papers identified, 1108
Number of papers weeded out, 1108
Number of papers excluded, 0
Number of papers included, 0

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

Number of papers identified, 1108
Number of papers weeded out, 1098
Number of papers excluded, 4
Number of papers included, 6

What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?
Number of papers identified, 1108
Number of papers weeded out, 1090
Number of papers excluded, 11
Number of papers included, 7

G.13 Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents
Review question: What is the effectiveness of intravenous osmotic agents in the management of cerebral oedema associated with diabetic ketoacidosis?
Number of papers identified, 88
Number of papers weeded out, 80
Number of papers excluded, 7
Number of papers included, 1

G.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin
Review questions:
When should intravenous insulin therapy be started and stopped in children and young people with diabetic ketoacidosis?
Number of papers identified, 389
Number of papers weeded out, 388
Number of papers excluded, 0
Number of papers included, 1

How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?
Number of papers identified, 389
Number of papers weeded out, 386
Number of papers excluded, 0
Number of papers included, 3

G.15 Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis
Review question: What is the effectiveness of routine anticoagulant prophylaxis to prevent venous thrombosis in children and young people with diabetic ketoacidosis?
(G.16) **Type 1 diabetes – retinopathy**

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

- Number of papers identified: 5684
- Number of papers weeded out: 5382
- Number of papers excluded: 69
- Number of papers included: 18

(G.17) **Type 1 diabetes – nephropathy**

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

- Number of papers identified: 2924
- Number of papers weeded out: 2819
- Number of papers excluded: 91
- Number of papers included: 14

(G.18) **Type 2 diabetes – education**

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

- Number of papers identified: 1435
- Number of papers weeded out: 1402
- Number of papers excluded: 33
- Number of papers included: 0

(G.19) **Type 2 diabetes – behavioural interventions**

Review questions:

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

- Number of papers identified: 1637
- Number of papers weeded out: 1624
- Number of papers excluded: 13
- Number of papers included: 0
What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 2 diabetes?
Number of papers identified, 1637
Number of papers weeded out, 1617
Number of papers excluded, 20
Number of papers included, 0

G.20 Type 2 diabetes – dietary advice
Review question: What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?
Number of papers identified, 2605
Number of papers weeded out, 2588
Number of papers excluded, 16
Number of papers included, 1

G.21 Type 2 diabetes – weight loss
Review question: Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?
Number of papers identified, 697
Number of papers weeded out, 624
Number of papers excluded, 27
Number of papers included, 1

G.22 Type 2 diabetes – metformin
Review question: What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?
Number of papers identified, 604
Number of papers weeded out, 581
Number of papers excluded, 22
Number of papers included, 1

G.23 Type 2 diabetes – HbA1c targets
Review question: What is the optimal HbA1c target for children and young people with type 2 diabetes?
Number of papers identified, 716
Number of papers weeded out, 706
Number of papers excluded, 10
Number of papers included, 0
G.24 **Type 2 diabetes – hypertension**  
Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?  
Number of papers identified, 3205  
Number of papers weeded out, 3190  
Number of papers excluded, 7  
Number of papers included, 8  

G.25 **Type 2 diabetes – dyslipidaemia**  
Review question: What is the optimal monitoring strategy for identifying dyslipidaemia in children and young people with type 2 diabetes?  
Number of papers identified, 1613  
Number of papers weeded out, 1595  
Number of papers excluded, 11  
Number of papers included, 7  

G.26 **Type 2 diabetes – retinopathy**  
Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?  
Number of papers identified, 2594  
Number of papers weeded out, 2575  
Number of papers excluded, 17  
Number of papers included, 2  

G.27 **Type 2 diabetes – nephropathy**  
Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?  
Number of papers identified, 2923  
Number of papers weeded out, 2913  
Number of papers excluded, 7  
Number of papers included, 3  

G.28 **Health economics**  
Number of papers identified, 2754  
Number of papers weeded out, 2731  
Number of papers excluded, 19  
Number of papers included, 2
Appendix H: Excluded studies

H.1 Diagnosis

Review question

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

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>J. M. Wenzlau, O. Moua, S. A. Sarkar, L. Yu, M. Revers, G. S. Eisenbarth, H. W. Davidson, and C. Hutton</td>
<td>Age of population not reported</td>
</tr>
<tr>
<td>E. Lindholm, E. Agardh, T. Tuomi, L. Groop, and C. D. Agardh. Classifying diabetes according to the new WHO clinical stages. Eur.J.Epidemiol. 17 (11):983-989, 2001.</td>
<td>Wrong population: has not categorised diabetes into the standard different types (T1D, T2D etc) but insulin-requiring for control (IRC) and non-insulin requiring (NIR)</td>
</tr>
<tr>
<td>S Oak, L K. Gilliam, M Landin-Olsson, C Torn, I Kockum, CR. Pennington, M J.</td>
<td>Wrong outcomes: not the presence of</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
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<tr>
<td>----------------------------------------------------------------------</td>
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</tr>
<tr>
<td>JC. Low, EI. Felner, AB. Muir, M. Brown, M. Dorcelet, L. Peng, and G. E. Umpierrez. Do obese children with diabetic ketoacidosis have type 1 or type 2 diabetes? Prim Care Diabetes 6 (1):61-65, 2012.</td>
<td>Wrong outcomes: pools together results for islet cell Abs and GAD Abs so can’t separate the two</td>
</tr>
<tr>
<td>JL. Mahon, JM. Sosenko, L Rafkin-Mervis, H Krause-Steinrauf, JM. Lachin, C Thompson, PJ. Bingley, E Bonifacio, JP. Palmer, GS. Eisenbarth, J. Wolfsdorf, JS. Styler, TrialNet Natural History Committee, and Diabetes TrialNet Study Group. The TrialNet Natural History Study of the Development of Type 1 Diabetes: objectives, design, and initial results. Pediat Diabetes 10 (2):97-104, 2009.</td>
<td>Wrong outcomes: does not give Ab results for the T1D pts; this is just the screening and baseline risk assessment paper. Wrong study population and design – presence of Abs in relatives and see if predicts development of diabetes</td>
</tr>
</tbody>
</table>
Excluded studies

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


Herold, JM. Lachin, P McGee et al., and Diabetes TrialNet Study Group. Fall in C-peptide during first 2 years from diagnosis: evidence of at least two distinct phases from composite Type 1 Diabetes TrialNet data. Diabetes 61 (8):2066-2073, 2012.


<table>
<thead>
<tr>
<th>Study</th>
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<td>Reason for exclusion</td>
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</tr>
<tr>
<td>MC Moreira, GM Lara, R Linden, LR Feksa, R G Tavares, SE de Matos Almeida, and DB Berlese. Frequency of the anti-glutamic acid decarboxylase immunological marker in patients with diabetes duration longer than three years in southern Brazil. Sao Paulo Med J 129 (3):130-133, 2011.</td>
<td>Age range of population not specified</td>
</tr>
<tr>
<td>AJ. Delli, Fariba Vaziri-Sani, Bengt Lindblad, Helena Elding-Larsson, Annelie Carlsson, Gun Forsander, Sten A. Ivarsson, et al. and Better Diabetes Diagnosis study group. Zinc transporter 8 autoantibodies and their association with SLC30A8 and HLA-DQ genes differ between immigrant and Swedish patients with newly diagnosed type 1 diabetes in the Better Diabetes Diagnosis study. Diabetes 61 (10):2556-2564, 2012.</td>
<td>Excluded even for children/young pple GL, because doesn’t give the actual % of pple (or the titre) who are Ab+ for the young pple or children’s subgroup</td>
</tr>
<tr>
<td>MH Black, Jean M. Lawrenz, Catherine Phikher, Lawrence M. Dolan, Andrea Anderson, Beatriz Rodriguez, Santica M. Marcovina, Elizabeth J. Mayer-Davis, Giuseppina Imperatore, Dana Dabelea, and Georgeanna Klingensmith. GL, because doesn’t give the actual % of patients with the markers pre-specified in our protocol</td>
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© 2014 National Collaborating Centre for Women’s and Children’s Health
<table>
<thead>
<tr>
<th>Study</th>
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<tbody>
<tr>
<td>S Miersch, Xiaofang Bian, Garrick Wallstrom, Sahar Sibani, Tanya Logvinenko, Clive H. Wasserfall, Desmond Schatz, Mark Atkinson, Ji Qiu, and Joshua Labaer. Serological autoantibody profiling of Type 1 diabetes by protein arrays. J Proteomics 94:486-496, 2013.</td>
<td>Doesn't give % of ppl with Abs or the titre</td>
</tr>
<tr>
<td>JM. Sosenko, Jay S. Skyler, Jerry P. Palmer, Jeffrey P. Krischer, et al Diabetes TrialNet Study Group, and Prevention Trial-Type Diabetes. The prediction of type 1 diabetes by multiple autoantibody levels and their incorporation into an autoantibody risk score in relatives of type 1 diabetic patients. Diabetes Care 36 (9):2615-2620, 2013.</td>
<td>Does not answer the question: uses markers as predictors of future development of T1D</td>
</tr>
<tr>
<td>L Yu, Fran Dong, Dongmei Miao, Alexandra R. Fouts, Janet M. Wenzlau, and Andrea K. Steck. Proinsulin/Insulin autoantibodies measured with</td>
<td>Wrong population: mix of children and young people, with no age subgroup analysis</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
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<tr>
<td>Electrochemical luminescent assay are the earliest indicator of prediabetic islet autoimmunity. Diabetes Care 36 (8):2266-2270, 2013.</td>
<td>Analysis</td>
</tr>
<tr>
<td>SY Chai, Xiao Yu Pan, Ke Xi Song, Yue Ye Huang, Fei Li, Xiao Yun Cheng, and Shen Qu. Differential patterns of insulin secretion and sensitivity in patients with type 2 diabetes mellitus and nonalcoholic fatty liver disease versus patients with type 2 diabetes mellitus alone. Lipids health dis. 13:7, 2014.</td>
<td>Adults but N&lt;50</td>
</tr>
<tr>
<td>C Ekhpebegh, Benjamin Longo-Mbenza, and Ernesto Blanco-Blanco. Islet immunity and beta cell reserve of indigenous Black South Africans with ketoacidosis at initial diagnosis of diabetes. Etn Dis 23 (2):196-201, 2013.</td>
<td>Unclear population: just says DKA. Most were later recognised as T2D (in the discussion section), but no analysis done by type of diabetes</td>
</tr>
<tr>
<td>N. M. Kamal Alanani and A. A. Alsulaimani. Epidemiological pattern of newly diagnosed children with type 1 diabetes mellitus, Taif, Saudi Arabia. Sci.World J. 2013, 2013.</td>
<td>Wrong population: mix of all ages, with no age subgroup analysis</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
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<td>----------------------------------------------------------------------</td>
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<tr>
<td>YH Kong, Min Sun Kim, and Dae Yeol Lee. Comparison of the prevalence of islet autoantibodies according to age and disease duration in patients with type 1 diabetes mellitus. Ann.pediatr.endocrinol.metab. 18 (2):65-70, 2013.</td>
<td>Wrong sample size: adult subgroup is N&gt;50; adult and young people mixed subgroup is also N&lt;50</td>
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<tr>
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<tbody>
<tr>
<td>R. A. Oram, T. J. McDonald, B. M. Shields, L. R. Pearson, and A. T. Hattersley. A large, population-based study demonstrates that most people with long duration Type 1 diabetes are insulin microsecretors and produce their own endogenous insulin. Diabet Med 31:10, 2014.</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>F Prodam, Francesco Cadario, Simonetta Bellone, Letizia Trovato, Stefania Moia, Erica Pozzi, Silvia Savastio, and Gianni Bona. Oestin levels are associated with C-peptide and antiinsulin antibodies at the onset, whereas unacylated and acylated ghrelin levels are not predictive of long-term metabolic control in children with type 1 diabetes. J Clin Endocrinol Metab 99 (4):E599-E607, 2014.</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>J. V. Sildsen, R. W. Thomsen, J. S. Nielsen, J. Rungby, S. P. Ulrichsen, K.</td>
<td>Conference abstract</td>
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<td>Study</td>
<td>Reason for exclusion</td>
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<tr>
<td>S. Hameed, S. Ellard, H. J. Woodhead, K. A. Neville, J. L. Walker, M. E. Craig,</td>
<td>Wrong population: children and young people</td>
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### Included studies

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<tr>
<td>Diagnosis and management of type 1 diabetes in children and young people</td>
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<tr>
<td>Ender Arikan, Teyfik Sabuncu, Esref M. Ozzer, and Huseyv Hatemi. The clinical characteristics of latent autoimmune diabetes in adults and its relation with chronic complications in metabolically poor controlled Turkish patients with Type 2 diabetes mellitus. J.Diabetes Complications 19 (5):254-258, 2005.</td>
<td>Wrong population: adults only</td>
</tr>
<tr>
<td>M. Hawa, Hubert Kolb, Nanette Schloot, Huriya Beyan, Stavroula A. Paschou,</td>
<td>Wrong population: adults only</td>
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<tr>
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<td>Reason for exclusion</td>
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<tr>
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<td>---------------------------------------------------</td>
</tr>
<tr>
<td>YP. Mahadeb, Damien Gruson, Martin Buyssechaert, and Michel P. Hermans. What are the characteristics of phenotypic type 2 diabetic patients with low-titer GAD65 antibodies? Acta Diabetol. 51 (1):103-111, 2014.</td>
<td>Wrong population: adults only</td>
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### Excluded studies

<table>
<thead>
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<tbody>
<tr>
<td>MA. Radtke, Kristian Midthjell, Tom I. L. Nilsen, and Valdemar Grill. Heterogeneity of patients with latent autoimmune diabetes in adults: linkage to autoimmunity is apparent only in those with perceived need for insulin treatment: results from the Nord-Trondelag Health (HUNT) study. Diabetes Care 32 (2):245-250, 2009.</td>
<td>Wrong population: adults only</td>
</tr>
<tr>
<td>Mi Oh Roh, Chan Hee Jung, Bo Yeon Kim, Ji Oh Mok, and Chul Hee Kim. The prevalence and characteristics of latent autoimmune diabetes in adults (LADA) and its relation with chronic complications in a clinical department of a university hospital in Korea. Acta Diabetol. 50 (2):129-134, 2013.</td>
<td>Wrong population: adults only</td>
</tr>
<tr>
<td>S. Zhang, Qi Sun, Kai Feng, Yong Fu, Ou Wang, Fan Ping, and Yuxiu Li. Clinical, biochemical, and immunological characteristics of newly diagnosed nonobese diabetic patients aged 18-45 years in China. J.Diabetes Complications 26 (1):40-43, 2012.</td>
<td>Wrong population: adults only</td>
</tr>
</tbody>
</table>
What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Anderson, B.J., Wolf, F.M., Burkhart, M.T., Cornell, R.G.</td>
<td>Effects of peer-group intervention on metabolic control of adolescents with IDDM. Randomized outpatient study. Diabetes Care, 12, 179-183, 1989</td>
</tr>
</tbody>
</table>

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<tr>
<td>Grey, M., Whittemore, R., Jaser, S., Ambrosino, J., Lindemann, E., Libert, L., Northrup, V., Dziura, J., Effects of coping skills training in school-age children with type 1 diabetes, Research in Nursing and Health, 32, 405-418, 2009</td>
<td>PICO not met: intervention not considered to be a form of structured education</td>
</tr>
<tr>
<td>Grey, M., Whittemore, R., Jeon, S., Jaser, S., Murphy, K., Faulkner, M., Delamater, A., Internet programs for youth with type 1 diabetes (T1D) improve outcomes, Diabetes, 61, A90-A92, 2012</td>
<td>PICO not met: intervention not considered to be a form of structured education</td>
</tr>
<tr>
<td>Hackett, A.F., Court, S., Mathews, J.N., McCowen, C., Do education groups help diabetics and their parents?, Archives of Disease in Childhood, 64, 997-1003, 1989</td>
<td>In included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (study design unclear; not clearly an RCT)</td>
</tr>
<tr>
<td>Hampson, S.E., Skinner, T.C., Hart, J., Storey, L., Gage, H., Foxcroft, D., Kimber, A., Craddock, S., McEvilly, E.A., Behavioral interventions for adolescents with type 1 diabetes: how effective are they?, [68 refs], Diabetes Care, 23, 1416-1422, 2000</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (individual RCTs are included in the guideline review)</td>
</tr>
<tr>
<td>Hampson, S.E., Skinner, T.C., Hart, J., Storey, L., Gage, H., Foxcroft, D., Kimber, A., Shaw, K., Walker, J., Effects of educational and psychosocial interventions for adolescents with diabetes mellitus: a systematic review, [148 refs], Health Technology Assessment (Winchester, England), 5, 1-79, 2001</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (individual RCTs are included in the guideline review)</td>
</tr>
<tr>
<td>Hanberger, L., Ludvigsson, J., Nordfeldt, S., Use of a web 2.0 portal to improve education and communication in young patients with families: randomized controlled trial, Journal of medical Internet research, 15, e175-, 2013</td>
<td>Web 2.0 portal was not a ‘structured’ education programme (there was no structured curriculum); the use of the portal was designed to be self-initiated by participants and their parents whenever needed, although there was access to communication with healthcare professionals</td>
</tr>
<tr>
<td>Hill-Briggs, F., Gemmell, L., Problem solving in diabetes self-management and control: A systematic review of the literature, Diabetes Educator, 33, 1032-1050, 2007</td>
<td>Systematic review: individual randomised controlled trials have been considered for inclusion</td>
</tr>
<tr>
<td>Holmes, C.S., Chen, R., Mackey, E., Grey, M., Streisand, R., Randomized clinical trial of clinic-integrated, low-intensity treatment to prevent deterioration of disease care in adolescents with type 1 diabetes, Diabetes Care, 37, 1535-1543, 2014</td>
<td>Wrong intervention (behavioural intervention)</td>
</tr>
<tr>
<td>Hood, K.K., Rohan, J.M., Peterson, C.M., Drotar, D., Interventions with adherence-promoting components in pediatric type 1 diabetes: meta-analysis of their impact on glycemic control, Diabetes Care, 33, 1658-1664, 2010</td>
<td>Systematic review: individual randomised controlled trials have been considered for inclusion</td>
</tr>
<tr>
<td>Howells, L., Wilson, A.C., Skinner, T.C., Newton, R., Morris, A.D., Greene, S.A., A randomized control trial of the effect of negotiated telephone support on glycemic control in young people with Type 1 diabetes, Diabetic Medicine, 19, 643-648, 2002</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (did not consider a structured form of education)</td>
</tr>
<tr>
<td>Husted, G.R., Thorsteinsson, B.A., Esbensen, B.A., Hommel, E., Zoffmann, V., Improving glycemic control and life skills in adolescents with type 1 diabetes: a randomised, controlled intervention study using the Guided Self-Determination-Young method in triads of adolescents, parents and health care providers integrated into routine paediatric outpatient clinics, BMC Pediatrics, 11, 55-, 2011</td>
<td>PICO not met: intervention not considered to be a form of structured education</td>
</tr>
<tr>
<td>Jonsson, L., Hallstrom, I., Lundqvist, A., A multi-disciplinary education process related to the discharging of children from hospital when the child has been diagnosed with type 1 diabetes—a qualitative study, BMC Pediatrics, 10, 36-, 2010</td>
<td>Not a randomised controlled trial</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Mannucci, E., Pala, L., Rotella, C.M., Long-term interactive group education for type 1 diabetic patients, Acta Diabetologica, 42, 1-6, 2005</td>
<td>Not a randomised controlled trial</td>
</tr>
<tr>
<td>McBroom, L.A., Enriquez, M., Review of family-centered interventions to enhance the health outcomes of children with type 1 diabetes. [36 refs], Diabetes Educator, 35, 428-438, 2009</td>
<td>Systematic review: individual randomised controlled trials have been considered for inclusion</td>
</tr>
<tr>
<td>Mopherson, A.C., Price, K., Does an interactive website provide additional support to young people participating in an educational intervention for type 1 diabetes?, Pediatric Diabetes, 13, 139-, 2012</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Muller, Nicole, Kloos, Christof, Samann, Alexander, Wolf, Gunter, Muller, Ulrich Alfons, Evaluation of a treatment and teaching refresher programme for the optimization of intensified insulin therapy in type 1 diabetes, Patient Education and Counseling, 93, 108-113, 2013</td>
<td>Participants aged between 16 and 70 years</td>
</tr>
<tr>
<td>Murphy, H.R., Rayman, G., Skinner, T.C., Psycho-educational interventions for children and young people with Type 1 diabetes. [52 refs], Diabetic Medicine, 23, 935-943, 2006</td>
<td>Systematic review: individual randomised controlled trials have been considered for inclusion</td>
</tr>
<tr>
<td>Pichert, J.W., Smeltzer, C., Snyder, G.M., Gregory, R.P.,</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population limited to young women with eating disturbance)</td>
</tr>
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</table>
### Excluded studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smeltzer, R., Kinzer, C.K., Traditional vs anchored instruction for diabetes-related nutritional knowledge, skills, and behavior, Diabetes Educator, 20, 45-48, 1994</td>
<td>criteria for 2015 review (no outcomes of interest reported)</td>
</tr>
<tr>
<td>Pichert, J.W., Snyder, G.M., Kinzer, C.K., Boswell, E.J., Problem solving anchored instruction about sick days for adolescents with diabetes, Patient Education and Counseling, 23, 115-124, 1994</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 review (no outcomes of interest reported)</td>
</tr>
<tr>
<td>Sansom-Daly, U.M., Peate, M., Wakefield, C.E., Bryant, R.A., Cohn, R.J., A systematic review of psychological interventions for adolescents and young adults living with chronic illness, Health Psychology, 31, 380-393, 2012</td>
<td>Systematic review: individual randomised controlled trials have been considered for inclusion</td>
</tr>
<tr>
<td>Satin, W., La Greca, A.M., Zigo, M.A., Skyler, J.S., Diabetes in adolescence: effects of multifamily group intervention and parent simulation of diabetes, Journal of Pediatric Psychology, 14, 259-275, 1999</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not considered to be a structured education programme)</td>
</tr>
<tr>
<td>Shernfali, D., A case manager plus psychoeducation reduced adverse outcomes in youth with type 1 diabetes, Evidence Based Nursing, 7, 42-42, 2004</td>
<td>Abstract</td>
</tr>
<tr>
<td>Srinivasan, B., Davies, M., Lawrence, I., Diabetes: glycaemic control in type 1, Clinical Evidence, 2008, 2008. . , 2008</td>
<td>Systematic review: individual randomised controlled trials have been considered for inclusion</td>
</tr>
<tr>
<td>Sundelin, J., Forsander, G., Mattsson, S.E., Family-oriented support at the onset of diabetes mellitus: a comparison of two group conditions during 2 years following diagnosis, Acta Paediatrica Acta Paediatr., 85, 49-55, 1996</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not a form of structured education)</td>
</tr>
<tr>
<td>Urban, A.D., Berry, D., Grey, M., Optimizing outcomes in adolescents with type 1 diabetes and their families, Journal of Clinical Outcomes Management, 11, 299-306, 2004</td>
<td>Systematic review: individual randomised controlled trials have been considered for inclusion</td>
</tr>
<tr>
<td>Wang, Y.C., Stewart, S.M., Mackenzie, M., Nakonezny, P.A., Edwards, D., White, P.C., A randomized controlled trial comparing motivational interviewing in education to structured diabetes education in teens with type 1 diabetes, Diabetes Care, 33, 1741-1743, 2010</td>
<td>This is a process evaluation study, not a clinical trial</td>
</tr>
<tr>
<td>Wysocki, T., Harris, M.A., Greco, P., Harvey, L.M., McDonnell, K., Elder Danda, C.L., Bubb, J., White, N.H., Social validity of support group and behavior therapy interventions for families of adolescents with insulin-dependent diabetes mellitus, Journal of Pediatric Psychology, 33, 1746, 2012</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (no outcomes of interest reported and the original study was also excluded)</td>
</tr>
</tbody>
</table>
H.3 Type 1 diabetes – behavioural interventions

Review question

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes: maintenance and generalization of effects on parent-adolescent communication, Behavior Therapy, 39, 33-46, 2008</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (the original study Wysocki 1997 was excluded; this article has also been excluded as only results from the 3-month follow-up are reported)</td>
</tr>
<tr>
<td>Randomized, controlled trial of behavior therapy for families of adolescents with insulin-dependent diabetes mellitus, Journal of Pediatric Psychology, 25, 23-33, 2000</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Boardway,R.H., Delamater,A.M., Tomakowski,J., Gutai,J.P.</td>
<td>Included in 2004 guideline review â€“ does not meet inclusion criteria for 2015 update review (follow-up does not meet required duration)</td>
</tr>
<tr>
<td>Stress management training for adolescents with diabetes, Journal of Pediatric Psychology, 18, 29-45, 1993</td>
<td>Secondary publication</td>
</tr>
<tr>
<td>Cakan,N., Ellis,D.A., Templin,T., Frey,M., Naar-King,S.</td>
<td>PICO not met - follow-up length insufficient</td>
</tr>
<tr>
<td>The effects of weight status on treatment outcomes in a randomized clinical trial of multisystemic therapy for adolescents with type 1 diabetes and chronically poor metabolic control, Pediatric Diabetes, 8, 206-213, 2007</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (pop not an RCT)</td>
</tr>
<tr>
<td>Channon,S., Smith,V., Gregory,J.W.</td>
<td>Interventions are not of interest</td>
</tr>
<tr>
<td>A pilot study of motivational interviewing in adolescents with diabetes, Archives of Disease in Childhood, 88, 680-683, 2003</td>
<td>Wrong study design (case-control, not RCT)</td>
</tr>
<tr>
<td>Chernoff,R.G., Ireys,H.T., DeVet,K.A., Kim,Y.J.</td>
<td>Wrong intervention (education)</td>
</tr>
<tr>
<td>A randomized, controlled trial of a community-based support program for families of children with chronic illness: pediatric outcomes, Archives of Pediatrics and Adolescent Medicine, 156, 533-539, 2002</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population does not match the inclusion criteria of the 2015 update review)</td>
</tr>
<tr>
<td>Chisholm,V., Gonzalez,A., Atkinson,L.</td>
<td>Interventions are not of interest</td>
</tr>
<tr>
<td>Interpersonal engagement mediates the relation between maternal affect and externalising behaviour in young children with type 1 diabetes, PLos ONE [Electronic Resource], 9, e97572, 2014</td>
<td>Wrong study design (case-control, not RCT)</td>
</tr>
<tr>
<td>Cho,E., Shin,S.H., Eun,S.H., Kim,J.Y., Nam,H.K., Lee,K.H., Rhee,Y.J.</td>
<td>Interventions are not of interest</td>
</tr>
<tr>
<td>Psychological characteristics of Korean children and adolescents with type 1 diabetes mellitus, Annals of Pediatric Endocrinology and Metabolism, 18, 122-127, 2013</td>
<td>Wrong study design (case-control, not RCT)</td>
</tr>
<tr>
<td>Daley,B.J.</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population unclear, stated as teenagers with diabetes)</td>
</tr>
<tr>
<td>Sponsorship for adolescents with diabetes, Health and Social Work, 17, 173-182, 1992</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not an intervention specified in the review protocol)</td>
</tr>
<tr>
<td>Randomized prospective study of self-management training with newly diagnosed diabetic children. [erratum appears in Diabetes Care 1990 Jul;13(7):819], Diabetes Care, 13, 492-498, 1990</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Ellis,D., Naar-King,S., Templin,T., Frey,M., Cunningham,P., Sheidow,A., Cakan,N., Idaliski,A.</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (intervention is an education programme rather than a behavioural intervention)</td>
</tr>
<tr>
<td>Multisystemic therapy for adolescents with poorly controlled type 1 diabetes: reduced diabetic ketoacidosis admissions and related costs over 5 years, Diabetes Care, 33, 2010</td>
<td>Conference abstract</td>
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<tr>
<td>Study</td>
<td>Reason for exclusion</td>
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<tr>
<td>24 months, Diabetes Care, 31, 1746-1747, 2008</td>
<td>Secondary publication</td>
</tr>
<tr>
<td>Ellis,D.A., Naar-King,S., Chen,X., Moltz,K., Cunningham,P.B., Idalski-Carcone,A., Multisystemic therapy compared to telephone support for youth with poorly controlled diabetes: findings from a randomized controlled trial, Annals of Behavioral Medicine, 44, 207-215, 2012</td>
<td>Secondary publication</td>
</tr>
<tr>
<td>Franklin,V.L., Waller,A., Pagliari,C., Greene,S.A., A randomized controlled trial of Sweet Talk, a text-messaging system to support young people with diabetes, Diabetic Medicine, 23, 1332-1338, 2006</td>
<td>PICO not met - support delivered by clinical staff not peers</td>
</tr>
<tr>
<td>Freteman,K.A., Duke,D.C., Harris,M.A., Behavioral health care for adolescents with poorly controlled diabetes via Skype: does working alliance remain intact?, Journal of Diabetes Science and Technology, 7, 727-735, 2013</td>
<td>Outcomes examined (working alliance inventory (WAI) subscale scores and the association between them and HbA1c) not of interest</td>
</tr>
<tr>
<td>Garcia-Perez,L., Pererste-lo-Perez,L., Serrano-Aguilar,P., Del,Mar Trujillo-Martin, Effectiveness of a psychoeducative intervention in a summer camp for children with type 1 diabetes mellitus, Diabetes Educator, 36, 310-317, 2010</td>
<td>PICO not met - intervention not relevant to this question</td>
</tr>
<tr>
<td>Greco,P., Pendley,J.S., McDonell,K., Reeves,G., A peer group intervention for adolescents with type 1 diabetes and their best friends, Journal of Pediatric Psychology, 25, 485-490, 2001</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not a comparative study and therefore does not meet the study design inclusion criteria)</td>
</tr>
<tr>
<td>Gregory,J.W., Channon,S., Motivational interviewing to improve blood-glucose control in childhood diabetes, Paediatrics and Child Health, 19, 331-334, 2009</td>
<td>Commentary</td>
</tr>
<tr>
<td>Grey,M., Whittemore,R., Jeon,S., Murphy,K., Faulkner,M.S., Delamater,A., TeenCope Study Group., Internet psycho-education programs improve outcomes in youth with type 1 diabetes, Diabetes Care, 36, 2475-2482, 2013</td>
<td>Education rather than behavioural intervention programme</td>
</tr>
<tr>
<td>Grey,M., Boland,E.A., Davidson,M., Lu,J., Tamborlane,W,V., Coping skills training for youth with diabetes mellitus has long-lasting effects on metabolic control and quality of life, Journal of Pediatrics, 137, 107-113, 2000</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population included participants up to the age of 20 years with no subgroups of younger participants reported)</td>
</tr>
</tbody>
</table>
| Grey,M., Boland,E.A., Davidson,M., Yu,C., Sullivan-Bolbay,S., Tamborlane,W.V., Short-term effects of coping skills training as adjunct to intensive therapy in adolescents, Diabetes Care, 21, 902-908, 1998 | Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population includes participants up to the age of 20 years but does not report subgroups for younger participants, and length of
### Excluded studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grey,M., Boland,E.A., Davidson,M., Yu,C., Tamborlane,W.V. Coping skills training for youths with diabetes on intensive therapy, Applied Nursing Research, 12, 3-12, 1999</td>
<td>Follow-up does not meet the inclusion criteria</td>
</tr>
<tr>
<td>Gross,A.M., Heimann,L., Shapiro,R., Schulz,R.M., Children with diabetes. Social skills training and hemoglobin A1c levels, Behavior Modification Behav.Modif., 7, 151-164, 1983</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (participants aged &lt; 20 years and no subgroup analysis for ages relevant to guideline)</td>
</tr>
<tr>
<td>Hampson,S.E., Skinner,T.C., Hart,J., Storey,L., Gage,H., Foxcroft,D., Kimber,A., Craddock,S., McEvilly,E.A., Behavioral interventions for adolescents with type 1 diabetes: how effective are they?. [68 refs], Diabetes Care, 23, 1416-1422, 2000</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (includes participants aged up to 21 years and does not report any subgroup analyses for younger participants)</td>
</tr>
<tr>
<td>Hampson,S.E., Skinner,T.C., Hart,J., Storey,L., Gage,H., Foxcroft,D., Kimber,A., Shaw,K., Walker,J., Effects of educational and psychosocial interventions for adolescents with diabetes mellitus: a systematic review, [148 refs], Health Technology Assessment (Winchester, England), 5, 1-79, 2001</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (the broad inclusion criteria for this health technology assessment (HTA) report did not match the 2015 review update criteria, but the report was checked for relevance of individual studies)</td>
</tr>
<tr>
<td>Harris,MA, Greco,P, Wysocki,T, White,NH, Family therapy with adolescents with diabetes: a litmus test for clinically meaningful change, Families, Systems and Health, 24, 441-446, 2001</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (no outcomes of interest)</td>
</tr>
<tr>
<td>Harris,MA, Mertlich,D, Piloting home-based behavioral family systems therapy for adolescents with poorly controlled diabetes, Children's Health Care, 32, 65-79, 2003</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not an RCT)</td>
</tr>
<tr>
<td>Hernandez,C.A., Family focused teamwork prevented deterioration in diabetes control in children and adolescents, Evidence Based Nursing, 7, 10-10, 2004</td>
<td>Commentary</td>
</tr>
<tr>
<td>Holmes,C.S., Chen,R., Mackey,E., Grey,M., Streisand,R., Randomized clinical trial of clinic-integrated, low-intensity treatment to prevent deterioration of disease care in adolescents with type 1 diabetes, Diabetes Care, 37, 1535-1543, 2014</td>
<td>Data in study cannot be extracted</td>
</tr>
<tr>
<td>Insabella,G., Grey,M., Knafl,G., Tamborlane,W., The transition to young adulthood in youth with type 1 diabetes on intensive therapy, Pediatric Diabetes, 8, 228-234, 2007</td>
<td>PICO not met - age range of participants in original study was 12 to 20 years</td>
</tr>
<tr>
<td>Irey,H.T., Chernoff,R., DeVet,K.A., Kim,Y., Maternal outcomes of a randomized controlled trial of a community-based support program for families of children with chronic illnesses, Archives of Pediatrics and Adolescent Medicine, 155, 771-777, 2001</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (population not exclusively type 1 diabetes)</td>
</tr>
<tr>
<td>Kaplan,R.M., Chadwick,M.W., Schimmel,L.E., Social learning intervention to promote metabolic control in type I diabetes mellitus: pilot experiment results, Diabetes Care, 8, 152-155, 1985</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (length of follow-up did not meet the inclusion criteria)</td>
</tr>
<tr>
<td>Kawamura,T., Kawamura,K., Hirose,M., Hashimoto,T., Higashide,T., Kashihara,Y., Aono,S., Okajima,M., Oguru,M., Harai,H., Training of motivational interviewing to parents improved the glycemetic control of the childhood and Family Medicine Centre for Women's and Children's Health, 33, 439-446, 2015</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
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<tr>
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<tr>
<td>adolescent type 1 diabetes: A prospective randomized control trial, Pediatric Diabetes, 13, 26-, 2012</td>
<td></td>
</tr>
<tr>
<td>Kumar,V.S., Wentzell,K.J., Mikkelsen,T., Pentland,A., Laffel,L.M., The DAILY (Daily Automated Intensive LOG for Youth) trial: a wireless, portable system to improve adherence and glycemic control in youth with diabetes, Diabetes Technology and Therapeutics, 6, 445-453, 2004</td>
<td>PICO not met - study included children and young people with either type 1 diabetes or type 2 diabetes</td>
</tr>
<tr>
<td>Lapp,J., White,N.H., Social networking and peer support (SNAPS) in adolescents with type 1 diabetes mellitus (T1D): A pilot study, Diabetes, 61, A195-, 2012</td>
<td></td>
</tr>
<tr>
<td>Marrero,OG, Myers,G, Golden,MP, West,D, Adjustment to misfortune: the use of a social support group for adolescent diabetes, Pediatric and Adolescent Endocrinology, 10, 213-218, 1982</td>
<td></td>
</tr>
<tr>
<td>Matam,P., Kumaaraih,V., Munichhodappa,C., Kumar,K.M., Aravind,S., Behavioural intervention in the management of compliance in young type-1 diabetics, Journal of the Association of Physicians of India, 48, 967-971, 2000</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (length of follow-up did not meet the inclusion criteria for the 2015 update review)</td>
</tr>
<tr>
<td>Mendez,F.J., Belendez,M., Effects of a behavioral intervention on treatment adherence and stress management in adolescents with IDDM, Diabetes Care, 20, 1370-1375, 1997</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (not a comparative study)</td>
</tr>
<tr>
<td>Murphy,H.R., Wadham,C., Hassler-Hurst,J., Rayman,G., Skinner,T.C., Families and Adolescents Communication and Teamwork Study (FACTS) Group., Randomized trial of a diabetes self-management education and family teamwork intervention in adolescents with Type 1 diabetes, Diabetic Medicine, 29, e249-e254, 2012</td>
<td>PICO not met - intervention not relevant to this question</td>
</tr>
<tr>
<td>Murphy,H.R., Wadham,C., Rayman,G., Skinner,T.C., Approaches to integrating paediatric diabetes care and structured education: experiences from the Families, Adolescents, and Children's Teamwork Study (FACTS), Diabetic Medicine, 24, 1261-1268, 2007</td>
<td>PICO not met - intervention not relevant to this question</td>
</tr>
<tr>
<td>Newton,K.T., Ashley,A., Pilot study of a web-based intervention for adolescents with type 1 diabetes, Journal of Telemedicine and Telecare, 19, 443-449, 2013</td>
<td>7-week intervention outcomes were assessed through an exit survey</td>
</tr>
<tr>
<td>Nunn,E., King,B., Smart,C., Anderson,D., A randomized controlled trial of telephone calls to young patients with poorly controlled type 1 diabetes, Pediatric Diabetes, 13, 2-6, 2012</td>
<td>PICO not met - intervention was support from a healthcare professional</td>
</tr>
</tbody>
</table>

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### Excluded studies

**Diagnosis and management of type 1 diabetes in children and young people**

#### Study

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paterson, B.L., Multisystemic therapy improved adherence to blood glucose testing in adolescents with type 1 diabetes. Evidence Based Nursing, 9, 14-14, 2006</td>
<td>Commentary</td>
</tr>
<tr>
<td>Pendley, J.S., Kasmen, L.L., Miller, D.L., Donze, J., Swenson, C., Reeves, G., Peer and family support in children and adolescents with type 1 diabetes, Journal of Pediatric Psychology, 27, 429-438, 2002</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (non-comparative study and therefore does not meet the study design inclusion criteria)</td>
</tr>
<tr>
<td>Powell, P.W., Hilliard, M.E., Anderson, B.J., Motivational interviewing to promote adherence behaviors in pediatric type 1 diabetes, Current Diabetes Reports, 14, 531−, 2014</td>
<td>This is a literature review</td>
</tr>
<tr>
<td>Ridge, K., Bartlett, J., Cheah, Y., Thomas, S., Lawrence-Smith, G., Winkley, K., Ismail, K., Do the effects of psychological treatments on improving glycemic control in type 1 diabetes persist over time? A long-term follow-up of a randomized controlled trial, Psychosomatic Medicine, 74, 319-323, 2012</td>
<td>Secondary publication</td>
</tr>
<tr>
<td>Sassmann, H., de Hair, M., Danne, T., Lange, K., Reducing stress and supporting positive relations in families of children with type 1 diabetes; a randomized controlled study for evaluating the effects of the DELFIN parenting program, BMC Pediatrics, 12, 152, 2012</td>
<td>Although families with children aged 2 to 10 years were selected for the study, the main target population of the intervention was parents; for outcomes related to children, only mean Hb1Ac at 3-month follow-up was reported</td>
</tr>
<tr>
<td>Scaramuzza, A., Castellani, G., Lorini, R., Insulin abuse in an adolescent with insulin-dependent diabetes mellitus, European Journal of Pediatrics, 155, 526−, 1996</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (this is a letter)</td>
</tr>
<tr>
<td>Schafer, L.C., Glasgow, R.E., McCaul, K.D., Increasing the adherence of diabetic adolescents, Journal of Behavioral Medicine, 5, 353-362, 1982</td>
<td>Included in 2004 guideline review - does not meet inclusion criteria for 2015 update review (case series, not an RCT)</td>
</tr>
<tr>
<td>Serlachius, A., Frydenberg, E., Northam, E., Cameron, F., A randomised trial of a psychosocial program to improve glycaemic control and psychosocial wellbeing in adolescents with type 1 diabetes, Pediatric Diabetes, 12, 20-, 2011</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Skocić-Milena, Rudan, Vlasta, Brajkovic-Lovorka, Marcinko, Darko, Relationship among psychopathological dimensions, coping mechanisms, and glycemic control in a Croatian sample of adolescents with diabetes mellitus type 1, European Child &amp; Adolescent Psychiatry, 19, 525-533, 2010</td>
<td>Wrong study design (cohort study not an RCT)</td>
</tr>
<tr>
<td>Sullivan-Bolyai, S., Grey, M., Deatrick, J., Gruppuso, P., Giralis, P., Tamborlane, W., Helping other mothers effectively work at raising young children with type 1 diabetes, Diabetes Educator, 30, 476-484, 2004</td>
<td>PICO not met - outcomes of interest not reported</td>
</tr>
<tr>
<td>Sundelin, J., Forsander, G., Mattsson, S.E., Family-oriented support at the onset of diabetes mellitus: a comparison of two group conditions during 2 years following diagnosis, Acta PaediatricaActa Paediatric., 85, 49-55, 1996</td>
<td>Included in 2004 guideline review â€“ does not meet inclusion criteria for 2015 update review (not intervention of...</td>
</tr>
</tbody>
</table>
H.4 Type 1 diabetes – multiple daily injections

Review question

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influence of intensive diabetes treatment on quality-of-life outcomes in the diabetes control and complications trial, Diabetes Care, 19, 195-203, 1996</td>
<td>PICO criteria not met - comparison is between 3 or more injections per day and 1-2 injections per day</td>
</tr>
<tr>
<td>Effect of intensive diabetes treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus: Diabetes Control and Complications Trial. Diabetes Control and Complications Trial Research Group, Journal of Pediatrics, 125, 177-188, 1994</td>
<td>PICO criteria not met - comparison is between 3 or more injections per day and 1-2 injections per day</td>
</tr>
<tr>
<td>Weight gain associated with intensive therapy in the diabetes control and complications trial. The DCCT Research Group, Diabetes Care, 11, 567-573, 1988</td>
<td>PICO criteria not met - comparison is between 3 or more injections per day and 1-2 injections per day</td>
</tr>
<tr>
<td>Effects of intensive diabetes therapy on neuropsychological function in adults in the Diabetes Control and Complications Trial, Annals of Internal Medicine, 124, 379-388, 1996</td>
<td>PICO criteria not met - comparison is between 3 or more injections per day and 1-2 injections per day</td>
</tr>
<tr>
<td>Acharya,S.H., Philip,S., Viswanath,A.K., Boroujerdi,M., Waugh,N.R., Pearson,D.W.M., Glycaemic control and body mass index in late-adolescents and young adults with Type 1 diabetes mellitus: A population-based study, Diabetic</td>
<td>PICO (Patient Intervention Comparator Outcome) criteria not met - age range is 15-25 years, data for insulin regimen comparisons not reported separately for guideline age range</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
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<tr>
<td>Medicine, 25, 360-364, 2008</td>
<td></td>
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<tr>
<td>Al-Khawari,M., Al-Ruwayeh,A., Al-Doub.K., Algrove,J., Adolescents on basal-bolus insulin can fast during Ramadan, Pediatric Diabetes, 11, 96-100, 2010</td>
<td>PICO criteria not met - participants are fasting during Ramadan with follow-up &lt; 4 months</td>
</tr>
<tr>
<td>Allen,C., LeCaire,T., Palta,M., Daniels,K., Meredith,M., D’Alessio,D.J., Wisconsin Diabetes Registry Project, Risk factors for frequent and severe hypoglycemia in type 1 diabetes, Diabetes Care, 24, 1878-1881, 2001</td>
<td>PICO criteria not met - comparison is between 3 or more injections per day or continuous subcutaneous insulin infusion (CSII) and less than 3 injections per day</td>
</tr>
<tr>
<td>Anderson,D.G., Multiple daily injections in young patients using the ezY-BICC bolus insulin calculation card, compared to mixed insulin and CSII, Pediatric Diabetes, 10, 304-309, 2009</td>
<td>PICO criteria not met - age range is 1-20 years and data for relevant comparisons not reported separately for guideline age range</td>
</tr>
<tr>
<td>Azar,S.T., Birbiri,A., Nocturnal blood pressure elevation in patients with type 1 diabetes receiving intensive insulin therapy compared with that in patients receiving conventional insulin therapy, Journal of Clinical Endocrinology and Metabolism, 83, 3190-3193, 1998</td>
<td>PICO criteria not met - comparison is between 2 and 3 or more injections per day</td>
</tr>
<tr>
<td>Azar,S.T., Zalloua,P.A., Zantout,M.S., Shahine,C.H., Salti,I., Leptin levels in patients with type 1 diabetes receiving intensive insulin therapy compared with those in patients receiving conventional insulin therapy, Journal of Endocrinological Investigation, 25, 724-726, 2002</td>
<td>PICO criteria not met - age range includes 18 years, guideline age range not reported separately</td>
</tr>
<tr>
<td>Bangstad,H.J., Danne,T., Deeb,L., Jarosz-Chobot,P., Urakami,T., Hanas,R., Insulin treatment in children and adolescents with diabetes, Pediatric Diabetes, 10, 82-99, 2009</td>
<td>Study criteria not met - consensus guideline</td>
</tr>
<tr>
<td>Baroni,M., Vialettes,B., Pozzilli,P., The glucose evaluation trial for remission (GETREM): A european effort to evaluate insulin-dependent diabetes mellitus in the first year after diagnosis, Diabetes and Metabolism, 23, 264-265, 1997</td>
<td>Study criteria not met - description of trial protocol only</td>
</tr>
<tr>
<td>Bayrakdar,A., Noureddin,S., Farhood,L., Nasrallah,M.P., Comparison of quality of life in a group of Lebanese type 1 diabetics on insulin pump and those on multiple daily injections, Journal Medical Libanais - Lebanese Medical Journal, 62, 22-26, 2014</td>
<td>The study does not show how many injections were given in the MDI group, wrong study design (cross-sectional study)</td>
</tr>
<tr>
<td>Blair,J.C., Peak,M., Gregory,J.W., What is the best way to deliver subcutaneous insulin to infants, children, and young people with type 1 diabetes mellitus?, BMJ (Online), 343, -, 2011</td>
<td>PICO criteria not met - continuous subcutaneous insulin infusion versus multiple daily injections</td>
</tr>
<tr>
<td>Blasetti,A., Di,Giulio C., Tocco,A.M., Verrotti,A., Tumini,S., Chiarelli,F., Altobelli,E., Variables associated with severe hypoglycemia in children and adolescents with type 1 diabetes: a population-based study, Pediatric Diabetes, 12, 4-10, 2011</td>
<td>PICO criteria not met - all participants were using multiple daily injections</td>
</tr>
<tr>
<td>Bloomgarden,Z.T., Diabetes issues in women and children, Diabetes Care, 26, 2457-2463, 2003</td>
<td>Study criteria not met - narrative review</td>
</tr>
<tr>
<td>Bolli,G.B., Rationale for using combinations of short-acting insulin analogue and NPH insulin at mealtime in the treatment of type 1 diabetes mellitus. [18 refs], Journal of Pediatric Endocrinology, 12 Suppl 3, 737-744, 1999</td>
<td>Study criteria not met - narrative review</td>
</tr>
<tr>
<td>Bulsara,M.K., Holman,C.D., Davis,E.A., Jones,T.W., The impact of a decade of changing treatment on rates of severe hypoglycemia in a population-based cohort of children with type 1 diabetes, Diabetes Care, 27, 2293-2298, 2004</td>
<td>PICO criteria not met - comparison is between 2 and 3 injections per day</td>
</tr>
</tbody>
</table>
Diagnosis and management of type 1 diabetes in children and young people

Excluded studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Callaghan,Brian C., Little,Ann A., Feldman,Eva L., Hughes,AC Richard, Enhanced glucose control for preventing and treating diabetic neuropathy, Cochrane Database of Systematic Reviews, - , 2012</td>
<td>PICO criteria not met - interventions are a mixture of advice, insulin, and pancreas transplant; data for young people included but not reported separately; references checked</td>
</tr>
<tr>
<td>Cengiz,E., Tamborlane,W.V., Martin-Frederiksen,M., Dziura,J., Weinzimer,S.A., Early pharmacokinetic and pharmacodynamic effects of mixing lispro with glargine insulin: results of glucose clamp studies in youth with type 1 diabetes, Diabetes Care, 33, 1009-1012, 2010</td>
<td>PICO criteria not met - follow-up &lt; 4 months</td>
</tr>
<tr>
<td>Centre for Reviews and Dissemination., Effect of intensive therapy on early macrovascular disease in young individuals with type 1 diabetes: a systematic review and meta-analysis (Structured abstract), Database of Abstracts of Reviews of Effects, - , 2012</td>
<td>PICO criteria not met - age range is 18-50 years</td>
</tr>
<tr>
<td>Chapman,T.M., Perry,C.M., Spotlight on insulin detemir in type 1 and 2 diabetes mellitus, Biodrugs, 19, 67-69, 2005</td>
<td>Study criteria not met - summary article; references checked</td>
</tr>
<tr>
<td>Chase,H.P., Rose,B., Hoops,S., Archer,P.G., Cribari,J.M., Techniques for improving glucose control in type 1 diabetes, Pediatrician, 12, 229-235, 1983</td>
<td>PICO criteria not met - number of injections per day not reported for all participants</td>
</tr>
<tr>
<td>Chase,H.P., Dixon,B., Pearson,J., Fiallo-Scharer,R., Walravens,P., Klingensmith,G., Rewers,M., Garg,S.K., Reduced hypoglycemic episodes and improved glycemic control in children with type 1 diabetes using insulin glargine and neutral protamine Hagedorn insulin, Journal of Pediatrics, 143, 737-740, 2003</td>
<td>PICO criteria not met - participants had a mixture of treatments before switching to basal-bolus regimen but these were not reported separately</td>
</tr>
<tr>
<td>Chase,H.P., Garg,S.K., Hoops,S.L., Harris,S., Wilcox,W., Use of the pen delivery system for intensive insulin therapy in college-age students with type I diabetes, Journal of Adolescent Health, 12, 373-376, 1991</td>
<td>PICO criteria not met - age range includes 18 years, but data for guideline age range not reported separately</td>
</tr>
<tr>
<td>Clarke,W.L., The Diabetes Control and Complications Trial: new challenges for the primary physician, Virginia Medical Quarterly, 121, 185-188, 1994</td>
<td>PICO criteria not met - multiple daily injections defined as 3 injections per day</td>
</tr>
<tr>
<td>Da,Silva,Jose!, Cardoso-Demartini,A.D.A., Liberatore,Junior,R. Paulino,M.F.V.M., De,Lemos Marini,S. Guerra-Junior,G., Rodrigues,A.G., Clinical and laboratory profile of pediatric and adolescent patients with type 1 diabetes, Jornal de Pediatria, 85, 490-494, 2009</td>
<td>PICO criteria not met - participants received 1, 2 or 3 injections per day; age range is 3-26 years</td>
</tr>
<tr>
<td>DAFNE Study Group, Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: dose adjustment for normal eating (DAFNE) randomised controlled trial, BMJ, 746-748, 2002</td>
<td>PICO criteria not met - age range is 18 years or older</td>
</tr>
</tbody>
</table>
### Excluded studies

#### Diagnosis and management of type 1 diabetes in children and young people

**Table:**

<table>
<thead>
<tr>
<th>Study</th>
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<tbody>
<tr>
<td>Dahl-Jorgensen, K., Torjesen, P., Hanssen, K.F., Sandvik, L., Aagenaes, O., Increase in insulin antibodies during continuous subcutaneous insulin infusion and multiple-injection therapy in contrast to conventional treatment, Diabetes, 1-5, 1987</td>
<td>PICO criteria not met - comparison is between 1 and 2 injections per day</td>
</tr>
<tr>
<td>Dej, Beaufort, C. Hypoglycemia during intensified insulin therapy of young children, Journal of Pediatric Endocrinology and Metabolism, 11, 153-158, 1998</td>
<td>PICO criteria not met - comparison is between 1-2 and 3 or more injections per day</td>
</tr>
<tr>
<td>Deiss, D., Kordonouri, O., Hartmann, R., Hopfenmuller, W., Lupke, K., Danne, T., Treatment with insulin glargine reduces asymptomatic hypoglycemia detected by continuous subcutaneous glucose monitoring in children and adolescents with type 1 diabetes, Pediatric Diabetes, 8, 157-162, 2007</td>
<td>PICO criteria not met - follow up &lt; 4 months</td>
</tr>
<tr>
<td>Deja, G., Jarosz-Chobot, P., Polanska, J., The rate of improvement in metabolic control in children with diabetes mellitus type 1 on insulin glargine depends on age, Experimental and Clinical Endocrinology and Diabetes, 115, 662-668, 2007</td>
<td>PICO criteria not met - comparison is between two versions of a multiple daily injection regimen</td>
</tr>
<tr>
<td>Downie, E., Craig, M.E., Hing, S., Cusumano, J., Chan, A.K., Donaghue, K.C., Continued reduction in the prevalence of retinopathy in adolescents with type 1 diabetes: role of insulin therapy and glycemic control, Diabetes Care, 34, 2368-2373, 2011</td>
<td>PICO criteria not met - multiple daily injections defined as 3 injections per day and results combined with those for CSII</td>
</tr>
<tr>
<td>Dunn, C.J., Plosker, G.L., Keating, G.M., McKeage, K., Scott, L.J., Insulin glargine: an updated review of its use in the management of diabetes mellitus, [111 refs], Drugs, 63, 1743-1777, 2008</td>
<td>PICO criteria not met - comparison is between two multiple daily injection regimens</td>
</tr>
<tr>
<td>Egger, M., Smith, G.D., Stettler, C., Diem, P., Risk of adverse effects of intensified treatment in insulin-dependent diabetes mellitus: a meta-analysis, Diabetic Medicine, 919-928, 1997</td>
<td>PICO criteria not met - all included trials are in adults (outside guideline age range)</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
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<td>---------------------------------------------------------------------</td>
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<tr>
<td>Fasching, P., Derfler, K., Maca, T., Kurzemmann, S., Howorka, K., Schneider, B., Zirm, M., Waldhausl, W.</td>
<td>PICO criteria not met - age range is 8-57 years</td>
</tr>
<tr>
<td>Franklin, V.L., Khan, F., Kennedy, G., Belch, J.J., Greene, S.A.</td>
<td>PICO criteria not met - cannot separate CSII and multiple daily injection results</td>
</tr>
<tr>
<td>Franklin, V.L., Waller, A., Pagliari, C., Greene, S.A., A randomized controlled trial of Sweet Talk, a text-messaging system to support young people with diabetes, Diabetic Medicine, 23, 1332-1338, 2006</td>
<td>PICO criteria not met - cannot separate CSII and multiple daily injection results</td>
</tr>
<tr>
<td>Garg, S.K., Carmain, J.A., Braddy, K.C., Anderson, J.H., Vignati, L., Jennings, M.K., Chase, H.P., Pre-meal insulin analogue insulin lispro vs Humulin R insulin treatment in young subjects with type 1 diabetes, Diabetic Medicine, 13, 47-52, 1996</td>
<td>PICO criteria not met - age range includes 18 years, with the guideline age range not reported separately</td>
</tr>
<tr>
<td>Garnock-Jones, K.P., Plosker, G.L., Insulin glulisine: A review of its use in the management of diabetes mellitus, Drugs, 69, 1035-1057, 2009</td>
<td>PICO criteria not met - comparison is between two multiple daily injection regimens</td>
</tr>
<tr>
<td>Gerstl, E.M., Rabi, W., Rosenbauer, J., Grobe, H., Hofer, S.E., Krause, U., Holl, R.W., Metabolic control as reflected by HbA1c in children, adolescents and young adults with type-1 diabetes mellitus: Combined longitudinal analysis including 27,035 patients from 207 centers in Germany and Austria during the last decade, European Journal of Pediatrics, 167, 447-453, 2008</td>
<td>PICO criteria not met - no data reported on insulin regimens</td>
</tr>
<tr>
<td>Gibb, D.M., Foot, A.B., May, B., Parish, H., Strang, S., Grant, D.B., Dunger, D.B., Human isophane or lente insulin? A double blind crossover trial in insulin dependent diabetes mellitus, Archives of Disease in Childhood, 65, 1334-1337, 1990</td>
<td>PICO criteria not met - both treatment arms received &lt; 4 injections per day</td>
</tr>
<tr>
<td>Golenko, A., Noczyńska, A., An evaluation of physical development and metabolic control in children with type 1 diabetes mellitus receiving treatment with various insulin regimens. Part 1, Diabetologia Doswiadamczalna i Kliniczna, 8, 115-123, 2008</td>
<td>PICO criteria not met - number of injections not reported</td>
</tr>
<tr>
<td>Granado, F., Olmedilla, B., Botella, F., Simal, A., Blanco, I.,</td>
<td>PICO criteria not met - age range is 14-35 years</td>
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<tr>
<td>Study</td>
<td>Reason for exclusion</td>
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<tr>
<td>Retinol and alpha-tocopherol in serum of type 1 diabetic patients with intensive insulin therapy: a long term follow-up study, Nutrition, 19, 128-132, 2003</td>
<td>PICO criteria not met - data reported for 2 and 3 injections per day only</td>
</tr>
<tr>
<td>Greene, S.A., Robertson, L., Royle, P., Robertson, A., Waugh, N., Rae, P., Patterson, C., A longitudinal observational study of insulin therapy and glycaemic control in Scottish children with Type 1 diabetes: DIABAUD 3, Diabetic Medicine, 23, 1216-1221, 2006</td>
<td></td>
</tr>
<tr>
<td>Grey, M., Boland, E.A., Tamborlane, W.V., Use of lispro insulin and quality of life in adolescents on intensive therapy, Diabetes Educator, 25, 934-941, 1999</td>
<td>PICO criteria not met - comparison is between two versions of a multiple daily injection regimen</td>
</tr>
<tr>
<td>Hanberger, L., Ludvigsson, J., Nordfeldt, S., Health-related quality of life in intensively treated young patients with type 1 diabetes, Pediatric Diabetes, 10, 374-381, 2009</td>
<td>Incomplete data for comparisons of interest</td>
</tr>
<tr>
<td>Hayes, R.L., Garnett, S.P., Clarke, S.L., Harkin, N.M., Chan, A.K., Ambler, G.R., A flexible diet using an insulin to carbohydrate ratio for adolescents with type 1 diabetes - a pilot study, Clinical Nutrition, 31, 705-709, 2012</td>
<td>PICO criteria not met - all participants were using multiple daily injections</td>
</tr>
<tr>
<td>Hecker, W., Grabert, M., Holl, R.W., Quality of paediatric IDDM care in germany: A multicentre analysis, Journal of Pediatric Endocrinology and Metabolism, 12, 31-38, 1999</td>
<td>PICO criteria not met - no comparative data reported</td>
</tr>
<tr>
<td>Hershey, T, Bhargava, N, Sadler, M, White, N.H., Craft, S, Conventional versus intensive diabetes therapy in children with type 1 diabetes: effects on memory and motor speed, Diabetes Care, 1318-1324, 1999</td>
<td>PICO criteria not met - comparison is between 3 or more injections per day and 1-2 injections per day</td>
</tr>
<tr>
<td>Holman, RR, Mayon-White, V, Orde-Peckar, C, Steemson, J, Smith, B, McPerson, K, Prevention of deterioration of renal and sensory-nervous function by more intensive management of insulin-dependent diabetic patients. A two-year randomised prospective study, Lancet, 204-208, 1983</td>
<td>PICO criteria not met - age range is 21-60 years</td>
</tr>
<tr>
<td>HOSTOMSKA, L., KOPECKY, A., Insulin mixtures in the treatment of diabetes in children, Review of Czechoslovak Medicine, 2, 261-264, 1956</td>
<td>PICO criteria not met - no comparisons of interest reported</td>
</tr>
<tr>
<td>Houtzagers, C.M., van, der, V, Multiple daily insulin injections: a multicentre study on acceptability and efficacy, Netherlands Journal of Medicine, 33, 16-25, 1988</td>
<td>PICO criteria not met - age range is 14-70 years, and follow-up &lt; 4 months</td>
</tr>
<tr>
<td>Houtzagers, CM, Bernsten, PA, van der Stap, H, van Maarschalkerweerd, WW, Lanting, P, Boen-Tan, I, Efficacy and acceptance of two intensified conventional insulin therapy regimens: a long-term cross-over comparison, Diabetic Medicine, 416-421, 1989</td>
<td>PICO criteria not met - age range is 18-63 years</td>
</tr>
<tr>
<td>Houtzagers, CM, Visser, SP, Bernsten, PA, van der Stap, H, van Maarschalkerweerd, WW, Heine, RJ, Multiple daily insulin injections improve self-confidence, Diabetic Medicine, 512-519, 1989</td>
<td>PICO criteria not met - age range is 18-65 years</td>
</tr>
<tr>
<td>Institut fuer Qualitaet und Wirtschaftlichkeit im, Gesundheitswesen., Rapid-acting insulin analogues in the treatment of diabetes mellitus type 1 (Structured abstract), Health Technology Assessment Database, - , 2012</td>
<td>Non-English language</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
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<tr>
<td>Jabbari,M., Bin-Abbas,B., Al-Fares,A., Basal-bolus insulin regimen using insulin detemir in type 1 diabetic Saudi children, Current Pediatric Research, 14, 108-110, 2010</td>
<td>PICO criteria not met - follow-up &lt; 4 months, &lt; 10 participants</td>
</tr>
<tr>
<td>Jackson,A., Ternand,C., Brunzell,J., Kleinschmidt,T., Dew,D., Milla,C., Moran,A., Insulin glargine improves hemoglobin A1c in children and adolescents with poorly controlled type 1 diabetes, Pediatric Diabetes, 4, 64-69, 2003</td>
<td>PICO criteria not met - comparison is between two versions of a multiple daily injection regimen</td>
</tr>
<tr>
<td>Jarosz-Chobot,P., Guthrie,D.W., Otto-Buczkowska,E., Koehler,B., Self-care of young diabetics in practice, Medical Science Monitor, 6, 129-132, 2000</td>
<td>PICO criteria not met - details of insulin regimens not reported</td>
</tr>
<tr>
<td>Karaguzel,G., Satilmis,A., Akcurin,S., Bircan,I., Comparison of breakfast and bedtime administration of insulin glargine in children and adolescents with Type 1 diabetes, Diabetes Research and Clinical Practice, 74, 15-20, 2006</td>
<td>PICO criteria not met - comparison is between two versions of a multiple daily injection regimen</td>
</tr>
<tr>
<td>Katz,M.L., Volkening,L.K., Anderson,B.J., Lafel,L.M., Contemporary rates of severe hypoglycaemia in youth with Type 1 diabetes: variability by insulin regimen, Diabetic Medicine, 29, 926-932, 2012</td>
<td>PICO criteria not met - number of injections not stated and regimens unclear</td>
</tr>
<tr>
<td>Khadilkar,V.V., Khadilkar,A.V., Concomitant use of insulin glargine and NPH in type 1 diabetes, Indian Pediatrics, 42, 796-800, 2005</td>
<td>PICO criteria not met - comparison is between two regimens of 2 injections per day</td>
</tr>
<tr>
<td>Kimura,S., Nose,O., Tajiir,H., Miki,K., Yabuschi,H., Shichiri,M., Harada,T., Efficacy of a multiple insulin injection regimen in teenagers with insulin-dependent diabetes. Carbohydrate and lipid oxidation measured by continuous indirect calorimetry, Diabetes Research and Clinical Practice, 4, 77-79, 1987</td>
<td>Study criteria not met - &lt; 10 participants</td>
</tr>
<tr>
<td>Knerr,I., Hofer,S.E., Holterhus,P.M., Nake,A., Rosenbauer,J., Weitzel,D., Wolf,J., Holl,R.W., Prevailing therapeutic regimes and predictive factors for prandial insulin substitution in 26 687 children and adolescents with Type 1 diabetes in Germany and Austria, Diabetic Medicine, 24, 1478-1481, 2007</td>
<td>Study criteria not met - no age range reported separately</td>
</tr>
<tr>
<td>Lawson,M.L., Gerstein,H.C., Tsui,E., Zinnman,B., Effect of intensive therapy on early macrovascular disease in young individuals with type 1 diabetes. A systematic review and meta-analysis, Diabetes Care, 22 Suppl 2, B35-B39, 1999</td>
<td>PICO criteria not met - all included trials were in adults</td>
</tr>
<tr>
<td>Limbert,C., Schwinghandl,J., Haas,J., Roth,R., Borkenstein,M., Severe hypoglycaemia in children and adolescents with IDDM: frequency and associated factors, Journal of Diabetes and its Complications, 7, 216-220, 1993</td>
<td>PICO criteria not met - age range is 4-25 years</td>
</tr>
<tr>
<td>Linn,T., Orta,K., Laube,H., Federlin,K., Intensive therapy in adult insulin-dependent diabetes mellitus is associated with improved insulin sensitivity and reserve: a randomized, controlled, prospective study over 5 years in newly diagnosed patients, Metabolism: Clinical and Experimental, 45, 1508-1513, 1996</td>
<td>PICO criteria not met - comparison is between 3 or more injections per day and 1-2 injections per day</td>
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<tr>
<td>McCaughey,E.S., Betts,P.R., Rowe,D.J., Improved diabetic control in adolescents using the Penject syringe for multiple insulin injections. Diabetic Medicine, 3, 234-236, 1986</td>
<td>PICO criteria not met - length of follow-up &lt; 4 months</td>
</tr>
<tr>
<td>McKeage,K., Goo,K.L., Insulin glargine: a review of its therapeutic use as a long-acting agent for the management of type 1 and 2 diabetes mellitus. [70 refs], Drugs, 61, 1599-1624, 2001</td>
<td>PICO criteria not met - comparison is between two multiple daily injection regimens</td>
</tr>
<tr>
<td>Menon,P.S.N., Virmani,A., Rationale of insulin therapy in insulin-dependent diabetes mellitus in children, Indian Pediatrics, 27, 1201-1208, 1990</td>
<td>Study criteria not met - narrative review</td>
</tr>
<tr>
<td>Microalbuminuria Collaborative Study Group, Intensive therapy and progression to clinical albuminuria in patients with insulin-dependent diabetes mellitus and microalbuminuria, BMJ, 973-977, 1995</td>
<td>PICO criteria not met - age range 17-59 years</td>
</tr>
<tr>
<td>Mohn,A., Strang,S., Wernicke-Panten,K., Lang,A.M., Edge,J.A., Dunger,D.B., Nocturnal glucose control and free insulin levels in children with type 1 diabetes by use of the long-acting insulin HOE 901 as part of a three-injection regimen, Diabetes Care, 23, 557-559, 2000</td>
<td>PICO criteria not met - both treatment arms include fewer than 4 injections per day</td>
</tr>
<tr>
<td>Mortensen,H.B., Outcome of quality management in pediatric diabetes care, Hormone Research, 50, 57-61, 1998</td>
<td>Incomplete data for comparisons of interest</td>
</tr>
<tr>
<td>Mortensen,H.B., Villumsen,J., Volund,A., Petersen,K.E., Nerup,J., Relationship between insulin injection regimen and metabolic control in young Danish type 1 diabetic patients. The Danish Study Group of Diabetes in Childhood, Diabetic Medicine, 9, 834-839, 1992</td>
<td>PICO criteria not met - multiple daily injections defined as 3 injections per day</td>
</tr>
<tr>
<td>Muhlhauser,I., Bruckner,I., Berger,M., Cheta,D., Jorgens,V., Ionescu-Tirgoviste,C., Scholz,V., Mincu,I., Evaluation of an intensified insulin treatment and teaching programme as routine management of type 1 (insulin-dependent) diabetes. The Bucharest-Dusseldorf Study, Diabetologia, 30, 681-690, 1987</td>
<td>PICO criteria not met - comparison is between 2 and &gt; 2 injections per day</td>
</tr>
<tr>
<td>Nathan,D.M., McKirrick,C., Larkin,M., Schaffran,R., Singer,D.E., Glycemic control in diabetes mellitus: Have changes in therapy made a difference?, American Journal of Medicine, 100, 157-163, 1996</td>
<td>PICO criteria not met - age range includes over 18 years, data for relevant comparisons not reported separately for guideline age range</td>
</tr>
<tr>
<td>Nguyen,T.M., Renukuntla,V.S., Heptulla,R.A., Mixing insulin aspart with detemir does not affect glucose excursion in children with type 1 diabetes, Diabetes Care, 33, 1750-1752, 2010</td>
<td>PICO criteria not met - follow-up &lt; 4 months</td>
</tr>
<tr>
<td>Ollenschlaeger,G, Hummerich,W, Stetten,M, Reincke,M, Allolio,B, Winkelmann,W, Management and efficacy of intensified insulin therapy - starting in outpatients, Klinische</td>
<td>PICO criteria not met - mean age of participants outside guideline age range</td>
</tr>
</tbody>
</table>
### Excluded studies

<table>
<thead>
<tr>
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<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wochenschrift, 60-65, 1989</td>
<td>Incomplete data for comparisons of interest</td>
</tr>
<tr>
<td>Olsen, B.S., Johanesen, J., Sjolie, A.K., Borch-Johnsen, K., Hougaard, P., Thorsteinsson, B., Premming, S., Marinelli, K., Mortensen, H.B., Metabolic control and prevalence of microvascular complications in young Danish patients with Type 1 diabetes mellitus, Diabetic Medicine, 16, 79-85, 1999</td>
<td>PICO criteria not met - no information on insulin regimens reported</td>
</tr>
<tr>
<td>Pais, V., Burkot, I., Buccino, D., Daneman, D., Is there a relationship between type of insulin regimen and dietary intake in adolescents with type 1 diabetes?, Canadian Journal of Diabetes, 34, 334-339, 2010</td>
<td>PICO criteria not met - no relevant comparisons reported</td>
</tr>
<tr>
<td>Paleta, M., Shen, G., Allen, C., Klein, R., D'Alessio, D., Longitudinal patterns of glycemic control and diabetes care from diagnosis in a population-based cohort with type 1 diabetes, American Journal of Epidemiology, 144, 954-961, 1996</td>
<td>Non-English language</td>
</tr>
<tr>
<td>Paus, P.N., Jervell, J., Berg, T.J., Frost, T., Larsen, S., NovoPen. An aid in multi-injection insulin therapy], Tidsskrift for den Norske Laegeforening : tidsskrift for praktisk medicin, ny række, 106, 1943-1946, 1986</td>
<td>This study is an observational study</td>
</tr>
<tr>
<td>Pieber, T.R., Treichel, H.C., Hompesch, B., Philotheou, A., Mordhorst, L., Gall, M.A., Robertson, L.I., Comparison of insulin detemir and insulin glargine in subjects with Type 1 diabetes using intensive insulin therapy, Diabetic Medicine, 24, 635-642, 2007</td>
<td>PICO criteria not met - age range is 18 years and older</td>
</tr>
<tr>
<td>Rabbone, I., Scaramuzzo, A.E., Ignaccolo, M.G., Tinti, D., Sicignano, S., Redaelli, F., De, Angelis L., Bosetti, A., Zuccotti, G.V., Cerutti, F., Carbohydrate counting with an automated bolus calculator helps to improve glycaemic control in children with type 1 diabetes using multiple daily injection therapy: an 18-month observational study, Diabetes Research and Clinical Practice, 103, 388-394, 2014</td>
<td>PICO criteria not met - mean age of participants is outside guideline age range</td>
</tr>
<tr>
<td>Reichard, P., Berglund, A., Britz, A., Levander, S., Rosenqvist, U., Hypoglycaemic episodes during intensified insulin treatment: increased frequency but no effect on cognitive function, Journal of Internal Medicine, 9-16, 1991</td>
<td>PICO criteria not met - mean age of participants is outside guideline age range</td>
</tr>
<tr>
<td>Rewers, M., Pihoker, C., Donagheue, K., Hanas, R., Swift, P., Klingensmith, G.J., Assessment and monitoring of glycemic control in children and adolescents with diabetes, Pediatric Diabetes, 10, 71-81, 2009</td>
<td>PICO criteria not met - comparison is between two multiple daily injection regimens</td>
</tr>
<tr>
<td>Reynolds, N.A., Wagstaff, A.J., Insulin aspart: a review of its use in the management of type 1 or 2 diabetes mellitus. [63 refs], Drugs, 64, 1957-1974, 2004</td>
<td>PICO criteria not met - age range is 18 years and older</td>
</tr>
<tr>
<td>Rogers, D.G., The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus, Clinical Pediatrics, 33, 378-, 1994</td>
<td>Study criteria not met - commentary article</td>
</tr>
<tr>
<td>Rosenbauer, J., Dost, A., Karges, B., Huglele, A., Stahl, A., Bachle, C., Gerstl, E.M., Kastendieck, C., Hofer, S.E., Holt, R.W., DPV Initiative and the German BMBF Competence Network Diabetes Mellitus., Improved metabolic control in children and adolescents with type 1 diabetes: a trend analysis using prospective multicenter data from Germany and Austria, Diabetes Care, 35, 80-86, 2012</td>
<td>PICO criteria not met - age of participants is &lt;20 years, data for comparison of interest not reported separately for guideline age range</td>
</tr>
<tr>
<td>Rosengren, A., Adlerberth, A., Bresater, L.E., Ehnborg, S., Weim, L., Multiple insulin injection therapy using an insulin pen - who benefits? A clinical 3-year follow-up study of 100 type 1 and 51 type 2 diabetic patients, Diabetes Research and Practice, 39, 2014</td>
<td>PICO criteria not met - age range is 17-72 years</td>
</tr>
</tbody>
</table>
Excluded studies

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
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<tr>
<td>and Clinical Practice, 20, 69-74, 1993</td>
<td>Study criteria not met - &lt; 10 participants</td>
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<tr>
<td>Rosilio,M., Cotton,J.B., Wieliczko,M.C., Gendrault,B., Carel,J.C.,</td>
<td>PICO criteria not met - comparison is between 1-2 and &gt; 3 injections per day</td>
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<td>Couvras,O., Ser.,N., Gillet,P., Sooskin,S., Garandeau,P., Stockens,C.,</td>
<td></td>
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<td>Luyer,B.L., Jos,J., Bony-Trifunovic,H., Bertrand,A.M., Leturcq,F.,</td>
<td></td>
</tr>
<tr>
<td>Lafuma,A., Bougneres,P.F., Factors associated with glycemic control: A</td>
<td></td>
</tr>
<tr>
<td>cross-sectional nationwide study in 2,579 French children with type 1</td>
<td></td>
</tr>
<tr>
<td>diabetes, Diabetes Care, 21, 1146-1153, 1998</td>
<td></td>
</tr>
<tr>
<td>Rosilio,M., Cotton,J.B., Wieliczko,M.C., Gendrault,B., Carel,J.C.,</td>
<td>PICO criteria not met - data reported for 2 versus 3 injections per day only</td>
</tr>
<tr>
<td>Couvras,O., Ser.,N., Gillet,P., Sooskin,S., Garandeau,P., Stockens,C.,</td>
<td></td>
</tr>
<tr>
<td>Luyer,B.L., Jos,J., Bony-Trifunovic,H., Bertrand,A.M., Leturcq,F.,</td>
<td></td>
</tr>
<tr>
<td>Lafuma,A., French Pediatric Diabetes Group, Bougneres,P.F., Factors</td>
<td></td>
</tr>
<tr>
<td>associated with glycemic control: A cross-sectional nationwide study</td>
<td></td>
</tr>
<tr>
<td>in 2,579 French children with type 1 diabetes. The French Pediatric</td>
<td></td>
</tr>
<tr>
<td>Diabetes Group, Diabetes Care, 21, 1146-1153, 1998</td>
<td></td>
</tr>
<tr>
<td>Rudolf,M.C., Sherwin,R.S., Markowitz,R., Bates,S.E., Genel,M.,</td>
<td>Study criteria not met - narrative review</td>
</tr>
<tr>
<td>Hochstadt,J., Tamborlane,W.V., Effect of intensive insulin treatment</td>
<td>Study criteria not met - &lt; 10 participants</td>
</tr>
<tr>
<td>on linear growth in the young diabetic patient, Journal of Pediatrics,</td>
<td></td>
</tr>
<tr>
<td>101, 333-339, 1982</td>
<td>Study criteria not met - narrative review</td>
</tr>
<tr>
<td>Salardi,S., Cacciari,E., Zucchini,S., Donati,S., Steri,L., Gualandi,</td>
<td>PICO criteria not met - multiple daily injections versus CSII</td>
</tr>
<tr>
<td>S., Mazzanti,L., Calliwa,R., Modifications of metabolic control in</td>
<td></td>
</tr>
<tr>
<td>type 1 diabetic children and adolescents: experience over the last 20</td>
<td></td>
</tr>
<tr>
<td>years, Journal of Pediatric Endocrinology, 10, 569-578, 1997</td>
<td></td>
</tr>
<tr>
<td>Schober,E., Schoenle,E., Van,Dyk J., Wernicke-Panten,K., Pediatric</td>
<td>PICO criteria not met - comparison is between two multiple daily injection</td>
</tr>
<tr>
<td>Study Group of Insulin Glargine, Comparative trial between insulin</td>
<td>regimens</td>
</tr>
<tr>
<td>glargine and NPH insulin in children and adolescents with type 1</td>
<td></td>
</tr>
<tr>
<td>diabetes, Diabetes Care, 24, 2005-2006, 2001</td>
<td></td>
</tr>
<tr>
<td>Schober,E., Schoenle,E., Van,Dyk J., Wernicke-Panten,K., Pediatric</td>
<td>PICO criteria not met - comparison is between two multiple daily injection</td>
</tr>
<tr>
<td>Study Group of Insulin Glargine., Comparative trial between insulin</td>
<td>regimens</td>
</tr>
<tr>
<td>glargine and NPH insulin in children and adolescents with type 1</td>
<td></td>
</tr>
<tr>
<td>diabetes mellitus, Journal of Pediatric Endocrinology, 15, 989-376,</td>
<td></td>
</tr>
<tr>
<td>2002</td>
<td></td>
</tr>
<tr>
<td>Shah,S.C., Malone,J.I., Simpson,N.E., A randomized trial of intensive</td>
<td>PICO criteria not met - is between 2 injections per day and continuous subcutaneous</td>
</tr>
<tr>
<td>insulin therapy in newly diagnosed insulin-dependent diabetes mellitus,</td>
<td>insulin infusion</td>
</tr>
<tr>
<td>New England Journal of Medicine, 320, 550-554, 1989</td>
<td>Study criteria not met - abstract only</td>
</tr>
<tr>
<td>Shalitin,S., Phillip,M., Which factors predict glycemic control in</td>
<td>PICO criteria not met - is between multiple daily injections and CSII</td>
</tr>
<tr>
<td>children diagnosed with type 1 diabetes before 6.5 years of age?, Acta</td>
<td></td>
</tr>
<tr>
<td>Diabetologica, 49, 355-362, 2012</td>
<td>Study criteria not met - abstract only</td>
</tr>
<tr>
<td>Shamoon,H., Duffy,H., Fleischer,N., Engel,S., Saenger,P., Strelzyn,M.,</td>
<td>PICO criteria not met - is between 3 or more injections per day and 1-2 injections</td>
</tr>
<tr>
<td>Litwak,M., Wylie-Rosett,J., Farkash,A., Geiger,D., Engel,H.,</td>
<td>per day</td>
</tr>
<tr>
<td>Fleischman,J., Pompi,D., Ginsberg,N., Glover,M., Brisman,M., Walker,E.,</td>
<td></td>
</tr>
<tr>
<td>Thomashunis,A., Gonzalez,J., The effect of intensive treatment of</td>
<td></td>
</tr>
<tr>
<td>diabetes on the development and progression of long-term complications</td>
<td></td>
</tr>
<tr>
<td>in insulin-dependent diabetes mellitus, New England Journal of</td>
<td></td>
</tr>
<tr>
<td>Medicine, 329, 977-986, 1993</td>
<td></td>
</tr>
<tr>
<td>Shukla,V.K., Otten,N., Insulin lispro: a critical evaluation (</td>
<td>Study criteria not met - abstract only</td>
</tr>
<tr>
<td>Structured abstract), Health Technology Assessment Database, -, 2012</td>
<td>Study criteria not met - abstract only</td>
</tr>
<tr>
<td>Simpson,D., McCormack,P.L., Keating,G.M., lyseng-Williamson,K.A.,</td>
<td>PICO criteria not met - is between two multiple daily injection regimens</td>
</tr>
<tr>
<td>Insulin lispro: A review of its use in the management of diabetes</td>
<td>Study criteria not met - abstract only</td>
</tr>
<tr>
<td>mellitus, Drugs, 67, 407-454, 2007</td>
<td>Study criteria not met - abstract only</td>
</tr>
<tr>
<td>Siu,A., Poon,C.Y., Pharmacologic management in pediatric type 1</td>
<td>Study criteria not met - abstract only</td>
</tr>
<tr>
<td>diabetes mellitus, U.S, 33, - , 2008</td>
<td>Study criteria not met - abstract only</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
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<td>Small,M., MacRury,S., Boal,A., Paterson,KR, MacCuish,AC,</td>
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<td>Comparison of conventional twice daily subcutaneous insulin</td>
<td></td>
</tr>
<tr>
<td>administration and a multiple injection regimen (using the NovoPen)</td>
<td></td>
</tr>
<tr>
<td>in insulin-dependent diabetes mellitus, Diabetes Research, 85-89,</td>
<td></td>
</tr>
<tr>
<td>1988</td>
<td></td>
</tr>
<tr>
<td>Smith,C.P., Dunger,D.B., Mitten,S., Hewitt,J., Spowart,K.,</td>
<td>PICO criteria not met - follow-up &lt; 4 months</td>
</tr>
<tr>
<td>Grant,D.B., Savage,M.O., A comparison of morning and</td>
<td></td>
</tr>
<tr>
<td>bed-time ultralente administration when using multiple</td>
<td></td>
</tr>
<tr>
<td>injections in adolescence, Diabetic Medicine, 5, 352-355, 1988</td>
<td></td>
</tr>
<tr>
<td>Soliman,A.T., Omar,M., Rizk,M.M., El Awwa A.,</td>
<td>PICO criteria not met - both treatment arms received fewer than 4 injections per day</td>
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<tr>
<td>AlGhobashy,F.M., Glycaemic control with modified intensive</td>
<td></td>
</tr>
<tr>
<td>insulin injections (MII) using insulin pens and premixed insulin</td>
<td></td>
</tr>
<tr>
<td>in children with type-1 diabetes: a randomized controlled trial,</td>
<td></td>
</tr>
<tr>
<td>Journal of Tropical Pediatrics, 52, 276-281, 2006</td>
<td></td>
</tr>
<tr>
<td>Srinivasan,B., Davies,M., Lawrence,I., Diabetes: glycaemic control</td>
<td>PICO criteria not met - multiple daily injections versus CSII</td>
</tr>
<tr>
<td>in type 1, Clinical Evidence, 2008, 2008, -. 2008</td>
<td></td>
</tr>
<tr>
<td>Sundelin,J., Forsander,G., Mattson,S.E., Family-oriented</td>
<td>PICO criteria not met - educational intervention</td>
</tr>
<tr>
<td>support at the onset of diabetes mellitus: a comparison of two</td>
<td></td>
</tr>
<tr>
<td>group conditions during 2 years following diagnosis,</td>
<td></td>
</tr>
<tr>
<td>Acta Paediatrica, 85, 49-55, 1996</td>
<td></td>
</tr>
<tr>
<td>Svensson,J., Johannesen,J., Mortensen,H.B., Nordly,S., Improved</td>
<td>PICO criteria not met - no direct comparisons of interventions of interest</td>
</tr>
<tr>
<td>metabolic outcome in a Danish diabetic paediatric population aged</td>
<td></td>
</tr>
<tr>
<td>0-18 yr: Results from a nationwide continuous Registration,</td>
<td></td>
</tr>
<tr>
<td>Pediatric Diabetes, 10, 461-467, 2006</td>
<td></td>
</tr>
<tr>
<td>Svoren,B.M., Volkening,L.K., Butler,D.A., Moreland,E.C.,</td>
<td>PICO criteria not met - multiple daily injections defined as 3 or more injections per</td>
</tr>
<tr>
<td>Anderson,B.J., Laffel,L.M., Temporal trends in the treatment of</td>
<td>day</td>
</tr>
<tr>
<td>pediatric type 1 diabetes and impact on acute outcomes,</td>
<td></td>
</tr>
<tr>
<td>Swift,P.G., Diabetes in the young: from Leicester to Siena</td>
<td>Study criteria not met - narrative review</td>
</tr>
<tr>
<td>(via Oslo, Bethesda and Hvidore), Acta Bio-Medica de l Ateneo</td>
<td></td>
</tr>
<tr>
<td>Parmense, 76 Suppl 3, 7-13, 2005</td>
<td></td>
</tr>
<tr>
<td>Swift,P.G., Kennedy,J.D., Gerlis,L.S., Change to U-100 insulin</td>
<td>PICO criteria not met - follow-up &lt; 4 months</td>
</tr>
<tr>
<td>does not appear to affect insulin absorption, British Medical</td>
<td></td>
</tr>
<tr>
<td>Journal Clinical Research Ed., 286, 1015,-, 1983</td>
<td></td>
</tr>
<tr>
<td>Tan,S.H., Lee,B.W., The use of twice-daily insulin regimes in</td>
<td>PICO criteria not met - comparison is between 1 and 2 injections per day</td>
</tr>
<tr>
<td>insulin-dependent diabetic children, Journal of the Singapore</td>
<td></td>
</tr>
<tr>
<td>Paediatric Society, 25, 70-74, 1983</td>
<td></td>
</tr>
<tr>
<td>The Writing Team for the Diabetes Control and Complications</td>
<td>PICO criteria not met - comparison is between 3 or more injections per day and 1-2</td>
</tr>
<tr>
<td>Trial/Epidemiology of Diabetes Interventions and Complications</td>
<td>injections per day</td>
</tr>
<tr>
<td>Group Research, Effect of intensive therapy on the microvascular</td>
<td></td>
</tr>
<tr>
<td>complications of type 1 diabetes mellitus, JAMA, 2563-2569, 2002</td>
<td></td>
</tr>
<tr>
<td>Thompson,R.J., Agostini,K., Potts,L., Luscombe,J., Christie,D.,</td>
<td>The study only reported that the highest HbA1c was the highest in the twice-group</td>
</tr>
<tr>
<td>Viner,R., White,B., Hindmarsh,P.C., Deprivation and ethnicity</td>
<td>and lowest in the insulin therapy group in text; no comparison between MDI and</td>
</tr>
<tr>
<td>impact on diabetes control and use of treatment regimen,</td>
<td>mixed insulin injection was made.</td>
</tr>
<tr>
<td>Diabetic Medicine, 30, 491-494, 2013</td>
<td></td>
</tr>
<tr>
<td>Thomsett,M., Shield,G., Batch,J., Cotterill,A., How well are we</td>
<td>PICO criteria not met - comparison is between 1-2 and &gt; 2 injections per day</td>
</tr>
<tr>
<td>doing? Metabolic control in patients with diabetes,</td>
<td></td>
</tr>
<tr>
<td>Journal of Paediatrics and Child Health, 35, 479-482, 1999</td>
<td></td>
</tr>
<tr>
<td>Tonella,P., Fluck,C.E., Mullis,P.E., Metabolic control of type 1</td>
<td>Incomplete data for comparisons of interest</td>
</tr>
<tr>
<td>diabetic patients followed at the University Children's Hospital</td>
<td></td>
</tr>
<tr>
<td>in Berne: have we reached the goal?, Swiss Medical Weekly, 140, w13057,-, 2010</td>
<td></td>
</tr>
<tr>
<td>Tubiana-Rufi,N., Levy-Marchal,C., Mugnier,E., Czemichow,P., Long</td>
<td>PICO criteria not met - age range is 5-19.5 years, guideline age range not reported</td>
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<tr>
<td>term feasibility of multiple daily injections with insulin pens in</td>
<td></td>
</tr>
<tr>
<td>children and adolescents with diabetes, European Journal of</td>
<td></td>
</tr>
<tr>
<td>Pediatrics, 149, 80-83, 1989</td>
<td></td>
</tr>
<tr>
<td>Tupola,S., Rajantie,J., Maenpaa,J., Severe hypoglycaemia in children</td>
<td>PICO criteria not met - age range is 2-21 years, guideline age range not reported</td>
</tr>
<tr>
<td>and adolescents during multiple-dose insulin therapy, Diabetic</td>
<td></td>
</tr>
<tr>
<td>Medicine, 15, 695-699, 1998</td>
<td></td>
</tr>
<tr>
<td>Urakami,T., Kuwabara,R., Habu,M., Okuno,M., Suzuki,J., Takahashi,S.,</td>
<td>No information on outcomes of interest</td>
</tr>
<tr>
<td>Basal insulin requirement of youth with type 1 diabetes differs</td>
<td></td>
</tr>
<tr>
<td>according to age, Journal of Diabetes Investigation, 5, 442-444, 2014</td>
<td></td>
</tr>
<tr>
<td>Urakami,T., Suzuki,J., Yoshida,A., Saito,H., Ishige,M.,</td>
<td>PICO criteria not met - insulin regimen data not reported</td>
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<tr>
<td>Study</td>
<td>Reason for exclusion</td>
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<tr>
<td>----------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Takahashi,S., Mugishima,H., Association between sex, age, insulin regimens and glycemic control in children and adolescents with type 1 diabetes, Clinical Pediatric Endocrinology, 19, 1-6, 2010</td>
<td>separately for guideline age range</td>
</tr>
<tr>
<td>Viberti,G.C., Intensive therapy and progression to clinical albuminuria in patients with insulin dependent diabetes mellitus and microalbuminuria, British Medical Journal, 311, 973-977, 1995</td>
<td></td>
</tr>
<tr>
<td>Wagner,V.M., Muller-Godeffroy,E., von,Sengbusch S., Hager,S., Thyen,U., Age, metabolic control and type of insulin regime influences health-related quality of life in children and adolescents with type 1 diabetes mellitus, European Journal of Pediatrics, 164, 491-496, 2005</td>
<td>Study criteria not met - multiple daily injections defined as &gt; 3 injections per day</td>
</tr>
<tr>
<td>Wagner,V.M., Grabert,M., Holl,R.W., Severe hypoglycaemia, metabolic control and diabetes management in children with type 1 diabetes in the decade after the Diabetes Control and Complications Trial -- a large-scale multicentre study, European Journal of Pediatrics, 164, 73-79, 2005</td>
<td>Study criteria not met - cannot separate CSII data from multiple daily injections</td>
</tr>
<tr>
<td>White,N.H., Intensive diabetes therapy is effective in children, American Family Physician, 50, 407-, 1994</td>
<td>Study criteria not met - comparison is between 1-2 and 2-4 injections per day</td>
</tr>
<tr>
<td>Wierusz-Wysocka,B., Wysocki,H., Byks,H., Zozulinska,D., Wykretowicz,A., Kazmierczak,M., Metabolic control quality and free radical activity in diabetic patients, Diabetes Research and Clinical Practice, 27, 193-197, 1995</td>
<td>Study criteria not met - age range 17-51 years and follow-up &lt; 4 months</td>
</tr>
<tr>
<td>Williams,R.M., Dunger,D.B., Insulin treatment in children and adolescents. [50 refs], Acta Paediatrica, 93, 440-446, 2004</td>
<td>Study criteria not met - narrative review</td>
</tr>
<tr>
<td>Wilson,D.P., Fesmire,J.D., Endres,R.K., Blackett,P.R., Increased levels of HDL-cholesterol and apolipoprotein A-I after intensified insulin therapy for diabetes, Southern Medical Journal, 78, 636-638, 1985</td>
<td>Study criteria not met - age range 9-21 years, guideline age range not reported separately</td>
</tr>
<tr>
<td>Wintergerst,K.A., Hinkle,K.M., Barnes,C.N., Omoruyi,A.O., Foster,M.B., The impact of health insurance coverage on pediatric diabetes management, Diabetes Research and Clinical Practice, 90, 40-44, 2010</td>
<td>PICO criteria not met - age range includes 18 years, guideline age range not reported separately</td>
</tr>
<tr>
<td>Wysocki,T., Diabetes self-management profile for flexible insulin regimens: Cross-sectional and longitudinal analysis of psychometric properties in a pediatric sample, Diabetes Care, 28, 2034-2035, 2005</td>
<td>PICO criteria not met - comparison is continuous glucose monitoring versus usual monitoring</td>
</tr>
<tr>
<td>Ying,A.K., Lairson,D.R., Giardino,A.P., Bondy,M.L., Zaheer,I., Haymond,M.W., Heptulla,R.A., Predictors of direct costs of diabetes care in pediatric patients with type 1 diabetes, Pediatric Diabetes, 12, 177-182, 2011</td>
<td>PICO criteria not met - multiple daily injections defined as 3 or more injections per day</td>
</tr>
</tbody>
</table>
H.5  Type 1 diabetes – HbA1c targets

Review question

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jarosz-Chobot,P., Polanska,J., Mysiowiec,M., Szadkowska,A., Fendler,W., Kaminska,H., Chumiecki,M., Mianoewka,B., Techmanska,I., Sztangierska,B., Mlynarski,W., PolPeDiab study group, Multicenter cross-sectional analysis of values of glycated haemoglobin (HbA1c) in Polish children and adolescents with long-term type 1 diabetes in Poland: PolPeDiab study group, Pediatric endocrinology, diabetes, and metabolism, 18, 125-129, 2012</td>
<td>No targets specified. No threshold for HbA1c in analysis. No relevant outcomes reported. Study assesses whether children and young people with different HbA1c values have stable HbA1c levels.</td>
</tr>
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</table>

H.6  Type 1 diabetes – blood glucose targets

Review question

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashwell,S.G., Gebbie,J., Home,P.D., Optimal timing of injection of once-daily insulin glargine in people with Type 1 diabetes using insulin lispro at meal-times, Diabetic Medicine, 23, 46-52, 2006</td>
<td>PICO not met: adult participants only</td>
</tr>
<tr>
<td>Boot,M., Volkening,L.K., Butler,D.A., Laffel,L.M., The impact of blood glucose and HbA1c goals on glycaemic control in children and adolescents with Type 1 diabetes, Diabetic Medicine, 30, 333-337, 2013</td>
<td>PICO not met: outcomes of interest not given</td>
</tr>
<tr>
<td>Fullerton,B., Jeitler,K., Siebenhofer,A., Intensive glucose control versus conventional glucose control for type 1 diabetes mellitus, Cochrane Database of Systematic Reviews, 2, CD009122-, 2014</td>
<td>The review was about both children and adults. The study on children (Wysocki et al. 2003) does not meet the protocol in terms of intervention (that is, the comparison groups (intensive and usual care)not only differed in terms of Hb1Ac targets during treatment, but also other interventions such as education and behavioural interventions).</td>
</tr>
<tr>
<td>Fullerton,Birgit, Berghold,Andrea, Jeitler,Klaus, Siebenhofer,Andrea, Intensive glucose control versus conventional glucose control for type 1 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2011</td>
<td>Protocol for a systematic review</td>
</tr>
<tr>
<td>Marcason,W., Is There a Recommended Target Range for Blood Glucose for the Type 1 Diabetic Endurance Athlete?, Journal of the Academy of Nutrition and Dietetics, 112, 2092-, 2012</td>
<td>Neither a study nor a systematic review</td>
</tr>
<tr>
<td>Rankin,D., Cooke,D.D., Heller,S., Elliott,J., Amiel,S., Lawton,J., UK National Institute for Health Research (NIHR)</td>
<td>PICO not met: adult participants only</td>
</tr>
</tbody>
</table>
### H.7 Type 1 diabetes – blood glucose monitoring

#### Review questions

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose Adjustment for Normal Eating (DAFNE) Study Group., Experiences of using blood glucose targets when following an intensive insulin regimen: a qualitative longitudinal investigation involving patients with Type 1 diabetes, Diabetic Medicine, 29, 1079-1084, 2012</td>
<td>PICO not met: no long-term outcomes assessed</td>
</tr>
<tr>
<td>Scaramuzza,A.E., Iafusco,D., Santoro,L., Bosetti,A., De,Palma A., Spiri,D., Mameli,C., Zuccotti,G.V., Timing of bolus in children with type 1 diabetes using continuous subcutaneous insulin infusion (TiBoDi Study), Diabetes Technology and Therapeutics, 12, 149-152, 2010</td>
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</table>

#### Excluded studies

<table>
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<tr>
<th>Reason for exclusion</th>
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<tbody>
<tr>
<td>PICO not met: no long-term outcomes assessed</td>
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<tr>
<td>PICO not met - intervention examined did not include blood glucose targets</td>
</tr>
<tr>
<td>PICO not met - study does not report relationship between blood glucose levels and HbA1c</td>
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<tr>
<td>Study</td>
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<tr>
<td>----------------------------------------------------------------------</td>
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<tr>
<td>Haupt, E., Herrmann, R., eckel-Timp, A., Vogel, H., Haupt, A., Walter, C.</td>
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<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
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<tbody>
<tr>
<td>Excluded studies</td>
<td></td>
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<tr>
<td>Diagnosis and management of type 1 diabetes in children and young people</td>
<td></td>
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<tr>
<td>Excluded studies</td>
<td></td>
</tr>
<tr>
<td>Imperatore,G., Loots,B., Bell,R., Lawrence,J.M., SEARCH</td>
<td></td>
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<tr>
<td>Anderson,A., Bloch,C.A., Naughton,M., Seid,M., Yi</td>
<td></td>
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<tr>
<td>Wysocki,T., Green,L., Huxtable,K., Blood glucose monitoring by diabetic adolescents: compliance and metabolic control, Health Psychology, 8, 267-284, 1989</td>
<td></td>
</tr>
<tr>
<td>Schiffrin,A., Belmonte,M., Multiple daily self-glucose monitoring: Its essential role in long-term glucose control in insulin-dependent diabetic patients treated with pump and multiple subcutaneous injections, Diabetes Care, 5, 479-484, 1982</td>
<td></td>
</tr>
<tr>
<td>Vervoort,T., Goubert,L.T., Vandenbossche,H., van,Aken,S., Matthys,D., Crombez,G., Child's and parents' catastrophizing about pain is associated with procedural fear in children: A study in children with diabetes and their mothers, Psychological Reports, 109, 879-895, 2011</td>
<td>The study did not have a comparator group; the participants appeared to have 1 finger prick test only</td>
</tr>
<tr>
<td>Wyszocki,T., Green,L., Huxtable,K., Blood glucose monitoring by diabetic adolescents: compliance and metabolic control, Health Psychology, 8, 267-284, 1989</td>
<td></td>
</tr>
<tr>
<td>No comparator group, and data were not reported according to age groups as study included mixed ages</td>
<td></td>
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<tr>
<td>PICO not met - study examined education in use of a real-time continuous glucose monitoring device</td>
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<tr>
<td>PICO not met - both randomised groups used 4 or fewer blood glucose tests per day</td>
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<tr>
<td>PICO not met - study does not report relationship between self-monitoring of blood glucose and glycaemic control</td>
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<tr>
<td>PICO not met - study does not report numerical data on the outcomes of interest</td>
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<tr>
<td>PICO not met - non-randomised study comparing 2 tests per day with 4 or more tests per day</td>
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<tr>
<td>Adult population</td>
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<tr>
<td>PICO not met - study examined factors associated with ‘good’ glycaemic control compared with ‘poor’ glycaemic control</td>
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<tr>
<td>PICO not met - study does not report the correlation between self-monitoring of blood glucose and glycaemic control</td>
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<tr>
<td>PICO not met - study examined incentives for self-monitoring of blood glucose, not different frequencies of self-monitoring</td>
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</table>
What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bode,B.W., Clinical utility of the continuous glucose monitoring system, Diabetes Technology and Therapeutics, 2 Suppl 1, S35-S41, 2000</td>
<td>Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (case study only)</td>
</tr>
<tr>
<td>Chase,H.P., Beck,R., Tamborlane,W., Buckingham,B., Maurus,N., Tsaklidian,E., Wysocki,T., Weinzimer,S., Kollman,C., Ruedy,K., Xing,D., A randomized multicenter trial comparing the GlucoWatch Biographer with standard glucose monitoring in children with type 1 diabetes, Diabetes Care, 28, 1101-1106, 2005</td>
<td>GlucoWatch G2 Biographer has been withdrawn from the market</td>
</tr>
<tr>
<td>Chetty,V.T., Almulla,A., Odueyungbo,A., Thabane,L., The effect of continuous subcutaneous glucose monitoring (CGMS) versus intermittent whole blood finger-stick glucose monitoring (SBGM) on hemoglobin A1c (HBA1c) levels in Type I diabetic patients: a systematic review, Diabetes Research and Clinical Practice, 81, 79-87, 2008</td>
<td>Superseded by more recent systematic reviews</td>
</tr>
<tr>
<td>Cobry,E., Chase,H.P., Burdick,P., McMann,K., Yetzer,H., Scrimgeour,L., Use of CoZmonitor in youth with type 1 diabetes, Pediatric Diabetes, 9, 148-151, 2008</td>
<td>PICO not met - study related to integration of capillary blood glucose monitoring and insulin pump therapy</td>
</tr>
<tr>
<td>Deiss,D., Hartmann,R., Schmidt,J., Kordonouri,O., Results of a randomised controlled cross-over trial on the effect of continuous subcutaneous glucose monitoring (CGMS) on glycaemic control in children and adolescents with type 1 diabetes, Experimental and Clinical Endocrinology and Diabetes, 114, 63-67, 2006</td>
<td>Included in the Cochrane systematic review (Langendam 2012)</td>
</tr>
<tr>
<td>Deiss,Dorothee, Bolinder-Jan, Riveline, Jean Pierre,</td>
<td>Included in the Cochrane systematic review (Langendam 2012)</td>
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<td>Study</td>
<td>Reason for exclusion</td>
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<tr>
<td>Battelino, Tadej, Bosi, Emanuele, Tubiana-Rufi, Nadia, Kerr, David,</td>
<td></td>
</tr>
<tr>
<td>Phillip, Moshe, Improved Glycemic Control in Poorly Controlled</td>
<td></td>
</tr>
<tr>
<td>Patients with Type 1 Diabetes Using Real-Time Continuous Glucose</td>
<td></td>
</tr>
<tr>
<td>Monitoring, Diabetes Care, 29, 2730-2732, 2006</td>
<td></td>
</tr>
<tr>
<td>Gandhi, G.Y., Kovalaske, M., Kudva, Y., Walsh, K., Elamian, M.B.,</td>
<td>Individual studies checked for inclusion and all except for the GlucoWatch studies are included in the</td>
</tr>
<tr>
<td>Beers, M., Coyle, C., Goalen, M., Murad, M.S., Erwin, P.J., Corpus,</td>
<td>Cochrane systematic review (Langendam 2012)</td>
</tr>
<tr>
<td>J., Monori, V.M., Murad, M.H., Efficacy of continuous glucose</td>
<td></td>
</tr>
<tr>
<td>monitoring in improving glycemic control and reducing hypoglycemia:</td>
<td></td>
</tr>
<tr>
<td>a systematic review and meta-analysis of randomized trials, Journal</td>
<td></td>
</tr>
<tr>
<td>of Diabetes Science and Technology, 5, 952-965, 2011</td>
<td></td>
</tr>
<tr>
<td>Guevara, D., Paiva, I., Balista, C., Barros, L., Carrilho, F., A1c,</td>
<td>The study was carried out among adults; retrospective in design, and made no comparison between finger-prick blood glucose testing and CGMS</td>
</tr>
<tr>
<td>glucose variability and hypoglycemia risk in patients with type 1</td>
<td></td>
</tr>
<tr>
<td>diabetes, Minerva Endocrinologica, 39, 127-133, 2014</td>
<td></td>
</tr>
<tr>
<td>Hirsch, I.B., Abelseth, J., Bode, B.W., Fischer, J.S., Kaufman, F.R.,</td>
<td>Included in the Cochrane systematic review (Langendam 2012)</td>
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<tr>
<td>Mastrototaro, J., Parkin, C.G., Wolpert, H.A., Buckingham, B.A.,</td>
<td></td>
</tr>
<tr>
<td>Sensor-augmented insulin pump therapy: results of the first</td>
<td></td>
</tr>
<tr>
<td>randomized treat-to-target study, Diabetes Technology and</td>
<td></td>
</tr>
<tr>
<td>Therapeutics, 10, 377-383, 2008</td>
<td></td>
</tr>
<tr>
<td>Hoeks, L.B., Greven, W.L., de Valk, H.W., Real-time continuous</td>
<td>Superseded by more recent systematic reviews</td>
</tr>
<tr>
<td>glucose monitoring system for treatment of diabetes: a systematic</td>
<td></td>
</tr>
<tr>
<td>review, Diabetic Medicine, 28, 386-94, 2011</td>
<td></td>
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<tr>
<td>Juvenile Diabetes Research Foundation Continuous Glucose Monitoring</td>
<td></td>
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<tr>
<td>Study Group, Beck, R.W., Hirsch, I.B., Lafler, L., Tamborlane, W.V.,</td>
<td>Included in the Cochrane systematic review (Langendam 2012)</td>
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<tr>
<td>Bode, B.W., Buckingham, B., Chase, P., Clemons, R., Fiillo-Scharer,</td>
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<td>Study Group, Beck, R.W., Lawrence, J.M., Lafler, L., Wysocki, T.,</td>
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<td>Xing, D., Huang, E.S., Ives, B., Kollman, C., Lee, J., Ruedy, K.J.,</td>
<td></td>
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<tr>
<td>Tamborlane, W.V., Quality-of-life measures in children and adults</td>
<td></td>
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<tr>
<td>with type 1 diabetes: Juvenile Diabetes Research Foundation</td>
<td></td>
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<tr>
<td>Continuous Glucose Monitoring randomized trial, [Erratum appears in</td>
<td></td>
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<tr>
<td>Diabetes Care. 2010 Dec;33(12):2725], Diabetes Care, 33, 2175-2177,</td>
<td></td>
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<td>Study Group, Tamborlane, W.V., Beck, R.W., Bode, B.W., Buckingham,</td>
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<td>B., Chase, H.P., Clemons, R., Fiillo-Scharer, R., Fox, L.A.,</td>
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<td>Gilliam, L.K., Hirsch, I.B., Huang, E.S., Kollman, C., Kowalski, A.J.,</td>
<td></td>
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<tr>
<td>Kaufman, F.R., Gibson, L.C., Halvorson, M., Carpenter, S., Fisher,</td>
<td>Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (not a randomised study)</td>
</tr>
<tr>
<td>L.K., Pfikkecheewanont, P., A pilot study of the continuous glucose</td>
<td></td>
</tr>
<tr>
<td>monitoring system: clinical decisions and glycemic control after its</td>
<td></td>
</tr>
<tr>
<td>use in pediatric type 1 diabetic subjects, Diabetes Care, 24, 2030-2034, 2001</td>
<td></td>
</tr>
<tr>
<td>Kordonouri, O., Hartmann, R., Pankowska, E., Rami, B., Kapellen,</td>
<td>An abstract</td>
</tr>
<tr>
<td>T., Coutant, R., Lange, K., Danne, T., Follow-up of patients with</td>
<td></td>
</tr>
<tr>
<td>sensor-augmented pump therapy during the first year of diabetes-pediatric onset study, Pediatric Diabetes, 12, 29-, 2011</td>
<td></td>
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<tr>
<td>Kordonouri, O., Hartmann, R., Pankowska, E., Rami, B., Kapellen,</td>
<td>Secondary publication of an included study</td>
</tr>
<tr>
<td>T., Coutant, R., Lange, K., Danne, T., Sensor augmented pump therapy</td>
<td></td>
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<tr>
<td>from onset of type 1 diabetes: late follow-up results of the Pediatric Onset Study, Pediatric Diabetes, 13, 515-518, 2012</td>
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<td>Kordonouri, O., Hartmann, R., Pankowska, E., Rami, B., Kapellen,</td>
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<td>from onset of type 1 diabetes: Late follow-up results of the Pediatric ONSET Study, Diabetologia, 54, 541-, 2011</td>
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<td>Kordonouri, O., Pankowska, E., Rami, B., Kapellen, T.,</td>
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<tr>
<td>Coutant, R., Hartmann, R., Lange, K., Knip, M., Danne, T., 2012</td>
<td>Sensor-augmented pump therapy from the diagnosis of childhood type 1 diabetes: results of the Paediatric Onset Study (ONSET) after 12 months of treatment, Diabetologia, 53, 2487-2495, 2010</td>
</tr>
<tr>
<td>Lange, K., Coutant, R., Danne, T., Kapellens, T., Pankowska, E., 2010</td>
<td>Included in the Cochrane systematic review (Langendam 2012)</td>
</tr>
<tr>
<td>Lawton, M.L., M. M. McInnes, K., Clarson, C., 2003</td>
<td>Minimum length of follow-up not met and objective not pertinent to this review question</td>
</tr>
<tr>
<td>Ludvigsson, J., Hansa, R., 2012</td>
<td>Continuous subcutaneous glucose monitoring improved metabolic control in pediatric patients with type 1 diabetes: a controlled crossover study, Pediatrics, 111, 933-938, 2003</td>
</tr>
<tr>
<td>Ly, T.T., Hewitt, J., Davey, R.J., Lim, E.M., Davis, E.A., 2011</td>
<td>Included in 2004 guideline review - copy could not be obtained for consideration in 2015 update review</td>
</tr>
<tr>
<td>Ly, T.T., Hewitt, J., Davey, R.J., Lim, E.M., Davis, E.A., 2011</td>
<td>Included in 2004 guideline review - copy could not be obtained for consideration in 2015 update review</td>
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<tr>
<td>Markowitz, J.T., Pratt, K., Aggarwal, J., Volkering, L.K., 2012</td>
<td>The original study (Juvenile Diabetes Research Foundation (JDFR) trial) was included in the Cochrane systematic review (Langendam 2012)</td>
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<tr>
<td>O'Connell, M.A., Donath, S., O'Neal, D.N., Colman, P.G., 2009</td>
<td>Included in the Cochrane systematic review (Langendam 2012)</td>
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<tr>
<td>Racci, D., Sulmont, V., Reznik, Y., Guerci, B., Renard, E., 2009</td>
<td>Not strictly a systematic review and superseded by more recent systematic reviews</td>
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<tr>
<td>Racci, D., Sulmont, V., Reznik, Y., Guerci, B., Renard, E., 2009</td>
<td>Included in the Cochrane systematic review (Langendam 2012)</td>
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<tr>
<td>Schiaffini, R., Ciampalini, P., Fierabracci, A., Spera, S., 2002</td>
<td>Objective is not relevant to the review question</td>
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<tr>
<td>Schiaffini, R., Ciampalini, P., Fierabracci, A., Spera, S., 2002</td>
<td>Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (cohort study only)</td>
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<tr>
<td>Sequeira, P.A., Montoya, L., Ruelas, V., Xing, D., Chen, V., 2013</td>
<td>Age of participants was 18 years and over</td>
</tr>
<tr>
<td>Schiaffini, R., Ciampalini, P., Fierabracci, A., Spera, S., 2002</td>
<td>Included in Cochrane systematic review (Langendam 2012)</td>
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</table>
Diagnosis and management of type 1 diabetes in children and young people

Excluded studies

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<tr>
<th>Study</th>
<th>Reason for exclusion</th>
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<tbody>
<tr>
<td>system on glycemic control in type 1 diabetic patients: systematic review and meta-analysis of randomized trials, European Journal of Endocrinology, 166, 567-574, 2012</td>
<td></td>
</tr>
<tr>
<td>Tansley, M., Laffel, L., Cheng, J., Beck, R., Coffey, J., Huang, E., Kollman, C., Lawrence, J., Lee, J., Ruedy, K., Tamborlane, W., Wysocki, T., Xing, D., Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group., Satisfaction with continuous glucose monitoring in adults and youths with Type 1 diabetes, Diabetic Medicine, 28, 1118-1122, 2011</td>
<td>Outcome not compared between intervention and comparator groups</td>
</tr>
<tr>
<td>Wojciechowski, P., Rys, P., Lipowska, A., Gaweska, M., Malecki, M.T., Efficacy and safety comparison of continuous glucose monitoring and self-monitoring of blood glucose in type 1 diabetes: systematic review and meta-analysis, Polskie Archiwum Medycyny Wewntrznej, 121, 333-343, 2011</td>
<td>All the studies included are covered by the Cochrane systematic review (Langendam 2012)</td>
</tr>
<tr>
<td>Yates, K., Hasnat, Milton A., Dear, K., Ambler, G., Continuous glucose monitoring-guided insulin adjustment in children and adolescents on near-physiological insulin regimens: a randomized controlled trial, Diabetes Care, 29, 1512-1517, 2006</td>
<td>Included in the Cochrane systematic review (Langendam 2012)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bergenthal, R.M., Tamborlane, W.V., Ahmann, A., Buse, J.B., Dailey, G., Davis, S.N., Joyce, C., Peoples, T., Perkins, B.A., Welsh, J.B., Will, S.M., Wood, M.A., Study Group., Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes.[Erratum appears in N Engl J Med. 2010 Sep 9;363(11):1092], New England Journal of Medicine, 363, 311-320, 2010</td>
<td>Participants were randomly assigned to insulin pump therapy group or injection therapy group and then given a form of continuous glucose monitoring; unable to tell whether any differences in groups is due to the form of CGMS used or to the therapy received</td>
</tr>
<tr>
<td>Bode, B.W., Clinical utility of the continuous glucose monitoring system, Diabetes Technology and Therapeutics, 2 Suppl 1, S35-S41, 2000</td>
<td>Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (case study only)</td>
</tr>
<tr>
<td>Chase, H.P., Beck, R.W., Xing, D., Tamborlane, W.V., Coffey, J., Fox, L.A., Ives, D., Keady, J., Kollman, C., Laffel, L., Ruedy, K.J., Continuous glucose monitoring in youth with type 1 diabetes: 12-month follow-up of the juvenile diabetes research foundation continuous glucose monitoring randomized trial, Diabetes Technology and Therapeutics, 12, 507-515, 2010</td>
<td>A sub-study: the original study was excluded</td>
</tr>
<tr>
<td>Chetty, V.T., Almulia, A., Odueyungbo, A., Thabane, L., The effect of continuous subcutaneous glucose monitoring (CGMS) versus intermittent whole blood finger-stick glucose monitoring (SBGM) on hemoglobin A1c (HBA1c) levels in Type 1 diabetic patients: a systematic review. [34 refs], Diabetes Research and Clinical Practice, 81, 79-87, 2008</td>
<td>PICO not met: comparator was self-monitoring of blood glucose</td>
</tr>
<tr>
<td>Danne, T., Lange, K., Kordonouri, O., Real-time glucose sensors in children and adolescents with type-1 diabetes. [64 refs], Hormone Research, 70, 193-202, 2008</td>
<td>Not a systematic review</td>
</tr>
<tr>
<td>Deiss, D., Hartmann, R., Schmidt, J., Kordonouri, O., Results</td>
<td>PICO not met: outcome data not been presented as</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
</tr>
<tr>
<td>---------------------------------------------------------------------</td>
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<tr>
<td>of a randomised controlled cross-over trial on the effect of</td>
<td>specified in the protocol</td>
</tr>
<tr>
<td>continuous subcutaneous glucose monitoring (CGMS) on glycaemic</td>
<td></td>
</tr>
<tr>
<td>control in children and adolescents with type 1 diabetes,</td>
<td></td>
</tr>
<tr>
<td>Experimental and Clinical Endocrinology and Diabetes, 114, 63-67,</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td></td>
</tr>
<tr>
<td>Edelman, S.V., Bailey, T.S., Continuous glucose monitoring health</td>
<td>Review article: individual studies checked for inclusion</td>
</tr>
<tr>
<td>outcomes. Diabetes Technology and Therapeutics, 11 Suppl 1, S68-S74,</td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td></td>
</tr>
<tr>
<td>Halvorson, M., Carpenter, S., Kaiserman, K., Kaufman, F.R., A pilot</td>
<td>Not an RCT</td>
</tr>
<tr>
<td>trial in pediatrics with the sensor-augmented pump:</td>
<td></td>
</tr>
<tr>
<td>combining real-time continuous glucose monitoring with the insulin</td>
<td></td>
</tr>
<tr>
<td>Hoeks, L.B., Greven, W.L., de Valk, H.W., Real-time continuous</td>
<td>Systematic review: individual studies checked for inclusion</td>
</tr>
<tr>
<td>glucose monitoring system for treatment of diabetes: a systematic</td>
<td></td>
</tr>
<tr>
<td>review, Diabetic Medicine, 28, 386-94, 2011</td>
<td></td>
</tr>
<tr>
<td>Hovorka, R., Elleri, D., Thabit, H., Allen, J.M., Leelarathna, L.,</td>
<td>The intervention and comparator were not as specified in the protocol (real-time CGMS versus real-time CGMS closed loop)</td>
</tr>
<tr>
<td>El-Khairi, R., Kumareswaran, K., Caldwell, K., Calhoun, P., Kollman,</td>
<td></td>
</tr>
<tr>
<td>C., Murphy, H.R., Acerini, C.L., Wilinska, M.E., Nodale, M., Dunger,</td>
<td></td>
</tr>
<tr>
<td>D.B., Overnight closed-loop insulin delivery in young people with</td>
<td></td>
</tr>
<tr>
<td>type 1 diabetes: A free-living, randomized clinical trial, Diabetes</td>
<td></td>
</tr>
<tr>
<td>Care, 37, 1204-1211, 2014</td>
<td></td>
</tr>
<tr>
<td>Juvenile Diabetes Research Foundation Continuous Glucose Monitoring</td>
<td>A secondary analysis of an RCT</td>
</tr>
<tr>
<td>Study Group, Beck, R.W., Buckingham, B., Miller, K., Wolpert, H.,</td>
<td></td>
</tr>
<tr>
<td>Xing, D., Block, J.M., Chase, H.P., Hirsch, I., Kollman, C., Laffel,</td>
<td></td>
</tr>
<tr>
<td>L., Lawrence, J.M., Milaszewski, K., Ruedy, K.J., Tamborlane, W.V.,</td>
<td></td>
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<tr>
<td>Factors predictive of use and of benefit from continuous glucose</td>
<td></td>
</tr>
<tr>
<td>monitoring in type 1 diabetes, Diabetes Care, 32, 1947-1953, 2009</td>
<td></td>
</tr>
<tr>
<td>Juvenile Diabetes Research Foundation Continuous Glucose Monitoring</td>
<td></td>
</tr>
<tr>
<td>Study Group, Beck, R.W., Lawrence, J.M., Laffel, L., Wysocki, T.,</td>
<td>PICO not met: the comparator is self-monitoring of blood glucose only</td>
</tr>
<tr>
<td>Xing, D., Huang, E.S., Ives, B., Kollman, C., Lee, J., Ruedy, K.J.,</td>
<td></td>
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<tr>
<td>Tamborlane, W.V., Quality-of-life measures in children and adults</td>
<td></td>
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<td>with type 1 diabetes: Juvenile Diabetes Research Foundation</td>
<td></td>
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<tr>
<td>Continuous Glucose Monitoring randomized trial [Erratum appears in</td>
<td></td>
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<tr>
<td>Diabetes Care, 2010 Dec;33(12):2725], Diabetes Care, 33, 2175-2177,</td>
<td></td>
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<tr>
<td>2010</td>
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<tr>
<td>Klonoft, D.C., Continuous glucose monitoring study does not</td>
<td>Not an RCT</td>
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<tr>
<td>demonstrate benefit in children and adolescents, Journal of</td>
<td></td>
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<tr>
<td>Pediatrics, 154, 463-464, 2009</td>
<td></td>
</tr>
<tr>
<td>Laffel, L.M., Hsu, W.C., McGill, J.B., Meneghini, L., Volkening,</td>
<td>Paediatric data not reported separately; participants with type 1 diabetes and those</td>
</tr>
<tr>
<td>L.K., Continued use of an integrated meter with electronic logbook</td>
<td>with type 2 diabetes cannot be distinguished</td>
</tr>
<tr>
<td>maintains improvements in glycaemic control beyond a randomized,</td>
<td></td>
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<tr>
<td>controlled trial, Diabetes Technology and Therapeutics, 9, 254-264,</td>
<td></td>
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<tr>
<td>2007</td>
<td></td>
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<tr>
<td>Lagarde, W.H., Barrows, F.P., Davenport, M.L., Kang, M., Guess, H.A.,</td>
<td>PICO not met: comparator was self-monitoring of blood glucose(although CGMS data were collected, they were not reported)</td>
</tr>
<tr>
<td>Calligouli, A.S., Continuous subcutaneous glucose monitoring in</td>
<td></td>
</tr>
<tr>
<td>children with type 1 diabetes mellitus: a single-blind, randomized,</td>
<td></td>
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<tr>
<td>controlled trial, Pediatric Diabetes, 7, 159-164, 2006</td>
<td></td>
</tr>
<tr>
<td>Langendam, M., Luijf, Y.M., Hoof, L., Devries, J.H., Mudder, A.H.,</td>
<td>Systematic review: individual articles checked for inclusion</td>
</tr>
<tr>
<td>Scholten, R.J., Continuous glucose monitoring systems for type 1</td>
<td></td>
</tr>
<tr>
<td>diabetes mellitus, Cochrane Database of Systematic Reviews, 1, CD008101-.2012,</td>
<td></td>
</tr>
<tr>
<td>Ly, T.T., Hewitt, J., Davey, R.J., Lim, E.M., Davis, E.A., Jones, T.</td>
<td>PICO not met: comparator was self-monitoring of blood glucose(although CGMS data were collected, they were not reported)</td>
</tr>
<tr>
<td>T.W., Improving epinephrine responses in hypoglycemia unawareness</td>
<td></td>
</tr>
<tr>
<td>with real-time continuous glucose monitoring in adolescents with</td>
<td></td>
</tr>
<tr>
<td>type 1 diabetes, Diabetes Care, 34, 50-52, 2011</td>
<td></td>
</tr>
<tr>
<td>Maahs, D.M., Calhoun, P., Buckingham, B.A., Chase, H.P., Hramiak, J.,</td>
<td>The trial included participants aged 15-45 years, but results were not stratified by age group</td>
</tr>
<tr>
<td>Lum, J., Cameron, F., Bequette, B.W., Aye, T., Paul, T., Slover, R.,</td>
<td></td>
</tr>
<tr>
<td>trial of a home system to reduce nocturnal hypoglycemia in type 1</td>
<td></td>
</tr>
<tr>
<td>diabetes, Diabetes Care, 37, 1885-1891, 2014</td>
<td></td>
</tr>
<tr>
<td>Maura, N., Fox, L., Engler, K., Beck, R.W., Continuous glucose</td>
<td>Not a systematic review</td>
</tr>
<tr>
<td>monitoring in type 1 diabetes, Endocrine, 43, 41-50,</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>O’Connell,M.A., Donath,S., O’Neal,D.N., Colman,P.G., Ambler,G.R., Jones,T.W., Davis,E.A., Cameron,F.J., Glycaemic impact of patient-led use of sensor-guided pump therapy in type 1 diabetes: a randomised controlled trial, Diabetologia, 52, 1250-1257, 2009</td>
<td>PICO not met: the comparator was self-monitoring of blood glucose</td>
</tr>
<tr>
<td>Pickup,J.C., Freeman,S.C., Sutton,A.J., Glycaemic control in type 1 diabetes during real time continuous glucose monitoring compared with self monitoring of blood glucose: meta-analysis of randomised controlled trials using individual patient data, BMJ, 343, d3805, 2011</td>
<td>Paediatic data not reported separately</td>
</tr>
<tr>
<td>Raccah,D., Sulmont,V., Reznik,Y., Guerci,B., Renard,E., Hanaire,H., Jeandidier,N., Nicolino,M., Incremental value of continuous glucose monitoring when starting pump therapy in patients with poorly controlled type 1 diabetes: the RealTrend study, Diabetes Care, 32, 2245-2250, 2009</td>
<td>PICO not met: the results were not stratified by age</td>
</tr>
<tr>
<td>Schiaffini,R., Ciampalini,P., Fierabracci,A., Spera,S., Borrelli,P., Bottazzo,G.F., Crino,A., The continuous glucose monitoring system (CGMS) in type 1 diabetic children is the way to reduce hypoglycemic risk, Diabetes/metabolism research and reviews, 18, 324-329, 2002</td>
<td>Included in 2004 guideline review - does not meet the inclusion criteria for the 2015 update review (cohort study only)</td>
</tr>
<tr>
<td>Soliman,A., DeSanctis,V., Yassin,M., Elalaily,R., Eldarsy,N.E., Continuous glucose monitoring system and new era of early diagnosis of diabetes in high risk groups, Indian Journal of Endocrinology and Metabolism, 18, 274-282, 2014</td>
<td>PICO not met: the results were not stratified by age</td>
</tr>
<tr>
<td>Tamborlane,W.V., Insulin pumps and continuous glucose monitoring in pediatric patients with type 1 diabetes mellitus, Endocrine Practice, 18, 13-16, 2012</td>
<td>Not a systematic review</td>
</tr>
<tr>
<td>Tansey,M., Laffel,L., Cheng,J., Beck,R., Coffey,J., Huang,E., Kollman,C., Lawrence,J., Lee,J., Ruedy,K., Tamborlane,W., Wysocki,T., Xing,D., Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group., Satisfaction with continuous glucose monitoring in adults and youths with Type 1 diabetes, Diabetic Medicine, 28, 1118-1122, 2011</td>
<td>A sub-study: the original study was excluded</td>
</tr>
</tbody>
</table>
H.8 Type 1 diabetes – blood ketone monitoring

Review question

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bashford, J., Acerini, C.L., How to use near-patient capillary ketone meters, Archives of Disease in Childhood Education and Practice, 97, 217-221, 2012</td>
<td>Narrative review article. Only relevant study cited is already included in review (Laffel et al., 2006)</td>
</tr>
<tr>
<td>Bektas, F., Eray, O., Sari, R., Akbas, H., Point of care blood ketone testing of diabetic patients in the emergency department, Endocrine Research, 30, 395-402, 2004</td>
<td>Monitoring in hospital</td>
</tr>
<tr>
<td>Bismuth, E., Laffel, L., Can we prevent diabetic ketoacidosis in children?, Pediatric Diabetes, 8, 24-33, 2007</td>
<td>Not a systematic review</td>
</tr>
<tr>
<td>Klocker, A.A., Phelan, H., Twigg, S.M., Craig, M.E., Blood beta-hydroxybutyrate vs. urine acetoacetate testing for the prevention and management of ketoacidosis in Type 1 diabetes: a systematic review, Diabetic Medicine, 30, 818-824, 2013</td>
<td>Systematic review. References checked - only relevant article is already included in this review (Laffel et al., 2006). Three other studies included in systematic review do not pertain to this question (all consider inpatient monitoring of ketones).</td>
</tr>
<tr>
<td>Lawrence, S.E., Diagnosis and treatment of diabetic ketoacidosis in children and adolescents, Paediatrics and Child Health, 10, 21-24, 2005</td>
<td>Review and recommendations (not a systematic review)</td>
</tr>
<tr>
<td>Vanelli, M., Chiari, G., Capuano, C., Iovane, B., Bernardini, A., Giacalone, T., The direct measurement of 3-beta-hydroxybutyrate enhances the management of diabetic ketoacidosis in children and reduces time and costs of treatment, Diabetes, Nutrition and Metabolism - Clinical and Experimental, 16, 312-316, 2003</td>
<td>Monitoring in hospital</td>
</tr>
</tbody>
</table>
## H.9 Type 1 diabetes – dietary advice

### Review questions

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aguilar, Maria J., Garcia, Pedro A., Gonzalez, Emilio, Perez, Maria C., Padilla, Carlos A.</td>
<td>A nursing educational intervention helped by One Touch UltraSmart improves monitoring and glycated haemoglobin levels in type 1 diabetic children, Journal of Clinical Nursing, 21, 1024-1032, 2012</td>
</tr>
<tr>
<td>Bishop, F.K., Maahs, D.M., Spiegel, G., Owen, D.</td>
<td>Excluded studies: not a randomised study, not an RCT. Only assesses ability of children and young people to count carbohydrates, not outcomes associated with carbohydrate counting</td>
</tr>
<tr>
<td>Forsander, G., Malmnolin, B., Eklund, C., Persson, B.</td>
<td>Relationship between dietary intake in children with diabetes mellitus type I, their management at diagnosis, social factors, anthropometry and glycaemic control, Scandinavian Journal of Nutrition/Näringforskning, 47, 75-84, 2003</td>
</tr>
<tr>
<td>Gilbertson, H.R., Brand-Miller, J.C., Thorburn, A.W., Evans, S., Chondros, P., Werther, G.A.</td>
<td>Study did not examine carbohydrate counting</td>
</tr>
<tr>
<td>Goksen, D., Ozen, S., Altkalinok, Y., Demir, G., Darcan, S.</td>
<td>Effects of carbohydrate counting method on metabolic control in children with type 1 diabetes, Pediatric Diabetes, 13, 142-142, 2012</td>
</tr>
<tr>
<td>Kaufman, F.R., Halvorson, M., Carpenter, S.</td>
<td>Use of a plastic insulin dosage guide to correct blood glucose levels out of the target range and for carbohydrate counting in subjects with type 1 diabetes, Diabetes Care, 22, 1252-1257, 1999</td>
</tr>
<tr>
<td>Lowe, J., Linjawi, S., Mensch, M., James, K., Attia, J.</td>
<td>Flexible</td>
</tr>
<tr>
<td>Non-randomised study</td>
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What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eating and flexible insulin dosing in patients with diabetes: Results of an intensive self-management course, Diabetes Research and Clinical Practice, 80, 439-443, 2008</td>
<td>Non-randomised study</td>
</tr>
<tr>
<td>Schmidt, S., Meidgaard, M., Serifovski, N., Storm, C., Christensen, T.M., Gade-Rasmussen, B., Norgaard, K., Use of an automated bolus calculator in MDI-treated type 1 diabetes: the BolusCal Study, a randomized controlled pilot study, Diabetes Care, 35, 984-990, 2012</td>
<td>All participants aged &gt; 18 years</td>
</tr>
</tbody>
</table>

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

Review question

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bektas, F., Eray, O., Sari, R., Akbas, H., Point of care blood ketone testing of diabetic patients in the emergency department, Endocrine Research, 30, 395-402, 2004</td>
<td>PICO not met - adult participants only.</td>
</tr>
</tbody>
</table>
H.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions

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

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

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

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

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

These 3 questions were addressed through a single search and there is one combined list of excluded studies.
**Study** | **Reason for exclusion**
---|---
Harris, G.D., Fiordalisi, I., Physiologic management of diabetic ketoacidemia. A 5-year prospective pediatric experience in 231 episodes. Archives of Pediatrics and Adolescent Medicine, 148, 1046-1052, 1994 | Not a comparative study
Klocker, A.A., Phelan, H., Twigg, S.M., Craig, M.E., Blood beta-hydroxybutyrate vs. urine acetoacetate testing for the prevention and management of ketoacidosis in Type 1 diabetes: a systematic review, Diabetic Medicine, 30, 818-824, 2013 | Systematic review of blood versus urine ketone testing
Naunheim, R., Jang, T.J., Banet, G., Richmond, A., McGill, J., Point-of-care test identifies diabetic ketoacidosis at triage, Academic Emergency Medicine, 13, 683-685, 2006 | Not a comparative study
Rewers, A., McFann, K., Chase, H.P., Bedside monitoring of blood beta-hydroxybutyrate levels in the management of diabetic ketoacidosis in children, Diabetes Technology and Therapeutics, 8, 671-676, 2006 | Not a comparative study

### H.12 Type 1 and type 2 diabetes – diabetic ketoacidosis- fluids

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

No articles were ordered for detailed consideration for this review question and so there is no excluded studies list.

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcillo,J.A., Intravenous fluid choices in critically ill children, Current Opinion in Critical Care, 20, 396-401, 2014</td>
<td>Discussion paper for reference checking. Relevant studies have been included in the guideline review.</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basnet,S., Venepalli,P.K., Andoh,J., Verhulst,S., Koirala,J., Effect of normal saline and half normal saline on serum electrolytes during recovery phase of diabetic ketoacidosis, Journal of Intensive Care Medicine, 29, 38-42, 2014</td>
<td>Normal saline was compared with half-normal saline; no additives of interest to the GDG were assessed.</td>
</tr>
<tr>
<td>Thuzar,M., Malabu,U.H., Tisdell,B., Sangla,K.S., Use of a standardised diabetic ketoacidosis management protocol improved clinical outcomes, Diabetes Research and Clinical Practice, 104, E8-E11, 2014</td>
<td>Patients &gt;= 16 years were included (mean age 30 years).</td>
</tr>
</tbody>
</table>
H.13  **Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents**

Review question

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>White, P.C., Dickson, B.A., Low morbidity and mortality in children with diabetic ketoacidosis treated with isotonic fluids, J Pediatr 2013 Sep;163(3):927, Journal of Pediatrics, 163, 761-766, 2013.</td>
<td>The dextrose assessed in this study, which is a type of additive, was not included in the protocol.</td>
</tr>
<tr>
<td>Wilson, H.K., Keuer, S.P., Lea, A.S., Boyd, A.E., III, Eknoyan, G., Phosphate therapy in diabetic ketoacidosis, Archives of Internal Medicine, 142, 517-520, 1982</td>
<td>PICO not met: adult population, mean age 26.8 years, range 14 to 58 years.</td>
</tr>
</tbody>
</table>

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

Review questions

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

All articles order for detailed consideration for this review question were included in the review and so there is no excluded studies list.

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

All articles order for detailed consideration for this review question were included in the review and so there is no excluded studies list.
H.15  Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis

Review question

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

No articles were ordered for detailed consideration for this review question and so there is no excluded studies list.

H.16  Type 1 diabetes – retinopathy

Review question

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>When to screen for retinopathy in children with diabetes, Consultant, 38, 1320, 1998</td>
<td>Summary of American Academy of Pediatrics guidelines only; no data reported</td>
</tr>
<tr>
<td>Progression of retinopathy with intensive versus conventional treatment in the Diabetes Control and Complications Trial. Diabetes Control and Complications Trial Research Group, Ophthalmology, 102, 647-661, 1995</td>
<td>Mean age 26.4 years; data on children and young people reported separately in an included study</td>
</tr>
<tr>
<td>Aiello,L.P., Diabetic retinopathy and other ocular findings in the diabetes control and complications trial/epidemiology of diabetes interventions and complications study, Diabetes Care, 37, 17-23, 2014</td>
<td>No stratification by age; full DCCT cohort, therefore, mean age &gt; 18 years</td>
</tr>
<tr>
<td>Al-Fifi,S.H., Intensive insulin treatment versus conventional regimen for adolescents with type 1 diabetes, benefits and risks, Saudi Medical Journal, 24, 485-487, 2003</td>
<td>Population included 12 to 18 year-olds; no stratification of prevalence of retinopathy within this age range</td>
</tr>
<tr>
<td>Amutha,A., Datta,M., Unnikrishnan,R., Anjana,R.M., Mohan,V., Clinical profile and complications of childhood- and adolescent-onset type 2 diabetes seen at a diabetes center in south India, Diabetes Technology and Therapeutics, 14, 497-504, 2012</td>
<td>No data on prevalence of retinopathy according to age or duration of diabetes</td>
</tr>
<tr>
<td>Betts,P.R., Logatchov,M., Volkov,I., Murphy,H., Dombrowskaya,N., Borzikh,S., Ivanova,I., Twyman,S., Vartan,J., An assessment of paediatric diabetes care in three centres in Russia and in Southampton, UK. The Paediatric Teams in Moscow, Tula, Tambov, Southampton, Diabetic Medicine, 16, 772-778, 1999</td>
<td>No stratification according to age or duration of diabetes; method of identifying retinopathy not reported</td>
</tr>
<tr>
<td>Cahill,M., Wallace,D., Travers,S., Lipinski,H., Aldington,S., Costigan,C., Mooney,D., Detection and prevalence of early diabetic retinopathy in juvenile diabetics with diabetes for 10 years or more, Eye, 14, 847-850, 2000</td>
<td>Fluorescein angiography used to identify retinopathy</td>
</tr>
<tr>
<td>Chiumello,G., Bognetti,E., Meschi,F., Carra,M., Balzano,E., Early diagnosis of subclinical complications in insulin dependent diabetic children and adolescents, Journal of Endocrinological Investigation, 12, 101-104, 1989</td>
<td>No stratification of retinopathy prevalence within age group (population age range 11.4 to 22.6 years)</td>
</tr>
<tr>
<td>Cobuz,M., Cobuz,G., Chronic complications of type 1 diabetes mellitus in children, Romanian Journal of Diabetes, Nutrition and Metabolic Diseases, 19, 301-309, 2012</td>
<td>Prevalence of retinopathy not grouped according to age or duration of diabetes; method of identifying retinopathy not reported</td>
</tr>
</tbody>
</table>
### Study Table

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Danne,T., Kordonouri,O., Casari,A., Tumini,S., Chiarelli,F., Recent advances on the pathogenesis and management of both diabetic retinopathy and nephropathy with particular reference to children and adolescents with Type 1 diabetes. [87 refs], Diabetes, Nutrition and Metabolism - Clinical and Experimental, 12, 136-144, 1999</td>
<td>Narrative review</td>
</tr>
<tr>
<td>Demirel,F., Tepe,D., Kara,O., Esen,I., Microvascular complications in adolescents with type 1 diabetes mellitus, JCRPE Journal of Clinical Research in Pediatric Endocrinology, 5, 145-149, 2013</td>
<td>No stratification by age or duration of diabetes</td>
</tr>
<tr>
<td>Donaghue,K.C., Chiarelli,F., Trotta,D., Allgrove,J., hl-Jorgensen,K., Microvascular and macrovascular complications associated with diabetes in children and adolescents, Pediatric Diabetes, 10, 195-203, 2009</td>
<td>Clinical guideline, no primary data</td>
</tr>
<tr>
<td>Donaghue,K.C., Craig,M.E., Chan,A.K., Fairchild,J.M., Cusumano,J.M., Verge,C.F., Crock,P.A., Hing,S.J., Howard,N.J., Silink,M., Prevalence of diabetes complications 6 years after diagnosis in an incident cohort of childhood diabetes, Diabetic Medicine, 22, 711-718, 2005</td>
<td>Prevalence of retinopathy recorded according to age, but data only provided graphically therefore unable to determine exact numbers</td>
</tr>
<tr>
<td>Donaghue,K.C., Fairchild,J.M., Craig,M.E., Chan,A.K., Hing,S., Cutler,L.R., Howard,N.J., Silink,M., Do all prepubertal years of diabetes duration contribute equally to diabetes complications?, Diabetes Care, 26, 1224-1229, 2003</td>
<td>No data on prevalence stratified by age or duration of diabetes</td>
</tr>
<tr>
<td>Downie,E., Craig,M.E., Hing,S., Cusumano,J., Chan,A.K., Donaghue,K.C., Continued reduction in the prevalence of retinopathy in adolescents with type 1 diabetes: role of insulin therapy and glycemic control, Diabetes Care, 34, 2368-2373, 2011</td>
<td>No data on prevalence of retinopathy according to age or duration of diabetes</td>
</tr>
<tr>
<td>EI,Asrar,M, Adly,A.A., EI,Hadidy,E, Abdelwahab,M.A., D-dimer levels in type 1 and type 2 diabetic children and adolescents; Relation to microvascular complications and dyslipidemia &quot;own data and review&quot;, Pediatric endocrinology reviews : PER, 9, 657-668, 2012</td>
<td>Ophthalmoscopy used to identify retinopathy; no stratification of prevalence according to age or duration of diabetes</td>
</tr>
<tr>
<td>Epps,M.C., Craig,M.E., Cusumano,J., Hing,S., Chan,A.K., Howard,N.J., Silink,M., Donaghue,K.C., Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes, Diabetes Care, 29, 1300-1306, 2006</td>
<td>No assessment of prevalence of retinopathy according to age or duration of diabetes</td>
</tr>
<tr>
<td>Florkowski,C.M., Scott,R.S., Coope,P.A., Graham,P.J., Moir,C.L., Age at diagnosis, glycaemic control and the development of retinopathy in a population-based cohort of Type 1 diabetic subjects in Canterbury, New Zealand, Diabetes Research and Clinical Practice, 52, 125-131, 2001</td>
<td>Ophthalmoscopy used to identify retinopathy; no assessment of prevalence according to age or duration of diabetes</td>
</tr>
<tr>
<td>Gallego,P.H., Craig,M.E., Hing,S., Donaghue,K.C., Role of blood pressure in development of early retinopathy in adolescents with type 1 diabetes: Prospective cohort study, BMJ, 337, 497-500, 2008</td>
<td>No stratification of prevalence according to age or duration of diabetes</td>
</tr>
</tbody>
</table>
### Diagnosis and management of type 1 diabetes in children and young people

#### Excluded studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holt, R.W., Lang, G.E., Grabert, M., Heinze, E., Lang, G.K., Debabar, K.M.</td>
<td>Diabetic retinopathy in pediatric patients according to age or duration of diabetes; data presented only graphically</td>
</tr>
<tr>
<td>Johnson, B., Elliott, J., Scott, A., Heller, S., Eisner, C.</td>
<td>Medical and psychological outcomes for young adults with Type 1 diabetes: No improvement despite recent advances in diabetes care, Diabetic Medicine, 31, 227-231, 2014</td>
</tr>
<tr>
<td>Klein, B.E., Moss, S.E., Klein, R.</td>
<td>Is menarche associated with diabetic retinopathy?, Diabetes Care, 13, 1034-1038, 1990</td>
</tr>
<tr>
<td>Klein, R., Klein, B.E., Moss, S.E., Davis, M.D., DeMets, D.L.</td>
<td>Retinopathy in young-onset diabetic patients, Diabetes Care, 8, 311-315, 1985</td>
</tr>
<tr>
<td>Kovacs, M., Mukerji, P., Drash, A., Iyengar, S., Biomedical and psychiatric risk factors for retinopathy among children with IDDM, Diabetes Care, 18, 1592-1599, 1995</td>
<td></td>
</tr>
<tr>
<td>Leccaire, T., Palta, M., Zhang, H., Allen, C., Klein, R., D’Alessio, D.</td>
<td>Lower-than-expected prevalence and severity of retinopathy in an incident cohort followed during the first 4-14 years of type 1 diabetes: the Wisconsin Diabetes Registry Study, American Journal of Epidemiology, 164, 143-150, 2006</td>
</tr>
<tr>
<td>Levy-Shraga, Y., Lerner-Geleva, L., Boyko, V., Graph-Barel, C., Mazor-Aronovitch, K., Modan-Moses, D., Pinhas-Hamiel, O.</td>
<td>No assessment of prevalence according to age or duration of diabetes; method of identifying retinopathy not reported</td>
</tr>
</tbody>
</table>
Excluded studies
Diagnosis and management of type 1 diabetes in children and young people

<table>
<thead>
<tr>
<th>Study</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Type 1 diabetes in pre-school children—long-term metabolic control, associated autoimmunity and complications, Diabetic Medicine, 29, 1291-1296, 2012</td>
<td>Method of identifying retinopathy not reported; no assessment of prevalence according to age or duration of diabetes</td>
</tr>
<tr>
<td>Lierre,M., Marre,M., Robert,J.J., Charpentier,G., Iannasci,F., Passa,P., Cross-sectional study of care, socioeconomic status and complications in young French patients with type 1 diabetes mellitus, Diabetes and Metabolism, 31, 41-46, 2005</td>
<td>No stratification according to age or duration of diabetes</td>
</tr>
<tr>
<td>Lueder,G.T., Pradhan,S., White,N.H., Risk of retinopathy in children with type 1 diabetes mellitus before 2 years of age, American Journal of Ophthalmology, 140, 930-931, 2005</td>
<td>Duplication of data already included in Donaghue 1999</td>
</tr>
<tr>
<td>Raman,V., Campbell,F., Holland,P., Chapman,T., Dabbs,T., 2011 retinopathy and maculopathy in Northland, New Zealand: Papiathip Hipp, Diabetes, Ophthalmology, 88, 613-618, 1981</td>
<td>No stratification according to age or duration of diabetes</td>
</tr>
<tr>
<td>Butler,G., Owens,D.R., Visual function in young IDDM patients over 8 years of age. A 4-year longitudinal study, Diabetes Care, 20, 1724-1730, 1997</td>
<td>No stratification of prevalence according to age or duration of diabetes</td>
</tr>
<tr>
<td>Minuto,N., Emmanuele,V., Vannati,M., Russo,C., Rebora,C., Panarello,S., Pistorio,A., Lorini,R., d'Annunzio,G., Retinopathy screening in patients with type 1 diabetes diagnosed in young age using a non-mydratic digital stereoscopic retinal imaging, Journal of Endocrinological Investigation, 35, 389-394, 2012</td>
<td>No stratification of prevalence according to age or duration of diabetes</td>
</tr>
<tr>
<td>Nicoloff,G., Baydanoff,S., Stanimirova,N., Petrova,C., Christova,P., Relationship between anti-elastin IgG subclasses and the development of microvascular complications - A three-year follow-up study in children with Type 1 (insulin-dependent) diabetes mellitus, Central-European Journal of Immunology, 26, 12-16, 2001</td>
<td>No stratification of prevalence according to age or duration of diabetes</td>
</tr>
<tr>
<td>North,R.V., Farrell,U., Banford,D., Jones,C., Gregory,J.W., Butler,G., Owens,D.R., Visual function in young IDDM patients over 8 years of age. A 4-year longitudinal study, Diabetes Care, 20, 1724-1730, 1997</td>
<td>No assessment of prevalence according to age or duration of diabetes</td>
</tr>
<tr>
<td>Olsen,B.S., Johannesen,J., Sjolie,A.K., Borch-Johnsen,K., Hougardss,P., Thorsteinsson,B., Prammings,S., Marinelli,K., Mortensen,H.B., Metabolic control and prevalence of microvascular complications in young Danish patients with Type 1 diabetes mellitus. Danish Study Group of Diabetes in Childhood, Diabetic Medicine, 16, 79-85, 1999</td>
<td>Includes longitudinal data only but 13.5% of participants had retinopathy at baseline, and new incidence not reported; cannot assume new incidence for 4 years' follow up due to the potential for regression of retinopathy</td>
</tr>
<tr>
<td>Owen,D.R., Farrell,U., Jones,C., North,R., Screening for diabetic retinopathy in young insulin-dependent diabetics (Type I), Pediatric Reviews and Communications, 8, 50-55, 1994</td>
<td>Data on prevalence of retinopathy according to duration of diabetes presented only graphically; no data on prevalence stratified according to age</td>
</tr>
<tr>
<td>Mean age 62.7 years</td>
<td>No assessment of prevalence according to age or duration of diabetes</td>
</tr>
</tbody>
</table>
### Diagnosis and management of type 1 diabetes in children and young people

**Excluded studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rogers,D.G., White,N.H., Shalwitz,R.A., Palmberg,P., Smith,M.E., Santiago,J.V., The effect of puberty on the development of early diabetic microvascular disease in insulin-dependent diabetes, Diabetes Research and Clinical Practice, 3, 39-44. 1987</td>
<td>No assessment of prevalence according to age; although all participants had 5 to 7 years' duration of diabetes, the study did not include participants in puberty, or early post-pubertal stage therefore not representative of entire population of children and young people with type 1 diabetes</td>
</tr>
<tr>
<td>Salardi,S., Rubbi,F., Puglioli,R., Brancalone,A., Bacchi-Reggiani,L., Ragni,L., Cacciari,E., Diabetic retinopathy in childhood: long-term follow-up by fluorescein angiography beginning in the first months of disease, Journal of Pediatric Endocrinology, 19, 507-515, 2001</td>
<td>Fluorescein angiography used to identify retinopathy; no assessment of prevalence according to age or duration of diabetes</td>
</tr>
<tr>
<td>Verougstraete,C., Toussaint,D., De Schepper,J., Haentjens,M., Dorchy,H., First microangiographic abnormalities in childhood diabetes - Types of lesions, Graeef's Archive for Clinical and Experimental Ophthalmology, 229, 24-32, 1991</td>
<td>Fluorescein angiography used to identify retinopathy; no assessment of prevalence according to age or duration of diabetes</td>
</tr>
<tr>
<td>Wan Nazaimoon,W.M., Letchuman,R., Noraini,N., Ropilah,A.R., Zainal,M., Ismail,I.S., Wan Mohamad,W.B., Faridah,I., Singaraveloo,M., Sheriff,I.H., Khalid,B.A., Systolic hypertension and duration of diabetes mellitus are important determinants of retinopathy and microalbuminuria in young diabetics, Diabetes Research and Clinical Practice, 46, 213-221, 1999</td>
<td>Retinopathy assessed by ophthalmoscopy; mean age of participants 26.9 years</td>
</tr>
<tr>
<td>White,N.H., Cleary,P.A., Dahms,W., Goldstein,D., Malone,J., Tamborlane,W.V., Diabetes Control and Complications Trial (DCCT), Beneficial effects of intensive therapy of diabetes during adolescence: outcomes after the conclusion of the Diabetes Control and Complications Trial (DCCT), Journal of Pediatrics, 139, 804-812, 2001</td>
<td>No stratification of prevalence according to age or duration of diabetes</td>
</tr>
<tr>
<td>Wiltshire,E.J., Mohsin,F., Chan,A., Donaghue,K.C., Methylene tetrahydrofolate reductase and methionine synthase reductase gene polymorphisms and protection from microvascular complications in adolescents with type 1 diabetes, Pediatric Diabetes, 9, 448-553, 2008</td>
<td>No stratification of prevalence according to age or duration of diabetes</td>
</tr>
</tbody>
</table>

### H.17 Type 1 diabetes – nephropathy

**Review question**

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allen,T.J., Cooper,M.E., Gilbert,R.E., Winikoff,J., Skinni,S.L., Jerums,G., Serum total renin is increased before microalbuminuria in diabetes, Kidney International, 50, 902-907, 1996</td>
<td>Study involving adults</td>
</tr>
<tr>
<td>Alleyn,C.R., Volkening,L.K., Wolfson,J., Rodriguez-</td>
<td>The threshold (ACR &gt; 20 microg/mg) for confirmation of</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
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<tr>
<td>----------------------------------------------------------------------</td>
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</tr>
<tr>
<td>Ventura,A., Wood,J.R., Lafei.L.M., Occurrence of microalbuminuria in young people with Type 1 diabetes: importance of age and diabetes duration, Diabetic Medicine, 27, 532-537, 2010</td>
<td>microalbuminuria used in the study corresponds to an ACR of &gt; 2.26 mg/mmol, which is lower than the UK standard of 2.5 mg/mmol for males and 3.5 mg/mmol for females</td>
</tr>
<tr>
<td>Amin,R., Bah, T.K., Widmer.B., Dalton,R.N., Dunger,D.B., Longitudinal relation between limited joint mobility, height, insulin-like growth factor 1 levels, and risk of developing microalbuminuria: The Oxford Regional Prospective Study, Archives of Disease in Childhood, 90, 1039-1044, 2005</td>
<td>Only the numbers of microalbuminuria participants under or above 11 years were reported; no information about the population size in each age group and, therefore, prevalence cannot be calculated</td>
</tr>
<tr>
<td>Amin,R., Turner,C., Van,Aken S., Bah, T.K., Watts,A., Lindess,D.R., Dalton,R.N., Dunger,D.B., The relationship between microalbuminuria and glomerular filtration rate in young type 1 diabetic subjects: The Oxford Regional Prospective Study, Kidney International, 68, 1740-1749, 2005</td>
<td>Children and young people under 16 years diagnosed with type 1 diabetes were included; at 5 years’ duration, when microalbuminuria was measured, some of them were already over 18 years</td>
</tr>
<tr>
<td>Amin,R., Widmer.B., Dalton,R.N., Dunger,D.B., Unchanged incidence of microalbuminuria in children with type 1 diabetes since 1986: a UK based inception cohort, Archives of Disease in Childhood, 94, 258-262, 2009</td>
<td>No cumulative prevalence before the age of 18 years was reported; prevalence by diabetes duration was reported in Kaplan-Meier graph only</td>
</tr>
<tr>
<td>Amin,R., Widmer.B., Prevost,A.T., Schwarze,P., Cooper,J., Edge,J., Marcovcechio,L., Neil,A., Dalton,R.N., Dunger,D.B., Risk of microalbuminuria and progression to macroalbuminuria in a cohort with childhood onset type 1 diabetes: prospective observational study, BMJ, 336, 697-701, 2008</td>
<td>Prevalence by age for all types of microalbuminuria (including intermittent and persistent) were reported together</td>
</tr>
<tr>
<td>Bakman,M., Yuksel,B., Topaloglu,A.K., Mungan,N.O., Ozer,G., Risk factors for microalbuminuria in children and adolescents with insulin dependent diabetes mellitus, Annals of Medical Sciences, 10, 156-159, 2001</td>
<td>Just an overall prevalence for all participants was reported, no stratification according to age</td>
</tr>
<tr>
<td>Barkai,L., Van,Aken S., Lukac,K., Enhanced progression of urinary albumin excretion in IDDM during puberty, Diabetes Care, 21, 1019-1023, 1998</td>
<td>Just an overall prevalence was reported, no stratification according to age</td>
</tr>
<tr>
<td>Basiratnia,M., Abadi,S.F., Amirhakimi,G.H., Karamizadeh,Z., Karamifar,H., Ambulatory blood pressure monitoring in children and adolescents with type-1 diabetes mellitus and its relation to diabetic control and microalbuminuria, Saudi Journal of Kidney Diseases and Transplantation, 23, 311-315, 2012</td>
<td>Just an overall prevalence was reported, no stratification according to age</td>
</tr>
<tr>
<td>Bertalan,R., Gregory,J.W., Detecting diabetes complications in children, Practical Diabetes, 28, 352-357a, 2011</td>
<td>Background reading</td>
</tr>
<tr>
<td>Bojestig,M., Arnqvist,H.J., Karlberg,B.E., Ludvigsson,J., Unchanged incidence of severe retinopathy in a population of Type 1 diabetic patients with marked reduction of nephropathy, Diabetic Medicine, 15, 863-869, 1998</td>
<td>Only a cumulative incidence of nephropathy after 20 years’ follow-up was reported</td>
</tr>
<tr>
<td>Bojestig,M., Arnqvist,H.J., Karlberg,B.E., Ludvigsson,J., Glycemic control and prognosis in type 1 diabetic patients with microalbuminuria, Diabetes Care, 19, 313-317, 1996</td>
<td>Just an overall prevalence was reported, no stratification according to age</td>
</tr>
<tr>
<td>Bruno,G., Pagano,G., Low prevalence of microalbuminuria in young Italian insulin-dependent diabetic patients with short duration of disease: a population-based study, Piedmont Study Group for Diabetes Epidemiology, Diabetic Medicine, 13, 889-893, 1996</td>
<td>Microalbuminuria was tested on 1 overnight urine sample only</td>
</tr>
<tr>
<td>Campbell,F.M., Microalbuminuria and nephropathy in insulin dependent diabetes mellitus, Archives of Disease in Childhood, 73, 4-7, 1995</td>
<td>Background reading</td>
</tr>
<tr>
<td>Chiarelli,F., Verrotti,A., Morgese,G., Glomerular hyperfiltration increases the risk of developing microalbuminuria in diabetic children, Pediatric Nephrology, 9, 154-158, 1995</td>
<td>Only participants with hyperfiltration &gt; 140 ml/minute per 1.73 square metres were included in the study to assess the development of microalbuminuria</td>
</tr>
<tr>
<td>Cizmeciglu,F.M., Noyes,K., Bath,L., Kelnar,C., Audit of microalbumin excretion in children with type I diabetes, Journal of clinical research in pediatric endocrinology, 1, 136-143, 2009</td>
<td>Just an overall prevalence for the age group 10 to 16 years was reported, no further stratification</td>
</tr>
<tr>
<td>Cobas,R.A., Santos,B., Da,SilvaP, Neves,R., Gomes,M.B., Progression to microalbuminuria in patients with type 1 diabetes: A seven-year prospective study, Diabetology and metabolic syndrome, 3, -, 2011</td>
<td>Study subjects included those who were older than 18 years</td>
</tr>
<tr>
<td>Cobuz,M., Cobuz,G., Chronic complications of type 1 diabetes mellitus in children, Romanian Journal of Diabetes, Nutrition and Metabolic Diseases, 19, 301-309, 2012</td>
<td>Just an overall prevalence was reported, no stratification according to age</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
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<td>----------------------------------------------------------------------</td>
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<tr>
<td>type 1 diabetes. Diabetes Care, 36, 3863-3869, 2013</td>
<td>Just the number of microalbuminuria participants was reported, prevalence cannot be calculated</td>
</tr>
<tr>
<td>Couper,J.J., Staples,A.J., Cocciolone,R., Nairn,J., Badcock,N., Henning,P., Relationship of smoking and albuminuria in children with insulin-dependent diabetes, Diabetic Medicine, 11, 666-669, 1994</td>
<td>AER was tested on 1 urine sample only, not in line with the UK standard (at least 2 out of 3 consecutive urine collections over a period of 9 to 4 months)</td>
</tr>
<tr>
<td>Dahlquist,G., Rudberg,S., The prevalence of microalbuminuria in diabetic children and adolescents and its relation to puberty, Acta Paediatrica Scandinavica, 76, 795-800, 1987</td>
<td>Only an overall prevalence for all participants after 8 years’ follow-up was reported</td>
</tr>
<tr>
<td>Dahlquist,G., Stattn,E.L., Rudberg,S., Urinary albumin excretion rate and glomerular filtration rate in the prediction of diabetic nephropathy; a long-term follow-up study of childhood onset type-1 diabetic patients, Nephrology Dialysis Transplantation, 15, 1382-1386, 2001</td>
<td>Microalbuminuria was tested on a 24-hour urine collection only</td>
</tr>
<tr>
<td>D’Antonio,J.A., Ellis,D., Doff,B.H., Becker,D.J., Drash,A.L., Kuller,L.H., Orchard,T.J., Diabetes complications and glycemic control. The Pittsburgh Prospective Insulin-Dependent Diabetes Cohort Study Status Report after 5 yr of IDDM, Diabetes Care, 12, 694-70, 1999</td>
<td>Only an overall prevalence for the duration between 2 and 15 years was reported; no data stratified by age</td>
</tr>
<tr>
<td>Demirel,F., Tepe,D., Kara,O., Esen,I., Microvascular complications in adolescents with type 1 diabetes mellitus, JCRPE Journal of Clinical Research in Pediatric Endocrinology, 5, 145-149, 2013</td>
<td>Just an overall prevalence for all participants was reported, no stratification according to age</td>
</tr>
<tr>
<td>Donaghue,K.C., Craig,M.E., Chan,A.K., Fairchild,J.M., Usman,J., Howard,N.J., Silink,M., Prevalence of diabetes complications 6 years after diagnosis in an incident cohort of childhood diabetes, Diabetic Medicine, 22, 711-718, 2005</td>
<td>The threshold (AER &gt; 15 microg/minute)used for confirmation of microalbuminuria in the study corresponds to ACR &gt; 2.65mg/mmol for males and 2.96 mg/mmol for females, the threshold for females was lower than that of the UK standards (2.5 mg/mmol for males and 3.5 mg/mmol for females)</td>
</tr>
<tr>
<td>Donaghue,K.C., Fairchild,J.M., Chan,A., Hing,S.J., King,J., Howard,N.J., Silink,M., Diabetes microvascular complications in prepubertal children, Journal of Pediatric Endocrinology, 10, 579-585, 1997</td>
<td>Just an overall prevalence was reported, no stratification according to age</td>
</tr>
<tr>
<td>Donaghue,K.C., Fairchild,J.M., Craig,M.E., Chan,A.K., Hing,S., Cutler,L.R., Howard,N.J., Silink,M. Do all prepubertal years of diabetes duration contribute equally to diabetes complications?, Diabetes Care, 26, 1224-1229, 2003</td>
<td>Longitudinal study, data analysed were from the lastest assessment when selected participants were already older than 18 years</td>
</tr>
<tr>
<td>Dost,A., Klinkert,C., Kapellen,T., Lemmer,A., Naeye,A., Grabert,M., Kreuder,J., Holl,R.W., DPV,Science,I. Arterial hypertension determined by ambulatory blood pressure profiles: contribution to microalbuminuria risk in a multicenter investigation in 2,105 children and adolescents with type 1 diabetes, Diabetes Care, 31, 720-725, 2008</td>
<td>Just an overall prevalence was reported, no stratification according to age</td>
</tr>
<tr>
<td>Ebeling,P., Koivisto,V.A., Occurrence and interrelationships of complications in insulin-dependent diabetes in Finland, Acta Diabetologica, 34, 33-38, 1997</td>
<td>The youngest age group assessed ranged from 15 to 27 years</td>
</tr>
<tr>
<td>Elamin,A., li Omer,M.I., Ismail,B., Tuvelo,T., Microalbuminuria in young Sudanese patients with type 1 diabetes, Annals of Saudi Medicine, 13, 493-497, 1993</td>
<td>The study was undertaken in Sudan</td>
</tr>
<tr>
<td>Gorman,D., Sochett,E., Daneman,D., The natural history of microalbuminuria in adolescents with type 1 diabetes, Journal of Pediatrics, 134, 333-337, 1999</td>
<td>Just an overall prevalence was reported, no stratification according to age</td>
</tr>
<tr>
<td>Harvey,J.N., Allagoa,B., The long-term renal and retinal outcome of childhood-onset Type 1 diabetes, Diabetic Medicine, 21, 26-31, 2004</td>
<td>Mean AER values by age at onset of diabetes rather than microalbuminuria prevalence by age were reported</td>
</tr>
<tr>
<td>Holl,R.W., Grabert,M., Thon,A., Heinze,E., Urinary excretion of albumin in adolescents with type 1 diabetes: persistent versus intermittent microalbuminuria and relationship to duration of diabetes, sex, and metabolic control, Diabetes Care, 22, 1555-1560, 1999</td>
<td>Just numbers of microalbuminuria patients by age were reported, no prevalence or incidence can be calculated</td>
</tr>
<tr>
<td>Izumi,K., Hoshi,M., Kuno,S., Okuno,G., Yamazaki,Y.,</td>
<td>Just an overall prevalence for all participants was reported,</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>--------------------------------------------------------------</td>
</tr>
<tr>
<td>Ishihiki, G., Sasaki, A., Glycemic control, growth and complications in children with insulin-dependent diabetes mellitus—a study of children enrolled in a Summer camp program for diabetics in Kinki district, Japan, Diabetes Research and Clinical Practice, 28, 185-190, 1995</td>
<td>no stratification according to age</td>
</tr>
<tr>
<td>Janner, M., Knill, S.E., Diem, P., Zuppinger, K.A., Mulfis, P.E., Persistent microalbuminuria in adolescents with type I (insulin-dependent) diabetes mellitus is associated to early rather than late puberty. Results of a prospective longitudinal study, European Journal of Pediatrics, 153, 403-408, 1994</td>
<td>Just an overall prevalence for all participants was reported, no stratification according to age</td>
</tr>
<tr>
<td>Joner, G., Brinchmann-Hansen, O., Torres, C.G., Hanssen, K.F., A nationwide cross-sectional study of retinopathy and microalbuminuria in young Norwegian type 1 (insulin-dependent) diabetic patients, Diabetologia, 35, 1049-1054, 1992</td>
<td>Cut-off point for microalbuminuria was set at AER &gt; 15 microg/minute, which corresponds to ACR &gt;= 2.65 mg/mmol for males or &gt;= 2.96 mg/mmol for females, the threshold for females was lower than that of the UK standards (2.5 mg/mmol for males and 3.5 mg/mmol for females)</td>
</tr>
<tr>
<td>Jones, C.A., Leese, G.P., Kerr, S., Bestwick, K., Isherwood, D.I., Vora, J.P., Hughes, D.A., Smith, C., Development and progression of microalbuminuria in a clinic sample of patients with insulin dependent diabetes mellitus, Archives of Disease in Childhood, 78, 518-523, 1998</td>
<td>Prevalence by age for all types of microalbuminuria (including intermittent and persistent) was reported</td>
</tr>
<tr>
<td>Karavanaki, K., Baum, J.D., Coexistence of impaired indices of autonomic neuropathy and diabetic nephropathy in a cohort of children with type 1 diabetes mellitus, Journal of Pediatric Endocrinology, 16, 79-90, 2003</td>
<td>Just the number of persistent microalbuminuria participants was reported, no population size of age groups and no prevalence can be calculated</td>
</tr>
<tr>
<td>Kim, N.H., Pavkov, M.E., Knowler, W.C., Hanson, R.L., Weil, E.J., Curtis, J.M., Bennett, P.H., Nelson, R.G., Predictive value of albuminuria in American Indian youth with or without type 2 diabetes, Pediatrics, 125, e844-e851, 2010</td>
<td>Study involving adults &gt; 18 years</td>
</tr>
<tr>
<td>Laborde, K., Levy-Marchal, C., Kindermans, C., Dechaux, M., Czemichow, P., Sachs, C., Glomerular function and microalbuminuria in children with insulin-dependent diabetes, Pediatric Nephrology, 4, 39-43, 1990</td>
<td>Microalbuminuria was determined by 1 urine sample in the morning only</td>
</tr>
<tr>
<td>Lee, T.H., Han, S.H., The prevalence of complications in Korean diabetic subjects, Tohoku Journal of Experimental Medicine, 141 Suppl. 361-365, 1983</td>
<td>The youngest group started from 19 years of age, and just the number of microalbuminuria participants was reported</td>
</tr>
<tr>
<td>Levy-Shraga, Y., Lerner-Geva, L., Boyko, V., Graph-Barel, C., Mazor-Aronovitch, K., Modan-Moses, D., Pinhas-Hamiel, O., Type 1 diabetes in pre-school children—long-term metabolic control, associated autoimmunity and complications, Diabetic Medicine, 29, 1291-1296, 2012</td>
<td>Complications were grouped together and cumulative incidence of all complications was reported in a graph</td>
</tr>
<tr>
<td>Lievre, M., Marre, M., Robert, J.J., Charpentier, G., Iannaccioli, F., Passa, P., Diabetes, therapeutic Strategies and COmlications (DISCO) investigators, Cross-sectional study of care, socio-economic status and complications in young French patients with type 1 diabetes mellitus, Diabetes and Metabolism, 31, 41-46, 2005</td>
<td>Just an overall prevalence for all participants was reported, no stratification according to age</td>
</tr>
<tr>
<td>Likitmaskul, S., Wacharasindhu, S., Rawdaree, P., Ngarmukos, C., Deerochanawong, C., Suwanwaliakorn, S., Chetthakul, T., Bunnap, P., Kosachunhanun, N., Plengvidhaya, N., Leelawatana, R., Kritiyawong, S., Benjasuratwong, Y., Pratipanawatr, T., Thailand Diabetes Registry Project: Type of diabetes, glycemic control and prevalence of microvascular complications in children and adolescents with diabetes, Journal of the Medical Association of Thailand, 89, S10-S16, 2006</td>
<td>No microalbuminuria prevalence was reported</td>
</tr>
<tr>
<td>Majaliwa, E.S., Munubhi, E., Ramaiya, K., Mpembeni, R., Saniyia, A., Mohn, A., Chiarelli, F., Survey on acute and chronic complications in children and adolescents with type</td>
<td>Just the numbers of microalbuminuric participants by age group were reported, no prevalence can be calculated</td>
</tr>
</tbody>
</table>
## Excluded studies

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 diabetes at Muhimbili National Hospital in Dar es Salaam, Tanzania, Diabetes Care, 30, 2187-2192, 2007</td>
<td>Just an overall prevalence was reported, no stratification according to age</td>
</tr>
<tr>
<td>Marcevecchio,M.L., Dalton,R.N., Chiarelli,F., Dunger,D.B., A1C variability as an independent risk factor for microalbuminuria in young people with type 1 diabetes, Diabetes Care, 34, 1011-1013, 2011</td>
<td>Just an overall prevalence was reported, no stratification according to age</td>
</tr>
<tr>
<td>Marshall,S.M., Hackett,A., Court,S., Parkin,M., Alberti,K.G., Albumin excretion in children and adolescents with insulin-dependent diabetes, Diabetes Research, 3, 345-348, 1986</td>
<td>Cut-off point for microalbuminuria was set at AER &gt;14 microg/min, which corresponds to ACR &gt;=2.48mg/mmol for males or &gt;=2.71mg/mmol for females (lower than the UK standards)</td>
</tr>
<tr>
<td>Mathiesen,E.R., Saurbrey,N., Hommel,E., Parving,H.H., Prevalence of microalbuminuria in children with type 1 (insulin-dependent) diabetes mellitus, Diabetologia, 29, 640-643, 1986</td>
<td>Cut-off point for microalbuminuria was set at AER &gt;14 microg/min, which corresponds to ACR &gt;=2.48mg/mmol for males or &gt;=2.71mg/mmol for females (lower than the UK standards)</td>
</tr>
<tr>
<td>Matyka,K., Microalbuminuria in childhood diabetes, Journal of the Royal College of Physicians of Edinburgh, 39, 233-235, 2009</td>
<td>Not a primary study; summary of previous relevant publications</td>
</tr>
<tr>
<td>McVean,J.J., Eickhoff,J.C., MacDonald,M.J., Prevalence of early microalbuminuria in children with type 1 diabetes mellitus, Journal of Pediatric Endocrinology, 21, 469-471, 2008</td>
<td>ACR was tested on at least 1 random urine collection, including single urine sample</td>
</tr>
<tr>
<td>Midyett,L.K., Grunt,J., Simon,S.D., Noninvasive radial artery tonometry augmentation index and arterial albumin/creatinine levels in early adolescents with type 1 diabetes mellitus, Journal of Pediatric Endocrinology and Metabolism, 22, 531-537, 2009</td>
<td>ACRs by age and diabetes duration were only reported graphically</td>
</tr>
<tr>
<td>Moayeri,H., Dalili,H., Prevalence of microalbuminuria in children and adolescents with diabetes mellitus type I, Acta Medica Iranica, 44, 105-110, 2006</td>
<td>Just the number of microalbuminuria participants was reported, no prevalence by age can be calculated</td>
</tr>
<tr>
<td>Mogensen,C.E., Christensen,C.K., Predicting diabetic nephropathy in insulin-dependent patients, New England Journal of Medicine, 311, 89-93, 1984</td>
<td>Just an overall prevalence was reported, no stratification according to age</td>
</tr>
<tr>
<td>Mohsin,F., Craig,M.E., Cusumano,J., Chan,A.K., Hing,S., Lee,J.W., Slink,M., Howard,N.J., Donaghue,K.C., Discordant trends in microvascular complications in adolescents with type 1 diabetes from 1990 to 2002, Diabetes Care, 28, 1974-1980, 2005</td>
<td>Just an overall prevalence was reported, no stratification according to age</td>
</tr>
<tr>
<td>Moore,T.H., Shield,J.P., Prevalence of abnormal urinary albumin excretion in adolescents and children with insulin dependent diabetes: the MIDAC study. Microalbuminuria in Diabetic Adolescents and Children (MIDAC) research group, Archives of Disease in Childhood, 83, 239-243, 2000</td>
<td>Microalbuminuria prevalence was stratified by puberty status (which was not defined by age) rather than by age</td>
</tr>
<tr>
<td>Moore,T.H., Shield,J.P., Microalbuminuria in diabetic adolescents and children—feasibility phase of a national cross-sectional study, MIDAC Research Group, Journal of Diabetes and its Complications, 13, 122-128, 1999</td>
<td>Just an overall prevalence for all participants was reported, not stratified by age</td>
</tr>
<tr>
<td>Morgese,G., Chiarelli,F., La,Penna G., Verrotti,A., Early detection of nephropathy in juvenile diabetes. Journal of Endocrinological Investigation, 12, 139-140, 1989</td>
<td>Just an overall prevalence for all participants was reported, no stratification according to age</td>
</tr>
<tr>
<td>Mortensen,H.B., Epidemiology of microalbuminuria among children with and without diabetes. Danish Study Group of Diabetes in Childhood, Journal of Diabetes and its Complications, 8, 164-165, 1994</td>
<td>Just an overall prevalence was reported, no stratification according to age</td>
</tr>
<tr>
<td>Mortensen,H.B., Hougaaard,P., Ibsen,K.K., Parving,H.H., Petersen,K., Nerup,J., Marner,B., Holstein,V., Haase,H., Saurbrey,N., Klinge,I., Bille,T., Kreutzfeldt,J., Lund,H.I., Pedersen,I.L., Maclntyre,B., Rasmussen,S.W., Hobolth,N., Brems,M., Relationship between blood pressure and urinary albumin excretion rate in young Danish Type 1 diabetic patients: Comparison to non-diabetic children, Diabetic Medicine, 11, 155-161, 1994</td>
<td>Just the numbers of microalbuminuria participants for different age groups were reported, no prevalence can be calculated</td>
</tr>
<tr>
<td>Mortensen,H.B., Marinelli,K., Norgaard,K., Main,K., Kastrup,K.W., Ibsen,K.K., Villumsen,J., Parving,H.H., A nation-wide cross-sectional study of urinary albumin excretion rate, arterial blood pressure and blood glucose control in Danish children with type 1 diabetes mellitus, Diabetic Medicine, 7, 887-897, 1990</td>
<td>Prevalence stratified by age and duration was only reported only graphically</td>
</tr>
<tr>
<td>Mullis,P., Kochil,H.P., Zuppinger,K., Schwarz,H.P., Intermittent microalbuminuria in children with type 1 diabetes mellitus without clinical evidence of nephropathy, European Journal of Pediatrics, 147, 385-388, 1988</td>
<td>The threshold (AER &gt;15 microg/min) used for confirmation of microalbuminuria in the study corresponds to ACR &gt;2.65mg/mmol for males or 2.96 mg/mmol for females, the threshold for females was lower than that of the UK standards (2.5mg/mmol for males and 3.5mg/mmol for females)</td>
</tr>
<tr>
<td>Nazim,J., Dziatkowiak,H., Szefko,K., Six-year observation of adolescents with type 1 diabetes and microalbuminuria,</td>
<td>Age of participants ranged from 2.2 to 24 years</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Diabetologia Polska, 7, 166-170, 2000</td>
<td></td>
</tr>
<tr>
<td>Nicoloff,G., Baydanoﬀ,S., Stanimirova,N., Petrova,C., Christova,P.,</td>
<td>Only an overall prevalence for a wide age range (5 to 13 years) was reported</td>
</tr>
<tr>
<td>Detection of serum collagen type IV in children with type 1 (insulin-dependent) diabetes mellitus—a longitudinal study, Pediatric Diabetes, 2, 184-190, 2001</td>
<td></td>
</tr>
<tr>
<td>Olkere,A.N., Anochic,I.C., Eke,F.U., Prevalence of microalbuminuria among secondary school children, African Health Sciences, 12, 140-147, 2012</td>
<td>Study carried out in Nigeria</td>
</tr>
<tr>
<td>Quattrin,T., Waz,W.R., Duffy,L.C., Sheldon,M.W., Campos,S.P., Albini,C.H., Feld, I.G., Microalbuminuria in an adolescent cohort with insulin-dependent diabetes mellitus, Clinical Pediatrics, 34, 12-17, 1995</td>
<td>Just an overall prevalence for all participants was reported, no stratiﬁcation according to age</td>
</tr>
<tr>
<td>Raile,K., Galler,A., Hofer,S., Herbst,A., Dunstheimer,D., Busch,P.,</td>
<td>Just an overall prevalence was reported, no stratiﬁcation according to age</td>
</tr>
<tr>
<td>Rowe,D.J.F., Hayward,M., Bagga,H., Betts,P., Effect of glycaemic control and duration of disease on overnight albumin excretion in diabetic children, British Medical Journal, 289, 957-959, 1994</td>
<td>Just the number of microalbuminuria participants &gt; 12 years was reported, no prevalence can be calculated</td>
</tr>
<tr>
<td>Roy,M.S., Aﬄouf,M., Roy,A., Six-year incidence of proteinuria in type 1 diabetic African Americans, Diabetes Care, 30, 1807-1812, 2007</td>
<td>The study was carried out only among African Americans in the USA</td>
</tr>
<tr>
<td>Salardi,S., Caccian,E., Pascucci,M.G., Giambiasi,E., Tacconi,M.,</td>
<td>Cut-off point for microalbuminuria used in the study was 25mg/24h, which corresponds to ACR &gt;= 3.06mg/mmol in males and &gt;= 3.19 mg/mmol in females, the threshold for females was lower than that of the UK standards (2.5mg/24h for males and 3.5mg/mmol for females)</td>
</tr>
<tr>
<td>Selgado,P.P., Silva,I.N., Vieira,E.C., Simoes e Silva,AC., Risk factors for early onset of diabetic nephropathy in pediatric type 1 diabetes, Journal of Pediatric Endocrinology, 23, 1311-1320, 2010</td>
<td>Just an overall prevalence was reported, no stratiﬁcation according to age</td>
</tr>
<tr>
<td>Schultze,C.J., Konopelska-Bahu,T., Dalton,R.N., Carroll.T.A., Stratton,I., Gale,E.A., Neil,A., Dunger,D.B., Microalbuminuria prevalence varies with age, sex, and puberty in children with type 1 diabetes followed from diagnosis in a longitudinal study. Oxford Regional Prospective Study Group, Diabetes Care, 22, 495-502, 1999</td>
<td>Only the number of microalbuminuria participants aged &lt; 11 years was reported without the whole number of this age group, prevalence cannot be calculated</td>
</tr>
<tr>
<td>Schultze,C.J., Neil,H.A., Dalton,R.N., Konopelska,Bahu,T., Dunger,D.B., Oxford Regional Prospective Study Group, Blood pressure does not rise before the onset of microalbuminuria in children followed from diagnosis of type 1 diabetes. Oxford Regional Prospective Study Group, Diabetes Care, 24, 555-560, 2001</td>
<td>Just an overall prevalence was reported, no stratiﬁcation according to age</td>
</tr>
<tr>
<td>Scott,A.R., Toomath,R., Boucher,D., Bruce,R., Crook,N.,</td>
<td>Just an overall prevalence for participants aged between 12 and 26 years was reported</td>
</tr>
<tr>
<td>Sellers,E,A.C., Blydt-Hansen,T.D., Dean,H.J., Gibson,I.W., Birk,P.E., Ogborn,M., Macroalbuminuria and renal pathology in first nation youth with type 2 diabetes, Diabetes Care, 32, 766-790, 2009</td>
<td>Just an overall prevalence was reported, no stratiﬁcation according to age</td>
</tr>
<tr>
<td>Sen,A., Buyukgezib,A., Albumin excretion rate, serum insulin-like growth factor-I and glomerular ﬁltration rate in type I diabetes mellitus at puberty, Journal of Pediatric Endocrinology, 10, 209-215, 1997</td>
<td>Mean values of AER for age groups such as 10 to 12 years, and 13 to 14 years, were reported, but prevalence cannot be calculated</td>
</tr>
<tr>
<td>Shield,J.P.H., Hunt,L.P., Karachaliou,F., Karavanaki,K., Baum,J.D., Is microalbuminuria progressive?, Archives of Disease in Childhood, 73, 512-514, 1995</td>
<td>Just an overall prevalence was reported, no stratiﬁcation according to age</td>
</tr>
<tr>
<td>Simsek,D.G., Aycan,Z., Ozen,S., Cetinkaya,S., Kara,C., Abali,S., Demir,K., Tunc,O., Ucakturk,A., Asar,G., Bas,F., Cetinkaya,E., Aydin,M., Karaguzel,G., Orbak,Z., Siklar,Z.,</td>
<td>Only an overall prevalence was reported, no stratiﬁcation by age or diabetes duration</td>
</tr>
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<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
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<tbody>
<tr>
<td>Altinkik, A., Okten, A., Ozkan, B., Ocal, G., Semiz, S., Arslanoglu, I., Evliyaoglu, O., Bundak, R., Darcan, S., Diabetes care, glycemic control, complications, and concomitant autoimmune diseases in children with type 1 diabetes in Turkey: a multicenter study, Journal of clinical research in pediatric endocrinology, 5, 20-26, 2013</td>
<td>Just an overall prevalence was reported, no stratification according to age</td>
</tr>
<tr>
<td>Stone, M.L., Craig, M.E., Chan, A.K., Lee, J.W., Verge, C.F., Donahue, K.C., Natural history and risk factors for microalbuminuria in adolescents with type 1 diabetes: a longitudinal study, Diabetes Care, 29, 2072-2077, 2006</td>
<td>Just an overall prevalence was reported, no stratification according to age</td>
</tr>
<tr>
<td>Svensson, M., Eriksson, J.W., Dahlquist, G., Early glycemic control, age at onset, and development of microvascular complications in childhood-onset type 1 diabetes: a population-based study in northern Sweden, Diabetes Care, 27, 955-962, 2004</td>
<td>Participants’ age ranged from 1 to 20 years (small sample size of 19 participants only)</td>
</tr>
<tr>
<td>Tan, S.H., Lee, B.W., Low, P.S., Lee, C.P., Assessment of complications in children with insulin-dependent diabetes mellitus, Annals of the Academy of Medicine, Singapore, 14, 266-271, 1985</td>
<td>The overall prevalence was reported when participants had attained 21 years of age</td>
</tr>
<tr>
<td>Tsai, C.W., Kuo, C.C., Wu, C.F., Chien, K.L., Wu, V.C., Chen, M.F., Sung, F.C., Su, T.C., Associations of renal vascular resistance with albuminuria in adolescents and young adults, Nephrology Dialysis Transplantation, 26, 3943-3949, 2011</td>
<td>Nephropathy was identified by ICD codes of diabetic nephropathy diagnosis on hospital discharge records rather than by AER or ACR</td>
</tr>
<tr>
<td>Wan Nazaimoon, W.M., Letchuman, R., Noraini, N., Ropilah, A.R., Zainal, M., Ismail, I.S., Wan Mohamad, W.B., Faridah, I., Singaraveloo, M., Sheriff, I.H., Khalid, B.A., Systolic hypertension and duration of diabetes mellitus are important determinants of retinopathy and microalbuminuria in young diabetics, Diabetes Research and Clinical Practice, 46, 213-221, 1999</td>
<td>Study on young adults older than 18 years</td>
</tr>
<tr>
<td>Yokoyama, H., Uchigata, Y., Otani, T., Maruyama, A., Yano-Aoki, K., Kanematsu, S., Kasahara, T., Matsuura, N., Omori, Y., Development of diabetic nephropathy in Japanese patients with insulin-dependent diabetes mellitus: Tokyo Women's Medical College epidemiologic study, Journal of Diabetes and its Complications, 8, 7-12, 1994</td>
<td>Participants included those who were older than 18 years</td>
</tr>
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**H.18 Type 2 diabetes – education**

**Review question**

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armour, T.A., Norris, S.L., Jack, L.Jr., Zhang, X., Fisher, L., The effectiveness of family interventions in people with diabetes mellitus: a systematic review. [47 refs], Diabetic Medicine, 22, 1295-1305, 2005</td>
<td>PICO not met - no studies included children or young people with type 2 diabetes. Interventions were generally behavioural in nature.</td>
</tr>
<tr>
<td>Atak, N., Gurkan, T., Kose, K., The effect of education on knowledge, self management behaviours and self efficacy of patients with type 2 diabetes, Australian Journal of Advanced Nursing, 26, 66-74, 2008</td>
<td>PICO not met - adult participants only</td>
</tr>
<tr>
<td>Avdal, Elif, Kizilci, Senyi, Demirel, Neslihan, The effects of Web-based diabetes education on diabetes care results: a randomized control study. CIN: Computers, Informatics, Nursing, 29, TC29-TC34, 2011</td>
<td>PICO not met - adult participants only</td>
</tr>
<tr>
<td>Babamoto, K.S., Sey, K.A., Camilleri, A.J., Karfan, V.J., Catalasan, J., Morisky, D.E., Improving diabetes care and health measures among hispanics using community health</td>
<td>PICO not met - adult participants only</td>
</tr>
</tbody>
</table>
# Excluded studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
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<tbody>
<tr>
<td>workers: results from a randomized controlled trial, Health Education and Behavior, 36, 113-126, 2009</td>
<td>PICO not met - although age not explicitly stated as an inclusion criterion, mean age of participants was 58 years (-12 years).</td>
</tr>
<tr>
<td>Borgermans, Liesbeth, Goeders, Geert, Carine, Verbeke, Geert, Carbonez, An, Ivanova, Anna, Mathieu, Chantal, Heyman, Jan, Patients' experiences with patient-centred care are associated with documented outcome of care indicators for diabetes: findings from the Leuven Diabetes Project, International Journal of Care Pathways, 15, 65-75, 2011</td>
<td>PICO not met - participants with type 1 diabetes only</td>
</tr>
<tr>
<td>Campbell, E.M., Redman, S., Moffitt, P.S., Sanson-Fisher, R.W., The relative effectiveness of educational and behavioral instruction programs for patients with NIDDM: a randomized trial, Diabetes Educator, 22, 379-386, 1996</td>
<td>PICO not met. Although inclusion criteria only state &lt; 80 years, mean age of participants was 58.3 years</td>
</tr>
<tr>
<td>Colquhoun, E., Durry, Michael I., Cregan, Deirdre, Keenan, Patricia, Group work with diabetic adolescents, Irish Journal of Psychological Medicine, 5, 37-40, 1988</td>
<td>PICO not met - participants with type 1 diabetes, psychosocial intervention.</td>
</tr>
<tr>
<td>Daniëlle, Pacaud, Helen, Kelley, Angela, M., Mike, Chiasson, Successful Delivery of Diabetes Self-Care Education and Follow-Up through eHealth Media, Canadian Journal of Diabetes, 36, 257-262, 2012</td>
<td>PICO not met - adult participants only</td>
</tr>
<tr>
<td>Delamater, Alan M., Smith, Jeffrey A., Bubb, Jeanne, Davis, Susan Green, Gamble, Thomas, White, Neil H., Santiago, Julio V., Family-based behavior therapy for diabetic adolescents, Johnson, James H [Ed]; Johnson, Suzanne Bennett [Ed], 293-306, 1991</td>
<td>PICO not met - type of diabetes not described (but likely type 1) and behavioural intervention, not educational.</td>
</tr>
<tr>
<td>Flamm, M., Panisch, S., Winkler, H., Johansson, T., Weltgasser, R., Sonnichsen, A.C., Effectiveness of the Austrian disease management programme &quot;Therapie Aktiv&quot; for type 2 diabetes regarding the improvement of metabolic control, risk profile and guideline adherence: 2 years of follow up, Wiener Klinische Wochenschrift, 124, 639-646, 2012</td>
<td>PICO not met - adult participants only</td>
</tr>
<tr>
<td>Heinrich, E., Schaper, N.C., de Vries, N.K., Self-management interventions for type 2 diabetes: a systematic review, European Diabetes Nursing, 7, 71-76, 2010</td>
<td>PICO not met - only adult studies included</td>
</tr>
<tr>
<td>Jeffreys, H.L., Hemoglobin A1C value for evaluating a community diabetes education series, Internet Journal of Advanced Nursing Practice, 9, -6p, 2008</td>
<td>PICO not met - not an RCT, and adult participants only</td>
</tr>
<tr>
<td>Keeratiyutawong, P., Panpaku, L., Melkus, G.D.E., Panpakdee, O., Vorapongsthorn, T., Effectiveness of a self-management program for Thais with type 2 diabetes, Thai Journal of Nursing Research, 10, 85-97, 2006</td>
<td>PICO not met - adult participants only</td>
</tr>
<tr>
<td>LEE, Haejung, KIM, Myoung Soo, PARK, Kyung Yeon, PARK, Hyo Young Sook, KIM, In Joo, Effects of a problem-solving counseling program to facilitate intensified walking on Koreans with type 2 diabetes, Japan Journal of Nursing Science, 8, 129-139, 2011</td>
<td>PICO not met - adult participants only (&gt; 50 years), and not randomised</td>
</tr>
</tbody>
</table>
### Excluded studies

**Diagnosis and management of type 1 diabetes in children and young people**

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>McIlhenny, C.V., Guzic, B., Knee, D., Demuth, B., Roberts, J., Using technology to deliver healthcare education to rural patients, Rural and Remote Health, 11, 1-11, 2011</td>
<td>PICO not met - adult participants only</td>
</tr>
<tr>
<td>Moriyama, M., Nakano, M., Kuroe, Y., Nin, K., Niitani, M., Nakaya, T., Efficacy of a self-management education program for people with type 2 diabetes: results of a 12 month trial, Japan Journal of Nursing Science, 6, 51-63, 2009</td>
<td>No age restriction to enter study, but control and intervention groups had a mean age of 65.2 years (± 8.5 years) and 66.4 years (± 9.2 years), respectively.</td>
</tr>
<tr>
<td>Pieter, Agema, Diana, Sherifali, Determining the impact of an intervention to increase problem-solving skills in diabetes self-management: The Diabetes Problem-Solving Passport Pilot Study, Canadian Journal of Diabetes, 36, 199-203, 2012</td>
<td>PICO not met - adult participants only.</td>
</tr>
<tr>
<td>Subcliffe, Paul, Martin, Steven, Sturt, Jackie, Powell, John, Griffiths, Frances, Adams, Ann, Dale, Jeremy, Systematic review of communication technologies to promote access and engagement of young people with diabetes into healthcare, BMC Endocrine Disorders, 11, 1, 2011</td>
<td>PICO not met - studies included use of IT to communicate diabetes management, rather than educational tools. Only one educational Internet site included, and this study was not an RCT.</td>
</tr>
<tr>
<td>Tjam, E.Y., Sherifali, D., Steinacher, N., Hett, S., Physiological outcomes of an Internet disease management program vs. in-person counselling: a randomized, controlled trial, Canadian Journal of Diabetes, 30, 397-405, 2006</td>
<td>PICO not met - adults with type 1 or type 2 diabetes only.</td>
</tr>
<tr>
<td>TODAY Study Group, A Clinical Trial to Maintain Glycemic Control in Youth with Type 2 Diabetes, New England Journal of Medicine, 366, 2247-2256, 2012</td>
<td>PICO not met - behavioural intervention, not education.</td>
</tr>
<tr>
<td>Tshiananga, Jacques Kande Tshiang, Kocher, Serge, Weber, Christian, Emyi-Albrecht, Katrina, Berndt, Karsten, Neeser Kurt, The Effect of Nurse-led Diabetes Self-</td>
<td>PICO not met - includes articles with either adult participants or children and young people with type 1 diabetes</td>
</tr>
</tbody>
</table>
H.19 Type 2 diabetes – behavioural interventions

Review questions

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

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

These 2 questions were addressed through a single search and there is one combined list of excluded studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradshaw,B., The role of the family in managing therapy in minority children with type 2 diabetes mellitus, Journal of Pediatric Endocrinology, 15 Suppl 1, 547-551, 2002</td>
<td>Intervention not behavioural. Focused on administering care such as diet supervision.</td>
</tr>
<tr>
<td>Ellis,D.A., Naar-King,S., Chen,X., Moltz,K., Cunningham,P.B., Idalski-Carcone,A., Multisystemic therapy compared to telephone support for youth with poorly controlled diabetes: findings from a randomized controlled trial, Annals of Behavioral Medicine, 44, 207-215, 2012</td>
<td>Type 1 versus type 2 entered together as a confounding variable in a linear model. No analysis of the effect of the intervention on type 2 children and young people only.</td>
</tr>
<tr>
<td>Grey,M., Boland,E.A., Davidson,M., Yu,C., Sullivan-Boyal,S., Tamborlane,W.V., Short-term effects of coping skills training as adjunct to intensive therapy in adolescents, Diabetes Care, 21, 902-908, 1998</td>
<td>PICO not met: participants had type 1 diabetes only.</td>
</tr>
</tbody>
</table>
### Excluded studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>study patients with poorly controlled type 2 diabetes, a randomised controlled trial of a family-based intervention: protocol and pilot study, BMC Family Practice, 8, 36-, 2007</td>
<td>PICO not met: adult population &gt; 50 years.</td>
</tr>
<tr>
<td>LEE, Haejung, KIM, Myoung Soo, PARK, Kyung Yeon, PARK, Hyoung Sook, KIM, In Joo, Effects of a problem-solving counseling program to facilitate intensified walking on Koreans with type 2 diabetes, Japan Journal of Nursing Science, 8, 129-139, 2011</td>
<td>PICO not met: adult population. Mean ages of 57.3 years and 56.8 years in each group.</td>
</tr>
<tr>
<td>Lou, V.W.Q., Zhang, Y., Evaluating the effectiveness of a participatory empowerment group for Chinese type 2 diabetes patients, Research on Social Work Practice, 16, 491-499, 2006</td>
<td>PICO not met: adult population. Mean ages of 66.4 years and 65.2 years in each group.</td>
</tr>
<tr>
<td>Tjam, A., Shenfield, D., Steinacher, N., Hett, S., Physiological outcomes of an Internet disease management program vs. in-person counselling: a randomized, controlled trial, Canadian Journal of Diabetes, 30, 397-405, 2006</td>
<td>PICO not met: adult population; 77% of participants &gt; 40 years.</td>
</tr>
</tbody>
</table>

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### H.20 Type 2 diabetes – dietary advice

**Review question**

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albarracin, C.A., Fuqua, B.C., Evans, J.L., Goldfine, I.D., Chromium picolinate and biotin combination improves glucose metabolism in treated, uncontrolled overweight to obese patients with type 2 diabetes, Diabetes/Metabolism Research Reviews, 24, 41-51, 2008</td>
<td>PICO not met: excluded people aged &lt; 18 years</td>
</tr>
<tr>
<td>Bantle, J.P., Laine, D.C., Thomas, J.W., Metabolic effects of dietary fructose and sucrose in types I and II diabetic subjects, JAMA, 256, 3241-3246, 1986</td>
<td>PICO not met: adults only for type 2 diabetes (36-80 years)</td>
</tr>
</tbody>
</table>
Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?

### Study

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johnson,S.T., Newton,A.S., Chopra,M., Buckingham,J., Huang,T.T., Franks,P.W., Jetha,M.M., Ball,G.D.</td>
<td>In search of quality evidence for lifestyle management and glycemic control in children and adolescents with type 2 diabetes: A systematic review, BMC Pediatrics, 10, 97, 2010</td>
</tr>
<tr>
<td>Kimmonth,A.L., Angus,R.M., Jenkins,P.A.</td>
<td>Whole foods and increased dietary fibre improve blood glucose control in diabetic children, Archives of Disease in Childhood, 57, 187-194, 1982</td>
</tr>
<tr>
<td>Ooi,Peng Cheow, Loke, Cheong Seng</td>
<td>Sweet potato for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, 1-9, 2012</td>
</tr>
<tr>
<td>Ooi,Peng Cheow, Yassin,Zaitun, Hamid,TengkuAizan, Momordica charantia for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, 1-9, 2012</td>
<td></td>
</tr>
<tr>
<td>Thomas,Diana, Elliott, Elizabeth J.</td>
<td>Low glycaemic index, or low glycaemic load, diets for diabetes mellitus, Cochrane Database of Systematic Reviews, 1-9, 2009</td>
</tr>
</tbody>
</table>

### H.21 Type 2 diabetes – weight loss

Review question

Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?
<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garanty-Bogacka et al., 2011</td>
<td>PICO not met: proportion of participants with type 2 diabetes not reported</td>
</tr>
<tr>
<td>Gidding et al., 2011</td>
<td>PICO not met: outcomes of interest</td>
</tr>
<tr>
<td>Grinstein et al., 2003</td>
<td>Outcomes for participants with type 1 diabetes and type 2 diabetes not presented separately</td>
</tr>
<tr>
<td>Himpens et al., 2012</td>
<td>PICO not met: adults only</td>
</tr>
<tr>
<td>Horowitz et al., 2012</td>
<td>PICO not met: adults only</td>
</tr>
<tr>
<td>Inge et al., 2013</td>
<td>An observational study with no correlation analysis between weight loss and glycaemic control</td>
</tr>
<tr>
<td>Jesudason et al., 2013</td>
<td>All participants aged over 18 years</td>
</tr>
<tr>
<td>Kim et al., 2010</td>
<td>PICO not met: adults only</td>
</tr>
<tr>
<td>Kopelman et al., 2010</td>
<td>PICO not met: adults only</td>
</tr>
<tr>
<td>Korner et al., 2013</td>
<td>No data specifically on children and young people with type 2 diabetes; population of obese people, 1.1% of whom had type 2 diabetes</td>
</tr>
<tr>
<td>Lawrence et al., 2013</td>
<td>PICO not met: no outcomes of interest</td>
</tr>
<tr>
<td>Lee et al., 2012</td>
<td>PICO not met: adults only</td>
</tr>
<tr>
<td>Leslie et al., 2012</td>
<td>PICO not met: adults only</td>
</tr>
<tr>
<td>Manning et al., 1995</td>
<td>Paediatric data not reported separately</td>
</tr>
</tbody>
</table>
Excluded studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marinari,G.M., Papadis,F.S., Briatore,L., Adami,G., Scopinaro,N., Type 2 diabetes and weight loss following biliopancreatic diversion for obesity, Obesity Surgery, 16, 1440-1444, 2006</td>
<td>PICO not met: adults only</td>
</tr>
<tr>
<td>Narasimhan,S., Weinstock,R.S., Youth-onset type 2 diabetes mellitus: lessons learned from the TODAY study, Mayo Clinic Proceedings, 89, 806-816, 2014</td>
<td>This is a review of the TODAY RCT already included in the review</td>
</tr>
<tr>
<td>Shi,Y.F., Pan,C.Y., Hill,J., Gao,Y., Orlistat in the treatment of overweight or obese Chinese patients with newly diagnosed Type 2 diabetes, Diabetic Medicine, 22, 1737-1743, 2005</td>
<td>PICO not met: outcomes not of interest</td>
</tr>
<tr>
<td>TODAY Study Group., Safety and Tolerability of the Treatment of Youth-Onset Type 2 Diabetes: The TODAY experience, Diabetes Care, 36, 1765-1771, 2013</td>
<td>PICO not met: outcomes not of interest</td>
</tr>
</tbody>
</table>

H.22 Type 2 diabetes – metformin

Review question

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Al-Shareef,M.A., Samneh,A.F., Aljoudi,A.S., Clinical effect of Metformin in children and adolescents with type 2 diabetes mellitus: a systematic review and meta-analysis, Journal of Family and Community Medicine, 19, 68-73, 2012</td>
<td>Systematic review of trials including metformin: 3 trials in the meta-analysis, 1 already included in the evidence summary (Jones et al., 2002). Remaining 2 trials excluded as do not compare metformin to placebo</td>
</tr>
<tr>
<td>Bernardita,PradoA, Veronica, GaeteP, Francisca, CoronaH, Eldreth,PeraltaV, Paula, DonosoA, Ximena, RaimannT, Metabolic effect of metformin in obese adolescents at risk of diabetes mellitus type 2Efecto metabolico de la metformina</td>
<td>PICO (Patient Intervention Comparator Outcome) criteria not met - population did not have type 2 diabetes</td>
</tr>
</tbody>
</table>
## Diagnosis and management of type 1 diabetes in children and young people

### Excluded studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>en adolescentes obesas con riesgo de diabetes mellitus tipo 2, Revista Chilena de Pediatría, 83, 48-57, 2012</td>
<td>PICO criteria not met - population did not have type 2 diabetes</td>
</tr>
<tr>
<td>Centre for Reviews and Dissemination., Efficacy of metformin in the treatment of NIDDM: meta-analysis (:Structured abstract); Database of Abstracts of Reviews of Effects, -, 2012</td>
<td></td>
</tr>
<tr>
<td>Centre for Reviews and Dissemination., Efficacy of metformin in the treatment of NIDDM: meta-analysis (Structured abstract), Database of Abstracts of Reviews of Effects, -, 2014</td>
<td>No information in abstract</td>
</tr>
<tr>
<td>Clarson,C.L., Mahmud,F.H., Baker,J.E., Clark,H.E., McKay,W.M., Schautteet,V.D., Hill,D.J., Metformin in combination with structured lifestyle intervention improved body mass index in obese adolescents, but did not improve insulin resistance, Endocrine, 36, 141-146, 2009</td>
<td>PICO criteria not met - population did not have type 2 diabetes</td>
</tr>
<tr>
<td>Freemark,M., Liver dysfunction in paediatric obesity: a randomized, controlled trial of metformin, Acta Paediatrica, 96, 1326-1332, 2007</td>
<td>PICO criteria not met - population did not have type 2 diabetes</td>
</tr>
<tr>
<td>Freemark,M., Bursey,D., A therapeutic trial of metformin in obese adolescents predisposed to type 2 diabetes mellitus, Pediatric Research, 47, 128A, 2000, 2000</td>
<td>PICO criteria not met - population did not have type 2 diabetes</td>
</tr>
<tr>
<td>Freemark,M., Bursey,D., The effects of metformin on body mass index and glucose tolerance in obese adolescents with fasting hyperinsulinemia and a family history of type 2 diabetes, Pediatrics, 107, E55, 2001</td>
<td>PICO criteria not met - population did not have type 2 diabetes</td>
</tr>
<tr>
<td>Gottschalk,M., Danne,T., Vlajnic,A., Cara,J.F., Glimepiride versus metformin as monotherapy in pediatric patients with type 2 diabetes: a randomized, single-blind comparative study, Diabetes Care, 30, 790-794, 2007</td>
<td>PICO not met - comparator was not placebo</td>
</tr>
<tr>
<td>Hess,A.M., Sullivan,D.L., Metformin for prevention of type 2 diabetes, Annals of Pharmacotherapy, 38, 1283-1285, 2004</td>
<td>PICO criteria not met - population did not have type 2 diabetes</td>
</tr>
<tr>
<td>Johansen,K., Efficacy of metformin in the treatment of NIDDM. Meta-analysis, Diabetes Care, 22, 33-37, 1999</td>
<td>No data reported for children or young people with type 2 diabetes</td>
</tr>
<tr>
<td>Kane,M.P., bu-Baker,A., Busch,R.S., The utility of oral diabetes medications in type 2 diabetes of the young. [58 refs]. Current Diabetes Reviews, 1, 83-92, 2005</td>
<td>Study criteria not met - overview of medications for type 2 diabetes</td>
</tr>
<tr>
<td>Kay,J.P., Alemzadeh,R., Langley,G., D’Angelo,L., Smith,P., Holshouser,S., Beneficial effects of metformin in normoglycemic morbidly obese adolescents, Metabolism: Clinical and Experimental, 50, 1457-1461, 2001</td>
<td>PICO criteria not met - population did not have type 2 diabetes</td>
</tr>
<tr>
<td>List,J.F., Woo,V., Morales,E., Tang,W., Fiedorek,F.T., Sodium-glucose cotransport inhibition with dapagliflozin in type 2 diabetes, Diabetes Care, 32, 650-657, 2009</td>
<td>PICO criteria not met - population aged 18-79 years</td>
</tr>
<tr>
<td>Narasimhan,S., Weinstock,R.S., Youth-onset type 2 diabetes mellitus: lessons learned from the TODAY study, Mayo Clinic Proceedings, 89, 806-816, 2014</td>
<td>This is a review of the TODAY study</td>
</tr>
<tr>
<td>Saenz,Antonio, FernandezEsteban,Inmaculada, Maitaix,Angel, usejo Segura,Monica, Figuls,Marta, Moher,David, Metformin monotherapy for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2013</td>
<td>Participants aged over 18 years</td>
</tr>
<tr>
<td>Saenz,Antonio, Fernandez-Esteban,Inmaculada, Mataix,Angel, usejo Segura,Monica, Figuls,Marta, Moher,David, Metformin monotherapy for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2009</td>
<td>Systematic review of metformin versus placebo in adults with type 2 diabetes</td>
</tr>
</tbody>
</table>
H.23  Type 2 diabetes – HbA1c targets

Review question

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chou, H.S., Palmer, J.P., Jones, A.R., Waterhouse, B., Ferreira-Cornwell, C., Krebs, J., Goldstein, B., Initial treatment with fixed-dose combination rosiglitazone/glimepiride in patients with previously untreated type 2 diabetes, Diabetes, Obesity and Metabolism, 10, 626-637, 2008</td>
<td>PICO not met: excluded patients aged &lt;18 years</td>
</tr>
<tr>
<td>Dorchy, H., Roggemans, M.P., Willems, D., Glycated hemoglobin and related factors in diabetic children and adolescents under 18 years of age: a Belgian experience, Diabetes Care, 20, 2-6, 1997</td>
<td>PICO not met: type 1 diabetes only.</td>
</tr>
<tr>
<td>Rosenstock, J., Rood, J., Cobitz, A., Biswas, N., Chou, H., Garber, A., Initial treatment with rosiglitazone/metformin fixed-dose combination therapy compared with monotherapy with either rosiglitazone or metformin in patients with uncontrolled type 2 diabetes, Diabetes, Obesity and Metabolism, 8, 650-660, 2006</td>
<td>PICO not met: excluded patients aged &lt; 18 years.</td>
</tr>
<tr>
<td>Saenz, Antonio, Fernandez Estevez, Inmaculada, Mataix, Angel, usejo, Segura, Monica, Figuls, Marta, Moher, David, Metformin monotherapy for type 2 diabetes mellitus, Cochrane Database of Systematic Reviews, -, 2009</td>
<td>PICO not met: excluded patients aged &lt; 18 years.</td>
</tr>
<tr>
<td>Tong, P.C., Ko, G.T., So, W.Y., Chiang, S.C., Yang, X., Kong, A.P., Ozaki, R., Ma, R.C., Cockram, C.S., Chow, C.C., Chan, J.C., Use of anti-diabetic drugs and glycaemic control in type 2 diabetes-tThe Hong Kong Diabetes Registry, Diabetes Research and Clinical Practice, 82, 346-352, 2008</td>
<td>Children and young people were included in the study but no separate analyses were reported.</td>
</tr>
</tbody>
</table>

H.24  Type 2 diabetes – hypertension

Review question

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Al-Agha, A.E., Ocheltree, A., Shata, N., Prevalence of hypertension, Diabetes Research and Clinical Practice, 82, 346-352, 2008</td>
<td>Prevalence estimates (measurements of blood pressure and</td>
</tr>
</tbody>
</table>
### H.25 Type 2 diabetes – dyslipidaemia

#### Review question

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>hyperinsulinism, type 2 diabetes mellitus and metabolic syndrome among Saudi overweight and obese pediatric patients, Minerva Pediatria, 64, 623-631, 2012</td>
<td>lipids) are not provided with respect to a specific time since diagnosis - only mean age at diagnosis is provided with a wide age range</td>
</tr>
<tr>
<td>Bacha,F., Gidding,S.S., Caprio,S., Weinstock,R., Lynch,J., Hirst,K., High prevalence and rapid increase of cardiovascular disease risk factors in youth with type 2 diabetes: The today study group, Circulation, 127, -., 2013</td>
<td>Abstract only</td>
</tr>
<tr>
<td>Miller,J., Silverstein,J., How prevalent are diabetes-related complications in patients with youth-onset type 2 diabetes mellitus?:, Nature Clinical Practice Endocrinology and Metabolism, 3, 12-13, 2007</td>
<td>Commentary on a study weeded out as it compared type 2 diabetes with type 1 diabetes</td>
</tr>
<tr>
<td>Schober,E., Holl,R.W., Grabert,M., Thon,A., Rami,B., Kapellen,T., Seewi,O., Reinehr,T., Diabetes mellitus type 2 in childhood and adolescence in Germany and parts of Austria, European Journal of Pediatrics, 164, 705-707, 2005</td>
<td>Data not presented at specific timepoints since diagnosis (all cases are grouped together regardless of age or time since diagnosis)</td>
</tr>
<tr>
<td>Scott,C.R., Smith,J.M., Craddock,M.M., Pihoker,C., Characteristics of youth-onset noninsulin-dependent diabetes mellitus and insulin-dependent diabetes mellitus at diagnosis, Pediatrics, 100, 84-91, 1997</td>
<td>Data not reported according to time since diagnosis or by age group. Mean age and range are reported - range is very wide (8 to 19 years)</td>
</tr>
<tr>
<td>Urakami,T., Suzuki,J., Yoshida,A., Saito,H., Wada,M., Takahashi,S., Mugishima,H., Frequencies of factors of metabolic syndrome at diagnosis in children with T2DM, Pediatrics International, 51, 435-437, 2009</td>
<td>The same population was used by another included study. Methods are not clear about measurements taken pre-1990 (the included study states that blood pressure and lipids were not measured pre-1990)</td>
</tr>
<tr>
<td>Zdavkovic,V., Daneman,D., Hamilton,J., Presentation and course of Type 2 diabetes in youth in a large multi-ethnic city, Diabetic Medicine, 21, 1144-1148, 2004</td>
<td>Wide age range (8.8 to 17.5 years) with data not reported according to time since diagnosis</td>
</tr>
</tbody>
</table>

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H.26 Type 2 diabetes – retinopathy

Review question

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amutha,A., Datta,M., Unnikrishnan,R., Anjana,R.M., Mohan,V., Clinical profile and complications of childhood- and adolescent-onset type 2 diabetes seen at a diabetes center in south India, Diabetes Technology and Therapeutics, 14, 497-504, 2012</td>
<td>Mean age at screening for retinopathy 22.2 years (± 9.7 years). Prevalence of retinopathy stratified by duration of diabetes (&lt; 5, 5-10, 10-15 and &gt; 15 years) but not by age.</td>
</tr>
<tr>
<td>Danne,T., Kordonouri,O., Casani.A., Chiarelli,F., Diabetic retinopathy in childhood and adolescents, Diabetes, Nutrition and Metabolism - Clinical and Experimental, 12, 136-144, 1999</td>
<td>Narrative review article.</td>
</tr>
<tr>
<td>Donaghue,K.C., Fairchild,J.M., Craig,M.E., Chan,A.K., Hing,S., Cutler,L.R., Howard,N.J., Silink,M., Do all prepubertal years of diabetes duration contribute equally to diabetes complications?, Diabetes Care, 26, 1224-1229, 2003</td>
<td>Type 1 diabetes. Data on prevalence of retinopathy stratified by age or duration of diabetes not reported. Data reported as survival analysis only.</td>
</tr>
<tr>
<td>El,AsrarM, Adly,A.A., El,HadidyE, Abdelwahab,M.A., D-dimer levels in type 1 and type 2 diabetic children and adolescents; Relation to microvascular complications and dyslipidemia &quot;own data and review&quot;, Pediatric endocrinology reviews : PER, 9, 657-668, 2012</td>
<td>Ophthalmoscopy used for identification of retinopathy. No stratification of prevalence according to age or duration of diabetes.</td>
</tr>
<tr>
<td>Eppens,M.C., Craig,M.E., Cusumano,J., Hing,S., Chan,A.K., Howard,N.J., Silink,M., Donaghue,K.C., Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes, Diabetes Care, 29, 1300-1306, 2006</td>
<td>Prevalence of retinopathy not stratified by age or duration of diabetes. Age range for participants with type 2 diabetes not reported.</td>
</tr>
</tbody>
</table>
### H.27 Type 2 diabetes – nephropathy

**Review question**

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forster, A.S., Forbes, A., Dodhia, H., Connor, C., Du, Chemin A, Sivaprasad, S., Mann, S., Guilford, M.C., Changes in detection of retinopathy in type 2 diabetes in the first 4 years of a population-based diabetic eye screening program: Retrospective cohort study, Diabetes Care, 36, 2663-2669, 2013</td>
<td>Outcome not stratified by age. Population mean age not described, but likely to include adults as well as children and young people.</td>
</tr>
<tr>
<td>Jiialal, I., Welsh, N.H., Joubert, S.M., Rajput, M.C., Vascular complications in non-insulin-dependent diabetes in the young, South African Medical Journal, Suid-Afrikaanse Tydskrif Vir Geneeskunde, 62, 155-157, 1982</td>
<td>Age of patients not fully reported, but age of participants with retinopathy reported as 24 to 52 years, therefore likely to be inappropriate age group.</td>
</tr>
<tr>
<td>Study</td>
<td>Reason for exclusion</td>
</tr>
<tr>
<td>---------------------------------------------------------------------</td>
<td>----------------------------------------------------------</td>
</tr>
<tr>
<td>Maahs, D.M., Snively, B.M., Bell, R.A., Dolan, L., Hirsch, I.,</td>
<td>Just an overall prevalence was reported, no stratification</td>
</tr>
<tr>
<td>Imperatore, G., Linder, B., Marcovina, S.M., Mayer-Davis, E.J.,</td>
<td>according to age.</td>
</tr>
<tr>
<td>Pettitt, D.J., Rodriguez, B.L., Dabelea, D.</td>
<td></td>
</tr>
<tr>
<td>Higher prevalence of elevated albumin excretion in youth with type 2</td>
<td></td>
</tr>
<tr>
<td>than type 1 diabetes: the SEARCH for Diabetes in Youth study,</td>
<td></td>
</tr>
<tr>
<td>Diabetes Care, 30, 2593-2598, 2007</td>
<td></td>
</tr>
<tr>
<td>Shield, J.P.H., Lynn, R., Wan, K.C., Haines, L., Barrett, T.G.,</td>
<td>Just an overall prevalence was reported, no stratification</td>
</tr>
<tr>
<td>Management and 1 year outcome for UK children with type 2 diabetes,</td>
<td>according to age.</td>
</tr>
<tr>
<td>Archives of Disease in Childhood, 94, 206-209, 2009</td>
<td></td>
</tr>
<tr>
<td>TODAY Study Group., Rapid rise in hypertension and nephropathy in</td>
<td>Publication with error corrected on the TODAY clinical trial,</td>
</tr>
<tr>
<td>youth with type 2 diabetes: the TODAY clinical trial. [Erratum</td>
<td>relevant data to this review (which remain intact) have been</td>
</tr>
<tr>
<td>appears in Diabetes Care. 2013 Aug;36(8):2448], Diabetes Care, 36,</td>
<td>extracted from the original publication.</td>
</tr>
<tr>
<td>1735-1741, 2013</td>
<td></td>
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</table>

**H.28 Health economics**

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anderson, D.G., Multiple daily injections in young patients using</td>
<td>Right comparator, but no costs included</td>
</tr>
<tr>
<td>the ezy-BICC bolus insulin calculation card, compared to mixed</td>
<td></td>
</tr>
<tr>
<td>insulin and CSII, Pediatric Diabetes, 10, 304-309, 2009</td>
<td></td>
</tr>
<tr>
<td>Blair, J., Gregory, J.W., Peak, M., Insulin delivery by multiple</td>
<td>Commentary; no cost effectiveness</td>
</tr>
<tr>
<td>daily injections or continuous subcutaneous insulin infusion in</td>
<td></td>
</tr>
<tr>
<td>childhood: Addressing the evidence gap, Practical Diabetes, 29,</td>
<td></td>
</tr>
<tr>
<td>47-48, 2012</td>
<td></td>
</tr>
<tr>
<td>Centre for Reviews and Dissemination. The cost-effectiveness of</td>
<td>Cost utility analysis (CUA) conducted only in adult cohort</td>
</tr>
<tr>
<td>continuous glucose monitoring in type 1 diabetes (Provisional</td>
<td></td>
</tr>
<tr>
<td>abstract), NHS Economic Evaluation Database (NHSEED), -, 2010</td>
<td></td>
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<tr>
<td>Centre for Reviews and Dissemination. Continuous</td>
<td>CSII was not included in the 2015 update scope</td>
</tr>
<tr>
<td>subcutaneous insulin infusion versus multiple daily injections of</td>
<td></td>
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<tr>
<td>insulin: economic comparison in adult and adolescent Type 1 diabetes</td>
<td></td>
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<tr>
<td>mellitus in Australia (Structured abstract), NHS Economic Evaluation</td>
<td></td>
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<tr>
<td>Database (NHSEED), -, 2007</td>
<td></td>
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<tr>
<td>Chiari, G., Direct measurement of 3-B-hydroxybutyrate in the</td>
<td>Same study/data as Vanelli 2003: no economic evaluation,</td>
</tr>
<tr>
<td>management of diabetic ketoacidosis in children: A cost</td>
<td>only limited information on clinical cost (test, ICU)</td>
</tr>
<tr>
<td>effective enhancement in the management of diabetic ketoacidosis</td>
<td></td>
</tr>
<tr>
<td>in children, Diabetes Technology and Therapeutics, 13, 178-179, 2011</td>
<td></td>
</tr>
<tr>
<td>Couch, R., Jetha, M., Dryden, D.M., Hooton, N., Liang, Y., Durec,</td>
<td>No cost effectiveness model; comparator not clear</td>
</tr>
<tr>
<td>T., Sumano, E., Spooner, C., Milne, A., Gorman, K., Klassen, T.P.,</td>
<td></td>
</tr>
<tr>
<td>Diabetes education for children with type 1 diabetes mellitus and</td>
<td></td>
</tr>
<tr>
<td>their families (Structured abstract), Health Technology Assessment</td>
<td></td>
</tr>
<tr>
<td>Database, -, 2013</td>
<td></td>
</tr>
<tr>
<td>Gage, H., Hampson, S., Skinner, T.C., Hart, J., Storey, L., Foxcroft,</td>
<td>No cost effectiveness model for structured education versus</td>
</tr>
<tr>
<td>D., Kimber, A., Craddock, S., McEvilly, E.A., Educational and</td>
<td>usual care</td>
</tr>
<tr>
<td>psychosocial programmes for adolescents with diabetes: approaches,</td>
<td></td>
</tr>
<tr>
<td>outcomes and cost-effectiveness, [122 refs], Patient Education and</td>
<td></td>
</tr>
<tr>
<td>Counseling, 53, 333-346, 2004</td>
<td></td>
</tr>
<tr>
<td>Hampson, S.E., Skinner, T.C., Hart, J., Storey, L., Gage, H.,</td>
<td>No information on structured education programmes reported</td>
</tr>
<tr>
<td>Foxcroft, D., Kimber, A., Shaw, K., Walker, J., Effects of</td>
<td></td>
</tr>
<tr>
<td>educational and psychosocial interventions for adolescents with</td>
<td></td>
</tr>
<tr>
<td>diabetes mellitus: a systematic review, [148 refs], Health</td>
<td></td>
</tr>
<tr>
<td>Technology Assessment (Winchester, England), 5, 1-79, 2001</td>
<td></td>
</tr>
<tr>
<td>Health, Technology Assessment, Randomised controlled trial of</td>
<td>CSII was not included in the 2015 update scope</td>
</tr>
<tr>
<td>continuous subcutaneous insulin infusion compared to multiple</td>
<td></td>
</tr>
<tr>
<td>daily injection regimens in children and young people at diagnosis</td>
<td></td>
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<tr>
<td>of type 1 diabetes mellitus (Project record), Health Technology</td>
<td></td>
</tr>
<tr>
<td>Assessment Database, -, 2013</td>
<td></td>
</tr>
<tr>
<td>Health, Technology Assessment, Maximising engagement, motivation</td>
<td>Not reporting results</td>
</tr>
<tr>
<td>and long term change in a structured intensive education programme</td>
<td></td>
</tr>
<tr>
<td>in diabetes for children, young people and their families: child</td>
<td></td>
</tr>
<tr>
<td>and adolescent structured competencies approach to diabetes</td>
<td></td>
</tr>
<tr>
<td>education (Project record), Health Technology Assessment Database,</td>
<td></td>
</tr>
<tr>
<td>-, 2013</td>
<td></td>
</tr>
<tr>
<td>Huang, E.S., O’Grady, M., Basu, A., Winn, A., John, P., Lee, J.,</td>
<td>CUA conducted only in adult cohort</td>
</tr>
<tr>
<td>Meltzer, D., Kollman, C., Laffel, L., Tamborlane, W.,</td>
<td></td>
</tr>
</tbody>
</table>
### Appendix I: Evidence tables

The evidence tables from the 2004 guideline are presented in a separate document.

The evidence tables from the 2015 update are presented in a separate document, except for those related to the review question about diagnosis which are presented below.

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weinzimer, S., Wysocki, T., Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group., The cost-effectiveness of continuous glucose monitoring in type 1 diabetes. [Erratum appears in Diabetes Care. 2010 Sep;33(9):2129], Diabetes Care, 33, 1269-1274, 2010</td>
<td>Adult population</td>
</tr>
<tr>
<td>Laffel, L. M., Wentzell, K., Loughlin, C., Tovar, A., Moltz, K., Brink, S., Sick day management using blood 3-hydroxybutyrate (3-OHB) compared with urine ketone monitoring reduces hospital visits in young people with T1DM: a randomized clinical trial, Diabetic Medicine, 23, 278-284, 2006</td>
<td>Right comparator, but no costs or cost effectiveness model</td>
</tr>
<tr>
<td>Meltzer, D., Egleston, B., Stoffel, D., Dasbach, E., Effect of future costs on cost-effectiveness of medical interventions among young adults: the example of intensive therapy for type 1 diabetes mellitus, Medical Care, 38, 679-685, 2000</td>
<td>DCCT model included participants aged 13 to 39 years, thus costs and benefits associated with children and young people cannot be estimated from this trial</td>
</tr>
<tr>
<td>Nahata, L., Insulin therapy in pediatric patients with type 1 diabetes: continuous subcutaneous insulin infusion versus multiple daily injections. [12 refs], Clinical Pediatrics, 45, 503-508, 2006</td>
<td>Literature review, no cost data</td>
</tr>
<tr>
<td>Slover, I.I.R.H., Continuous glucose monitoring in children and adolescents, Current Diabetes Reports, 12, 510-516, 2012</td>
<td>Literature review, cost effectiveness information from Huang 2010</td>
</tr>
<tr>
<td>St, Charles M., Lynch, P., Graham, C., Minshall, M.E., A cost-effectiveness analysis of continuous subcutaneous insulin injection versus multiple daily injections in type 1 diabetes patients: a third-party US payer perspective, Value in Health, 12, 674-686, 2009</td>
<td>CSII was not included in the 2015 update scope</td>
</tr>
<tr>
<td>Vanelli, M., Chiari, G., Capuano, C., Iovane, B., Bernardini, A., Giacalone, T., The direct measurement of 3-beta-hydroxybutyrate enhances the management of diabetic ketoacidosis in children and reduces time and costs of treatment, Diabetes, Nutrition and Metabolism - Clinical and Experimental, 16, 312-316, 2003</td>
<td>No economic evaluation, only limited information on clinical cost (test, ICU)</td>
</tr>
</tbody>
</table>
I.1 Diagnosis

Review question

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

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

I.1.1 Population: young people only (all sample sizes)

Table 4: Andersson 2013 (NCGC reference 315)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
</table>

REF ID: Andersson 2013
### Table 5: Barker 2014 (NCGC reference 300)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barker et al.</td>
<td>Observation: prospective case-series</td>
<td>N=995 young people subgroup</td>
<td>Total N=3929 T1D adults, young people, and children</td>
<td>T1D: Fasting C-peptide, Stimulated C-peptide (results not given in study due to very small number of stim C-peptide mmts made)</td>
<td>Baseline, 1 and 5 years</td>
<td>T1D young people</td>
<td>Funding: Centro Internazionale Studi Diabete. Risk of bias: n/a lots of missing data at follow-up</td>
</tr>
</tbody>
</table>

#### Description

#### Notes
- **Inclusion criteria:** T1D (ADA and WHO criteria)
- **Exclusion criteria:** None given
- **Young people subgroup (age at onset >10 and ≤18 years)**
- **Diabetes type:** T1D
- **Diagnostic markers assessed:**
  - Fasting C-peptide
  - Stimulated C-peptide
- **Cutoffs for positivity:**
  - C-peptide: detection limit 0.01 nM
  - C-peptide+: 0.1 nmol/L
- **Outcome measure and effect sizes:**
  - C-peptide+: 0.1 nmol/L
- **Follow-up time:** Baseline, 1 and 5 years

### Table 6: Tung 2008 (NCGC reference 66)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y C Tung, JS Lee, WY Tsai, and PH Hsiao.</td>
<td>Observational: cross-sectional study</td>
<td>Total N=118 T1D (N=20 T2D young people and N=98 T1D children and young people)</td>
<td>Young people with diabetes type 2D</td>
<td>T2D: IC-PEPTIDE+</td>
<td>n/a</td>
<td>T2D young people (N=20)</td>
<td>Funding: Not reported</td>
</tr>
</tbody>
</table>

#### Description

#### Notes
- **Inclusion criteria:**
  - Newly diagnosed diabetes <18 years of age
  - Received neither oral hypoglycaemic agents nor insulin therapy before the study
- **Diagnostic markers assessed:**
  - IC-PEPTIDE
- **Cutoffs for positivity:**
  - IC-PEPTIDE+: 0.1 nmol/L
- **Follow-up time:** n/a

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### Reference: Tung 2008

**Study**

**Number of patients**
IAA, GADA and IA-2 were measured to confirm the Diagnosis

**Patient characteristics**
Exclusion criteria: None reported

**Diagnostic markers assessed**

**Length of follow-up**

**Outcome measure and effect sizes**

**Comments**

### Table 7: Shivaprasad 2014 (NCGC reference 325)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>REF ID: Shivaprasad 2014</td>
<td></td>
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<td></td>
<td>Risk of bias: n/a consecutive recruitment</td>
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</tbody>
</table>

#### Patient characteristics
- **Young people**
  - Diabetes type: T1D (N=21 newly Diagnosis)
  - Age, mean (SD): 11.0 (4.2) years
  - Duration of diabetes, mean (SD): 11.5 (14.4) months
  - Exclusion criteria: None given

- **Controls**
  - Diabetes type: T1D (N=21 newly Diagnosis)
  - Age, mean (SD): 11.0 (4.2) years
  - Duration of diabetes, mean (SD): 11.5 (14.4) months

### Table 8: Vermeulen 2011 (NCGC reference 250)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Vermeulen, I. Weets, M. Asanghanwa, J. Ruige, Gaal L. Van, C. Mathieu, B. Keymeulen, V. Lampasona, J. M. Wenzlau, J. C. Hutton, D. G.</td>
<td>Observation: case-control study</td>
<td>Taiwan</td>
<td>Total N=655 T1D (extra N=761 controls) Data here are for young people only: aged 10-39 (most were &gt;11 years)</td>
<td>T1D: GADA IA-2 ZnT8 Combinations</td>
<td>n/a</td>
<td>T1D young people (N=20)</td>
<td>Funding: Not reported</td>
</tr>
<tr>
<td></td>
<td>Single centre, Taiwan</td>
<td></td>
<td>Inclusion criteria: Newly diagnosed diabetes &lt;18 years of age</td>
<td>Cut-offs for positivity IC-PEPTIDE+: 0.1 nmol/L</td>
<td></td>
<td></td>
<td>Risk of bias: n/a</td>
</tr>
</tbody>
</table>

#### Patient characteristics
- **Young people**
  - Diabetes type: T1D controls (health)
  - Inclusion criteria: Newly diagnosed diabetes <18 years of age

#### Diagnostic markers assessed
- T1D: GADA IA-2 ZnT8
- Combinations

#### Outcome measure and effect sizes
- IC-PEPTIDE+: 0.1 nmol/L
- (range) 1.0 (0.5 – 5.1)

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### Table 9: Zanone 2003 (NCGC reference 79)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Single centre, Italy</td>
<td>Inclusion criteria: IDDM Adolescents (young people)</td>
<td></td>
<td>Cut-offs for positivity</td>
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<td></td>
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<td>Exclusion criteria: None reported</td>
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<td>fC-PEPTIDE+: not given</td>
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<td>ICA+: &gt;5 JDF units</td>
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<td>GAD65+: Index* of 0.069</td>
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<td>ICA+: &gt;5 JDF units</td>
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<td>Age, years, mean (range; SD)</td>
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<td>14.7 (11-18; 1.6)</td>
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<td>Duration of diabetes, years, mean (SD)</td>
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<td>52/48</td>
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</table>

*INDEX = sample cpm − negative control cpm /positive control cpm - negative control cpm
### I.1.2 Population: young people and adults (mixed population studies); N ≥50

#### Table 10: Besser 2011 (NCGC reference 300)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>R. Besser, J. Ludvigsson, A. Jones, T. McDonald, B. Shields, B. Knight, and A. Hattersley.</td>
<td>Observatioinal: cohort study</td>
<td>Adults from diabetes clinic, UK; young people from pediatric clinic, Sweden</td>
<td>Total N=72 T1D (mixture of young people and adults)</td>
<td>Young people (n=21) and adults diabetes type: T1D (n=72)</td>
<td>Patients underwent a standard mixed-meal tolerance test (MMTT)</td>
<td>T1D (N=75)</td>
<td>Association between 90-min sCP (1) and both the MMTT 120-min UCPCR and after the home evening meal.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inclusion criteria: T1D Young people (=&lt;19 years) and adults (≥18 years)</td>
<td>Age, years, median (IQR) Young (N=21)</td>
<td>14 (10.9-16.4)</td>
<td>18 (13-24)</td>
<td>In the pediatric cohort, correlations were also determined between AUC sCP and 120-min UCPCR. UCPCR cutoffs equivalent to 90-min sCP ≥0.2 nmol/L were derived using linear regression equations. UCPCR (120 min) following a home evening meal was compared with that after a MMTT.</td>
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<tr>
<td></td>
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<td></td>
<td>Age of Diagnosis: &lt;30 years on insulin since diagnosis</td>
<td>Adults (N=51)</td>
<td>33/67</td>
<td>51/49</td>
<td>Results: MMTT 120-min UCPCR was highly correlated to 90-min sCP (τ = 0.97; p&lt; 0.0001). UCPCR ≥0.53 nmol/mmol had 94% sensitivity/100% specificity for significant endogenous insulin secretion (90-min sCP ≥0.2 nmol/L). The 120-min postprandial evening meal UCPCR was highly correlated to 90-min sCP (τ = 0.91; p&lt; 0.0001). UCPCR ≥0.37 nmol/mmol had 84% sensitivity/97% specificity for sCP ≥0.2 nmol/L.</td>
</tr>
<tr>
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<td></td>
<td>Exclusion criteria: known renal impairment (eGFR&lt;60ml/min/1.73m^2) severe hypoglyc. within last 3 months; documented hypoglycaemia unawareness with a blood glucose &lt;3mmol/L, and HbA1c &gt;10%.</td>
<td>Diabetes duration, years, median (IQR)</td>
<td>2.6 (0.6-5.0)</td>
<td>21.4 (2.8-41.0)</td>
<td>Authors’ CONCLUSIONS: UCPCR measured during an MMTT or after a home meal is highly correlated with MMTT sCP. UCPCR testing is a</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>HbA1c, median (IQR), % Young</td>
<td>7.2 (6.6-7.9)</td>
<td>7.8 (6.9-9.0)</td>
<td>Risk of bias: n/a</td>
</tr>
<tr>
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<td></td>
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<td></td>
<td>Adults</td>
<td>7.6 (7.0-8.0)</td>
<td>7.4 (6.9-8.0)</td>
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<td></td>
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<td></td>
<td>To enrich for patients who had endogenous insulin secretion, 43% patients were either within 5 years of Diagnosis or known to still secrete C-peptide when previously tested.</td>
<td>sCP: collected at 0 and 90 min. Additional samples at 30, 60, and 120 min in pediatric patients (n=18), allowing area under the curve (AUC) to be calculated. Urine was collected as a fasting second morning void immediately before the start of the MMTT (0 min) and after 120 min. Significant endogenous insulin secretion was defined as 90-min sCP ≥0.2 nmol/L in accordance with the DCCT</td>
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</tr>
</tbody>
</table>

**Reference:** Besser 2011

**Study type:** Observational: cohort study

**Number of patients:** Adults from diabetes clinic, UK; young people from pediatric clinic, Sweden

**Patient characteristics:** Total N=72 T1D (mixture of young people and adults)

**Diagnostic markers assessed:** Patients underwent a standard mixed-meal tolerance test (MMTT)

**Length of follow-up:** N/A – immediate testing (up to 120 mins)

**Outcome measure and effect sizes:** T1D (N=75)

**Comments:** Association between 90-min sCP (1) and both the MMTT 120-min UCPCR and after the home evening meal.

**Funding:** Diabetes UK, Peninsula NIHR Clinical Research Facility, EC program Collaborative European Effort to Develop Diabetes Diagnostics; amidiabetesfon den (The Swedish Child Diabetes Foundation) and the Swedish Research Council.

**Risk of bias:** n/a
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Age, years, median (IQR)</td>
<td>25 (10)</td>
<td>M/F %</td>
<td>254 (60%)/168 (40%)</td>
<td>IA-2A index 123 (46)</td>
<td>IA-2A index 122 (83)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IA-2A index</td>
<td>91 (90)</td>
<td>3 Ab</td>
<td>89 (40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 Ab</td>
<td>74 (34)</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>ICA &amp; GADA</td>
<td>47 (21)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>ICA &amp; IA-2A</td>
<td>6 (3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>GADA &amp; IA-2A</td>
<td>21 (10)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>1 Ab</td>
<td>57 (26)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>ICA</td>
<td>1 (0.5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>GADA</td>
<td>49 (22)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>IA-2A</td>
<td>7 (3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>C-PEPTIDE</td>
<td>0.10 nmol/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>ICA512/IA-2-: Index* of IA-2A: Index* of 1.0 GADA+: Index* of 4.6 ICA+: &gt;4 JDF units</td>
<td>*INDEX = sample cpm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>GADA</td>
<td>72 (85)</td>
<td>Risk of bias: n/a</td>
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</tr>
</tbody>
</table>
### Reference

**Table 12: Brunova 2002 (NCGC reference 28)**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>J. Brunova, J. Bruna, M. Koning, M. Meyer, G. Joubert, and W. Mollentze. GAD65Ab and primary hypothyroidism in type 1 and 2 diabetic subjects.</td>
<td>Observational: cross-sectional study</td>
<td>Total N=192 (N=55 T1D and N=137 T2D)</td>
<td>Adults and young people Diabetes type: T2D T1D T1D N=55; T2D N=137 Age, years, (range) 13 – 85 years M/F % 50/50</td>
<td>T1D: GAD65 T2D: IC-PEPTIDE GAD65 Cut-offs for positivity IC-PEPTIDE+: not given GAD65+: not given</td>
<td>n/a</td>
<td>T1D (N=55)</td>
<td>Funding: Not reported Risk of bias: n/a</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>GAD65+</td>
<td>17/55 (30.9%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T2D (N=137)</td>
<td>GAD65+</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IC-PEPTIDE in GAD-patients, pmol/L (SD)</td>
<td>637.6 (503)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IC-PEPTIDE in GAD-patients, pmol/L (SD)</td>
<td>1168.1 (732)</td>
</tr>
</tbody>
</table>

P-C-PEPTIDE: Carried out in patients that were tested for C peptide within 1 week after diagnosis

At diagnosis:
Undetectable (<0.10 nmol/L):
Ab+: 30/123 (24.4%)
Ab-: 1/36 (2.8)
Low (<0.25 nmol/L)
Ab+: 72/123 (58.5)
Ab-: 2/36 (5.6)
Follow up:
Undetectable (<0.10 nmol/L):
Ab+: 13/123 (10.6)
Ab-: 3/36 (8.3)
Among all Ab- patients, 13/93 had low fasting P-C Peptide (0.25 nmol/L) and 12/13 had T1D
### Table 13: Laadhar 2007 (reference 30)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Exclusion criteria: None reported</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>T1D N=261</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>Age, years, mean (SD; range)</td>
<td>29.1 (1.9; 16-60)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Age at Diagnosis, years, mean (SD)</td>
<td>20.3 (10.3)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>M/F %</td>
<td>48/52</td>
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</table>

### Table 14: Lu 2014 (NCGC reference 321)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes (baseline)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>H Lu, F Hu, Y Zeng, L Zou, S Luo, Y Sun, H Liu, and L Sun. Ketosis onset type 2 diabetes</td>
<td>Observational: cross-sectional study</td>
<td>N=140</td>
<td>Adults and young people Diabetes type: T2D</td>
<td>T2D: Fasting C-PEPTIDE</td>
<td>n/a</td>
<td>T2D adults and young people f-C-PEP, pmol/L (SD)</td>
<td>Funding: Not reported Risk of bias: n/a</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inclusion criteria:</td>
<td></td>
<td></td>
<td></td>
<td>Ketosis group: 475.8 (406) Nonketotic group: 348.2 (283)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Newly diagnosed T2D Without islet-associated</td>
<td></td>
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</tbody>
</table>

REF ID: Lu 2014

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>T.McDonald, K. Colclough, R. Brown, B. Shields, M. Shepherd, P. Bingley, A. Williams, A. Hattersley, and Sian Ellard. Islet autoantibodies can discriminate maturity-onset diabetes of the young (MODY) from Type 1 diabetes. Diabet. Med. 28 (9):1028-1033, 2011.</td>
<td>Observational: cross-sectional study</td>
<td>Total N=616 N=98 T1D – adults and young people N=508 MODY – but adults only</td>
<td>Adults and young people Diabetes type: T1D MODY</td>
<td>T1D: GAD IA-2</td>
<td>n/a</td>
<td>T1D: 24/98 (24.5%) IA-2: 19/98 (94.5%)</td>
<td>Funding: None reported Risk of bias: n/a</td>
</tr>
<tr>
<td></td>
<td>UK study</td>
<td>Inclusion criteria: Clinical history of diabetes HbA1c &lt;6.0% MODY Diagnosis by genetic testing T1D Diagnosis in last 6 mths</td>
<td>Age, years, median (IQR)</td>
<td>&gt; 6 months</td>
<td></td>
<td>GAD+: 5 (1%) IA-2+: 0 (0%) GAD+ and/or IA-2+: 5/508 (1%)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Exclusion criteria: None given</td>
<td>Duration of diabetes, years, median (IQR)</td>
<td>Cut-offs for positivity</td>
<td></td>
<td>GAD+: 54 WHO units/ml (99th percentile) IA-2+: 15 WHO units/ml (99th percentile; lowest calibrator)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Age, years mean</td>
<td>44.8 47.0</td>
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<td></td>
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<td></td>
<td>M/F %</td>
<td>66 72</td>
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<td></td>
<td>BMI, mean</td>
<td>25.0 24.4</td>
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<td></td>
<td></td>
<td></td>
<td>HbA1c</td>
<td>11.0% 11.8%</td>
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<td></td>
<td></td>
<td>Drop-outs / missing data: none</td>
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### Table 16: Oram 2014 (NCGC reference 316)

<table>
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<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>Inclusion criteria: T1D for &gt;5 years Diagnosis at either &lt;30 years age (n=68) or &gt;30 years age with islet autoAbs present (n=6) All patients on insulin since Diagnosis.</td>
<td>Age at Diagnosis, median (IQR) 16 (9-23) years</td>
<td>C-peptide titres are compared using different assays; results not been extracted for this review as do not know which is the best (in terms of Diagnosis accuracy) assay method to use</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Exclusion criteria: None given</td>
<td>Male</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Duration of diabetes, median (IQR) 51% 30 (19-41 years)</td>
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<td></td>
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<td></td>
<td>BMI, median (IQR) 25 (23 – 28) kg/m2</td>
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<td></td>
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<td></td>
<td>HbA1c, median (IQR) 7.9 (7.2 – 9.0) kg/m2</td>
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</table>

### Table 17: Ota 2005 (NCGC reference 126)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up n/a</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Inclusion criteria: T1D classified by American diabetes association</td>
<td>T1D N=101</td>
<td>Cut-offs for positivity ICA512/IA-2: 0.4 U/mL GAD65+: 1.3 U/mL</td>
<td></td>
<td>GAD65+ IA-2+ 37 (32)</td>
<td>Risk of bias: n/a</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exclusion criteria: None reported</td>
<td>Age, years, mean (range; SD) 41.3 (14.0-89.0; 15.3)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Duration of diabetes, years, mean (SD) 10.4 (9.6)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>M/F % 47/54</td>
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</table>

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### Table 18: Rajalakshmi (NCGC reference 322)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>R Rajalakshmi, A Amutha, Harish Ranjani, Mohammed K. Ali, Ranjit Unnikrishnan, Ranjit Mohan Anjana, K. M. V. Narayan, and Viswanath Mohan. Prevalence and risk factors for diabetic retinopathy in Asian Indians with young onset type 1 and type 2 diabetes. J. Diabetes Complications 28 (3):291-297, 2014. REF ID: Rajalshmi 2014</td>
<td>Observational/cross-sectional study</td>
<td>N=300 T1D and T2D (N=150 of each)</td>
<td>Inclusion criteria: Diagnosis between ages 10 and 25 years Duration of diabetes &gt;2 years Diagnosis: FPG ≥126 mg/dL, and/or 2hr post-load glc level ≥200 mg/dL, or self-reported diabetes treated by a physician or on hypoglyc. Medications or insulin. T1D Diagnosis: accompanied by abrupt onset of symptoms like polyuria, polydipsia, or unexplained wt loss, DKA, asent insulin reserve, requirement of insulin from time of Diagnosis for control of hyperglycaemia. T2D Diagnosis: absence of ketosis, good B-cell functional reserve, absence of pancreatic calculi, and good response to oral hypoglyc. Agents for &gt;2 years. Exclusion criteria: None reported.</td>
<td>Adults and young people Diabetes type: T1D, T2D Adults and young people: T1D (n=150) T2D (n=150)</td>
<td>Fasting C-peptide, pmol/ml</td>
<td>n/a</td>
<td>Funding: Global diabetes research centre. Risk of bias: n/a no missing data</td>
</tr>
</tbody>
</table>

### Table 19: Samuelsson 2013 (NCGC reference 317)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
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<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>Study type</td>
<td>Number of patients</td>
<td>Patient characteristics</td>
<td>Diagnostic markers assessed</td>
<td>Length of follow-up</td>
<td>Outcome measure and effect sizes</td>
<td>Comments</td>
</tr>
<tr>
<td>-----------</td>
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<td>-----------</td>
</tr>
<tr>
<td>Anna Scholin, Agneta Siegbahn, Lars Lind, Christian Berne, Goran Sundkvist, Elisabeth Bjork, F. Anders Karlsson, and Diabetes Incidence Study in Sweden group. CRP and IL-6 concentrations are associated with poor glycemic control despite preserved beta-cell function during the first year after diagnosis of type 1</td>
<td>Observatio nal study: Diabetic incidence in Sweden study.</td>
<td>Total N= 100 T1D . N=3ter excluded as pregnant. Inclusion criteria: Not pregnant. Exclusion criteria: None reported</td>
<td>Age of T1D patients (n=97) at diagnosis T1D: C-peptide ICA+ GADA+ IA-2A+ C-peptide: reference interval for fasting plasma concentration was 0.25 to 0.75 nmol/L GADA index: &gt;4.6 u/ml IA-2A index: &gt;1.0</td>
<td>12 months</td>
<td>Assays divided into islet antibody positive (ab+) and negative (ab-) Ab+ (N=78) C peptide (nmol/l) 0.25 (0.04-1.4) ICA+ 58/78 (74%) GADA+ 69/78 (88%) IA-2A+ 55/78 (70%) Ab- (N=19 : 19.7%) C peptide (nmol/l) 0.34 (0.08-1.41) Total population (I have added Ab+ and Ab-) ICA+ 58/97 (59.8%) GADA+ 69/97 (71.1%) IA-2A+ 55/97 (56.7%) C-peptide – 0.25 + 0.34 /2 =</td>
<td>Funding: Supported by Grant from the Swedish Research Council, the Swedish Heart Lung Foundation, the Swedish Diabetes Association, the family Ernfors Fund, and the Juvenile Diabetes Foundation</td>
<td></td>
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</table>
### Table 21: Scholin 2004b (NCGC reference 112)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Exclusion criteria: None reported</td>
<td></td>
<td></td>
<td>ICA+ N=199/312 (64%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IA-2A+ N=162/294 (55%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>GADA+ N=229/295 (78%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IAA+ N=58/215 (27%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T1D Ab+ (n=307)</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 22: Scholin 2004c (NCGC reference 69)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Scholin, L. Bjorklund, H. Borg, H. Arnqvist, E. Bjork,</td>
<td>Observational:</td>
<td>Total N=312 (patients with blood samples at</td>
<td>Adults and young people Diabetes type: T1D</td>
<td>T1D: C-PEPTIDE GADA</td>
<td>8 years</td>
<td>T1D Baseline (N=312)</td>
<td>Funding: Juvenile diabetes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ICA+ N=199/312 (64%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>GADA 235/311 (76)</td>
<td></td>
</tr>
</tbody>
</table>
### Table 23: Scholin 2011 (NCGC reference 93)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Scholin, L. Nystrom, H. Arqvist, J. Bolinder, E. Bjork, C. Berne, F. A. Karlsson, and Diabetes Incidence Study Group. Proinsulin/C-peptide ratio, glucagon and remission in new-onset Type 1 diabetes mellitus in young adults. Diabet.Med.</td>
<td>Observational: cross-sectional study and prospective</td>
<td>Total recruited: N=203 N=78 T1D (had complete data at all the time-points and were confirmed T1D)</td>
<td>Adults and young people Diabetes type: T1D</td>
<td>T1D: IC-PEPTIDE Cut-offs for positivity IC-PEPTIDE+: not given</td>
<td>3 years follow-up post Diagnosis.</td>
<td>T1D (N=78)</td>
<td>Funding: Not reported Risk of bias: n/a</td>
</tr>
<tr>
<td></td>
<td>Swedish study</td>
<td></td>
<td></td>
<td>T1D T1D N=78</td>
<td>Age, years, mean (SD; range)</td>
<td>26.2 (6.0)</td>
<td></td>
</tr>
</tbody>
</table>
Table 24: Tridgell 2011 (NCGC reference 46)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM. Tridgell, C Speikerman, Richard S. Wang, and Carla J. Greenbaum. Interaction of onset and duration of diabetes on the percent of gad and ia-2 antibody-positive subjects in the type 1 diabetes genetics consortium database. Diabetes Care 34 (4):988-993, 2011. REF ID: Tridgell 2011</td>
<td>Observation at: cross-sectional study</td>
<td>Total N= 5,020 T1D</td>
<td>Adults and young people</td>
<td>T1D: GADA IA-2A GADA and/or IA-2A</td>
<td>n/a</td>
<td>T1D: onset aged 2-7 (N=1,739) -univariate analyses T1D: onset aged 8-13 years (N=1,767) -univariate analyses</td>
<td>Funding: T1D Genetics consortium, National institute of diabetes and digestive and kidney diseases, juvenile diabetes research foundation Risk of bias: n/a</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Diabetes type: T1D</td>
<td>Cut-offs for positivity GAD65+: NR ICA+: NR</td>
<td></td>
<td>GADA+ 35.7% IA-2+ 43.1%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>T1D N=5,020</td>
<td>Data for adults and young people has been separated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Age, years, median (range) 10 (2-52)</td>
<td>Duration of diabetes, years, median (range) 8 (0-66)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>M/F % 50.7%/49.3%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Exclusion criteria: None reported</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Exclusion criteria: Pregnant T2D</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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### Table 25: Vermeulen 2011 (NCGC reference 250)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Vermeulen, I. Weets, M. Asanghanwa, J. Ruige, Gaal L. Van, C. Mathieu, B. Keymeulen, V. Lampasona, J. M. Wenzlau, J. C. Hutton, D. G. Pipeleers, and F. K. Gorus. Contribution of antibodies against IA-2beta and zinc transporter 8 to classification of diabetes diagnosed under 40 years of age. Diabetes Care 34 (8):1760-1765, 2011.</td>
<td>Observational: Case-control study</td>
<td>Total N= 665 T1D (n=170 aged 0-9 years; n=223 aged 10-19 years; n=149 aged 20-29 years; n=113 aged 30-39 years)</td>
<td>Young people and adults (data separated for some age-groups and markers) DIABETES TYPE: T1D</td>
<td>T1D IA-2A IA-2βA ZnT8 IAA GADA Combination s</td>
<td>1 year</td>
<td>T1D Adults aged 20-29 (N=149) MARKER N (%)</td>
<td>Funding: Juvenile diabetes Research F, EU and Belgian fund for Scientific Research Risk of bias: n/a</td>
</tr>
<tr>
<td></td>
<td>Registry, Belgium</td>
<td>Inclusion criteria: Diagnosis with diabetes before age 40 Physician Diagnosis of T1D on clinical grounds and treated with insulin with 7 days after Diagnosis Blood sampled within 7 days after Tx started CONTROLS: sex-matched non-diabetic controls aged 0-39 years None had relatives with T1D.</td>
<td>T1D Age, years.</td>
<td>n=170: 0-9 years n=223: 10-19 years n=149: 20-29 years n=113 30-39 years</td>
<td>Median: 15 (IQR9-26) years</td>
<td>≥1 Ab+ (GADA, IA-2A or ZnT8) 207 (93)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>M/F</td>
<td>383 /272</td>
<td>IA-2A: ≥0.44% tracer binding IA-2βA: ≥0.39% tracer binding</td>
<td></td>
<td>≥1 Ab+ (GADA, IA-2A or ZnT8) 209 (94)</td>
<td></td>
</tr>
</tbody>
</table>
### Table 26: Wenzlau 2010 (NCGC Reference 55)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient characteristics</th>
<th>Diagnostic markers assessed</th>
<th>Length of follow-up</th>
<th>Outcome measure and effect sizes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>J. M. Wenzlau, M. Walter, T. J. Gardner, L. M. Frisch, L. Yu, G. S. Eisenbarth, A. G. Ziegler, H. W. Davidson, and J. C. Hutton.</td>
<td>Observational cross-sectional study</td>
<td>Total N=506</td>
<td>Adults and young people Diabetes type: T1D</td>
<td>T1D: C-PEPTIDE ZnT8 GADA IA-2</td>
<td>Group 1: 2.5 years Group 2: 7 years Group 3: 3-10.9 years</td>
<td>Group 1: New onset diabetes (n=21) baseline ZnT8A+ 85.7% GADA+ 95.2% IA-2A+ 90.5% C Peptide+ 100%</td>
<td>Funding: Childhood diabetes foundation, Denver; university of Colorado health sciences centre diabetes endocrinology research centre</td>
</tr>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Age, 20.3 9.8 11.4</td>
<td>Cut-offs for positivity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 (n=21) 2 (n=61) 3 (n=424)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>transporter 8 autoantibodies in type 1 diabetic human subjects. J.Clin.Endocrinol.Metab. 95 (10):4712-4719, 2010.</td>
<td>patients (4 years duration) Patients with longstanding diabetes (&gt;20 years) Exclusion criteria: None reported</td>
<td>years, median (SD; range)</td>
<td>(6.2; 12.2-34.6)</td>
<td>(5.2; 1.6-36.7)</td>
<td>(7.6; 0.5-52.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
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<td>---</td>
<td>---</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-PEPTIDE+: 3 pmol/mL ZnT8: index* of 0.015-0.020 ICA512/IA-2+: Index* of 0.032 GAD65+: Index* of 0.069</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*INDEX = \( \frac{\text{sample cpm} - \text{negative control cpm}}{\text{positive control cpm} - \text{negative control cpm}} \)

**Group 1: new onset diabetes at 12 years follow up (prevalence)**

| GADA+ | 85.7% |
| IA-2A+ | 90.5% |
| C Peptide+ | 5.7% |

Risk of bias: n/a

**Group 2: New onset T1D diabetes (n=61) Baseline**

| ZnT8A+ | 80.3% |
| GADA+ | 63.0% |
| IA-2A+ | 73.8% |
| C Peptide+ | NR |

**Group 2: New onset T1D diabetes (n=61) 12 years follow up**

| ZnT8A+ | 42.6% |
| GADA+ | 32.4% |
| IA-2A+ | 47.5% |
| C Peptide+ (detected >0.02 pmol/mL) | 27.8% |

**Group 2: patients with 4 years duration of T1D at 12 years follow up (prevalence)**

| GAD+ | 10.7% |
| CWCR | 8.9% |
| IA2+ | 16.1% |
| GAD/CWCR | 3.6% |
| GAD/IA2 | 10.7% |
| IA2/CWCR | 19.6% |
| GAD/CWCR/IA2 | 20% |
### Group 3: Patients with longstanding diabetes (>20 years)
(n=282)
12 year follow up (prevalence)

<table>
<thead>
<tr>
<th>Antibodies</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAD+</td>
<td>11.0%</td>
</tr>
<tr>
<td>CWCR</td>
<td>1.4%</td>
</tr>
<tr>
<td>IA2+</td>
<td>7.8%</td>
</tr>
<tr>
<td>GAD/CWCR</td>
<td>0.7%</td>
</tr>
<tr>
<td>GAD/IA2</td>
<td>7.1%</td>
</tr>
<tr>
<td>IA2 / CWCR</td>
<td>2.1%</td>
</tr>
<tr>
<td>GAD/CWCR/IA2</td>
<td>2.5%</td>
</tr>
</tbody>
</table>
J.1 Original (2004) forest plots

J.1.1 Type 1 diabetes – insulin preparations

Figure J.1: HbA1c – all included studies providing HbA1c levels; HbA1c is significantly lower with rapid-acting analogues than regular insulin; eleven parallel group studies with a total of 4246 patients showed a significant decrease in HbA1c levels (WMD −0.14%, 95% CI −0.19 to −0.08%); twelve crossover studies with a total of 2441 patients showed no difference in HbA1c (WMD 0.00, 95% CI −0.09 to 0.08)
Figure I.2: HbA1c – studies separated into children/young people and adults; three studies with a total of 545 children and young people investigated HbA1c levels; the studies did not show a significant difference between rapid-acting analogues and regular insulin (WMD –0.03%, 95% CI –0.21 to 0.14%); nine studies with a total of 1896 adult patients did not show a significant difference between rapid-acting analogues and regular insulin (WMD 0.01%, 95% CI –0.09 to 0.11%).

**Table 1:** Forest plot of studies comparing rapid-acting insulin analogue versus soluble insulin for HbA1c levels in children and young people and adults.

<table>
<thead>
<tr>
<th>Study</th>
<th>Rapid-acting Insulin analogue</th>
<th>Soluble Insulin</th>
<th>WMD (Mean)</th>
<th>Weight</th>
<th>WMD (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean (SD)</td>
<td>N</td>
<td>Mean (SD)</td>
<td>%</td>
</tr>
<tr>
<td>Children studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deeks 2005</td>
<td>55</td>
<td>8.40 (1.5)</td>
<td>69</td>
<td>8.28 (1.0)</td>
<td>8.13</td>
</tr>
<tr>
<td>Holcombe 2003</td>
<td>443</td>
<td>8.69 (1.2)</td>
<td>419</td>
<td>8.70 (1.0)</td>
<td>17.68</td>
</tr>
<tr>
<td>Rökk-Adams 2003</td>
<td>33</td>
<td>8.60 (0.5)</td>
<td>23</td>
<td>8.90 (1.4)</td>
<td>1.48</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>545</td>
<td>545</td>
<td></td>
<td></td>
<td>24.30</td>
</tr>
</tbody>
</table>

*Test for heterogeneity: CHI² = 12.62, df = 2, P = 0.00, I² = 0%*

**Test for overall effect:** Z = 2.36 (P = 0.02)

**Adult studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Rapid-acting Insulin analogue</th>
<th>Soluble Insulin</th>
<th>WMD (Mean)</th>
<th>Weight</th>
<th>WMD (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean (SD)</td>
<td>N</td>
<td>Mean (SD)</td>
<td>%</td>
</tr>
<tr>
<td>Anderson 1994</td>
<td>1026</td>
<td>6.93 (1.7)</td>
<td>1028</td>
<td>6.93 (1.7)</td>
<td>9.34</td>
</tr>
<tr>
<td>Pfister 1996</td>
<td>97</td>
<td>7.34 (0.8)</td>
<td>97</td>
<td>7.33 (0.8)</td>
<td>8.77</td>
</tr>
<tr>
<td>Holman 1997</td>
<td>199</td>
<td>7.60 (1.0)</td>
<td>199</td>
<td>7.50 (1.2)</td>
<td>12.21</td>
</tr>
<tr>
<td>Unger 1997</td>
<td>246</td>
<td>7.02 (1.0)</td>
<td>242</td>
<td>7.02 (1.0)</td>
<td>16.62</td>
</tr>
<tr>
<td>Davies 1997</td>
<td>10</td>
<td>6.86 (0.8)</td>
<td>10</td>
<td>6.86 (0.8)</td>
<td>0.33</td>
</tr>
<tr>
<td>Gart 2000</td>
<td>97</td>
<td>7.40 (1.2)</td>
<td>97</td>
<td>7.40 (1.2)</td>
<td>9.71</td>
</tr>
<tr>
<td>Akehurst 2000</td>
<td>85</td>
<td>8.21 (1.8)</td>
<td>88</td>
<td>8.21 (1.8)</td>
<td>12.14</td>
</tr>
<tr>
<td>Ferguson 2001</td>
<td>33</td>
<td>8.10 (1.3)</td>
<td>33</td>
<td>8.10 (1.3)</td>
<td>3.18</td>
</tr>
<tr>
<td>Possin-Gaff 2001</td>
<td>152</td>
<td>7.52 (1.5)</td>
<td>152</td>
<td>7.52 (1.5)</td>
<td>4.81</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>1094</td>
<td>1094</td>
<td></td>
<td></td>
<td>70.10</td>
</tr>
</tbody>
</table>

*Test for heterogeneity: CHI² = 33.92, df = 9, P < 0.00, I² = 70%*

**Test for overall effect:** Z = 9.14 (P < 0.00)

**Forest plot:** Studies are represented as squares proportional to their weight, with horizontal lines indicating the 95% confidence interval for the weighted mean difference (WMD). The vertical line at 0 represents no difference between the rapid-acting insulin analogue and soluble insulin.
Figure I.3: HbA1c – studies separated into type of analogue (insulin aspart and insulin lispro); HbA1c was significantly lower with both types of rapid-acting analogue when compared with regular insulin (insulin aspart with a total of 2281 patients: WMD −0.14% 95% CI −0.20 to −0.07%; insulin lispro with a total of 1965 patients: WMD −0.13%, 95% CI −0.24 to −0.02%); there was no significant difference in HbA1c reduction between studies using insulin aspart or insulin lispro.

**Figure I.4:** Hypoglycaemic episodes/30 days; there was no significant difference between rapid-acting analogues and regular insulin regarding hypoglycaemic episodes.
Figure I.5: Hypoglycaemic episodes/30 days with adults’ and children’s/young people’s studies separated; there was no significant difference between rapid-acting analogues and regular insulin regarding hypoglycaemic episodes in either adults or children/young people; furthermore, there was no apparent difference between children/young people and adults in terms of the number of hypoglycaemic episodes/30 days

Table I.5: Hypoglycaemic episodes/30 days — crossover studies

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Rapid-acting insulin analogue</th>
<th>Soluble insulin</th>
<th>RR (random)</th>
<th>Weight %</th>
<th>RR (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dejmek 1977</td>
<td>52</td>
<td>53</td>
<td>1.02 (0.89)</td>
<td>3.46</td>
<td>0.30 (0.25)</td>
</tr>
<tr>
<td>Insulin 2000</td>
<td>465</td>
<td>463</td>
<td>0.98 (0.85)</td>
<td>21.70</td>
<td>0.30 (0.25)</td>
</tr>
<tr>
<td>Parmal 2000</td>
<td>23</td>
<td>23</td>
<td>0.98 (0.84)</td>
<td>3.56</td>
<td>0.30 (0.25)</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>544</td>
<td>546</td>
<td>1.00 (0.88)</td>
<td>23.64</td>
<td>0.30 (0.25)</td>
</tr>
</tbody>
</table>

Test for heterogeneity: Q = 3.26, df = 2 (P = 0.30), I² = 0%

Test for overall effect: Z = 1.04 (P = 0.30)

Total (95% CI): 150.0

Test for heterogeneity: Q = 10.37, df = 1 (P = 0.001), I² = 71.0%

Test for overall effect: Z = 1.19 (P = 0.23)

Figure I.6: Patient preference — patients preferred rapid-acting analogues to regular insulin; the overall estimate contained significant heterogeneity, which could be due to statistical and/or clinical reasons; these data should, therefore, be interpreted with caution

Table I.6: Patient preference — overall

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Rapid-acting insulin analogue</th>
<th>Soluble insulin</th>
<th>RR (random)</th>
<th>Weight %</th>
<th>RR (random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crossover studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Holliman 1977</td>
<td>144/199</td>
<td>55/169</td>
<td>3.59 (2.09)</td>
<td>7.44</td>
<td>0.39 (0.23)</td>
</tr>
<tr>
<td>Colomer 1977</td>
<td>21/26</td>
<td>4/7</td>
<td>0.32 (0.16)</td>
<td>16.74</td>
<td>0.39 (0.23)</td>
</tr>
<tr>
<td>Cane 2000</td>
<td>25/34</td>
<td>24/34</td>
<td>1.03 (0.70)</td>
<td>0.30</td>
<td>1.03 (0.70)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>213</td>
<td>213</td>
<td>1.00 (0.86)</td>
<td>100.00</td>
<td>1.00 (0.86)</td>
</tr>
</tbody>
</table>

Test for heterogeneity: Q = 10.81, df = 3 (P = 0.01), I² = 71.0%

Test for overall effect: Z = 3.60 (P < 0.001)
Figure I.7: Patient preference – separated according to children's/young people's and adults’ studies; both children/young people and adults preferred rapid-acting insulin analogue to regular insulin; the overall result was heterogeneous, and only one study contributed data for studies in children and young people; heterogeneity could be due to statistical and/or clinical reasons; these data should, therefore, be interpreted with caution.

<table>
<thead>
<tr>
<th>Comparison:</th>
<th>Rapid-acting insulin analogue versus soluble insulin — children and young people from adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome:</td>
<td>Patient preference - crossover studies</td>
</tr>
<tr>
<td>Study or sub-category</td>
<td>Rapid-acting insulin analogue</td>
</tr>
<tr>
<td>Children studies</td>
<td>1623</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>22</td>
</tr>
<tr>
<td>Total events: 18 (Rapid-acting insulin), 4 (Soluble insulin)</td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.26 (P = 0.024)</td>
<td></td>
</tr>
</tbody>
</table>

Adult studies

<table>
<thead>
<tr>
<th>Comparison:</th>
<th>Rapid-acting insulin analogue versus soluble insulin — adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome:</td>
<td>Patient preference - crossover studies</td>
</tr>
<tr>
<td>Study or sub-category</td>
<td>Rapid-acting insulin analogue</td>
</tr>
<tr>
<td>Hollerman 1987 12</td>
<td>144/190</td>
</tr>
<tr>
<td>Campbell 1998 13</td>
<td>2125</td>
</tr>
<tr>
<td>Gade 2003 14</td>
<td>3994</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>360</td>
</tr>
<tr>
<td>Total events: 100 (Rapid-acting insulin), 55 (Soluble insulin)</td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: Chi$^2$ = 3.68, df = 2 (P = 0.11), I$^2$ = 75.99%</td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.17 (P = 0.032)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comparison:</th>
<th>Rapid-acting insulin analogue versus soluble insulin — adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome:</td>
<td>Patient preference - crossover studies</td>
</tr>
<tr>
<td>Study or sub-category</td>
<td>Rapid-acting insulin analogue</td>
</tr>
<tr>
<td>Hollerman 1987 12</td>
<td>144/190</td>
</tr>
<tr>
<td>Campbell 1998 13</td>
<td>2125</td>
</tr>
<tr>
<td>Gade 2003 14</td>
<td>3994</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>360</td>
</tr>
<tr>
<td>Total events: 100 (Rapid-acting insulin), 55 (Soluble insulin)</td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: Chi$^2$ = 3.68, df = 2 (P = 0.11), I$^2$ = 75.99%</td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.17 (P = 0.032)</td>
<td></td>
</tr>
</tbody>
</table>

J.1.2 Type 1 diabetes – exercise

Figure I.8: Ideal frequency of exercise – exercising one to three times/week compared with control (no exercise)

J.2 2015 update forest plots

J.2.1 Diagnosis

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

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

No meta-analyses were conducted for this review question and so there are no forest plots.
J.2.2 Type 1 diabetes – education
Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.3 Type 1 diabetes – behavioural interventions
Review question: What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.4 Type 1 diabetes – multiple daily injections
Review question: What is the effectiveness of multiple daily injections of insulin when compared with mixed insulin injections in improving glycaemic control in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.5 Type 1 diabetes – HbA1c targets
Review question: What is the optimal haemoglobin A1c (HbA1c) target for children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.6 Type 1 diabetes – blood glucose targets
Review question: What are the optimal blood glucose targets for children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.7 Type 1 diabetes – blood glucose monitoring
Review questions:
How frequently should finger-prick blood glucose testing be performed in children and young people with type 1 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

What is the effectiveness of finger-prick blood glucose testing compared with continuous glucose monitoring in children and young people with type 1 diabetes?
Figure 1: Continuous glucose monitoring versus capillary blood glucose monitoring – HbA1c at 6 months

Note: Hirsch 2008 Juvenile 2008 and Yates 2006 were reported in Langendam 2012 systematic review

Figure 2: Continuous glucose monitoring versus capillary blood glucose monitoring – severe hypoglycaemic episodes at 6 months

Note: Juvenile 2008 and Yates 2006 were reported in Langendam 2012 systematic review

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

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.8 Type 1 diabetes – blood ketone monitoring

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

No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.9 Type 1 diabetes – dietary advice

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

No meta-analyses were conducted for this review question and so there are no forest plots.

**J.2.10 Type 1 and type 2 diabetes – diabetic ketoacidosis – symptoms and signs**

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

No meta-analyses were conducted for this review question and so there are no forest plots.

**J.2.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations**

Review questions:

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

No meta-analyses were conducted for this review question and so there are no forest plots.

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

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

No meta-analyses were conducted for this review question and so there are no forest plots.

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

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

No meta-analyses were conducted for this review question and so there are no forest plots.

**J.2.12 Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids**

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

No meta-analyses were conducted for this review question and so there are no forest plots.

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

No meta-analyses were conducted for this review question and so there are no forest plots.

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

No meta-analyses were conducted for this review question and so there are no forest plots.

**J.2.13 Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents**

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

No meta-analyses were conducted for this review question and so there are no forest plots.

**J.2.14 Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin**

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

No meta-analyses were conducted for this review question and so there are no forest plots.

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

No meta-analyses were conducted for this review question and so there are no forest plots.

**J.2.15 Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis**

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

No meta-analyses were conducted for this review question and so there are no forest plots.

**J.2.16 Type 1 diabetes – retinopathy**

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

No meta-analyses were conducted for this review question and so there are no forest plots.
J.2.16.1  **Type 1 diabetes – nephropathy**  
Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 1 diabetes?  
No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.17  **Type 2 diabetes – education**  
Review question: What is the effectiveness of structured education programmes in improving clinical and patient outcomes in children and young people with type 2 diabetes?  
No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.18  **Type 2 diabetes – behavioural interventions**  
Review question: What is the effectiveness of behavioural interventions to promote engagement with clinical services in children and young people with type 2 diabetes?  
No meta-analyses were conducted for this review question and so there are no forest plots.

Review question: What is the effectiveness of behavioural interventions to improve outcomes in children and young people with type 2 diabetes?  
No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.19  **Type 2 diabetes – dietary advice**  
Review question: What is the effectiveness of dietetic advice to optimise glycaemic control in children and young people with type 2 diabetes?  
No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.20  **Type 2 diabetes – weight loss**  
Review question: Does weight loss in children and young people with type 2 diabetes who are overweight or obese improve glycaemic control as measured by HbA1c?  
No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.21  **Type 2 diabetes – metformin**  
Review question: What is the effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with usual care or placebo?  
No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.22  **Type 2 diabetes – HbA1c targets**  
Review question: What is the optimal HbA1c target for children and young people with type 2 diabetes?  
No meta-analyses were conducted for this review question and so there are no forest plots.

J.2.23  **Type 2 diabetes – hypertension**  
Review question: What is the optimal monitoring strategy for identifying hypertension in children and young people with type 2 diabetes?  
No meta-analyses were conducted for this review question and so there are no forest plots.
**J.2.24  Type 2 diabetes – dyslipidaemia**  
Review question: What is the optimal monitoring strategy for identifying dyslipidaemia in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

**J.2.25  Type 2 diabetes – retinopathy**  
Review question: What is the optimal monitoring strategy for identifying retinopathy in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.

**J.2.26  Type 2 diabetes – nephropathy**  
Review question: What is the optimal monitoring strategy for identifying nephropathy in children and young people with type 2 diabetes?

No meta-analyses were conducted for this review question and so there are no forest plots.
Appendix K: GRADE tables

K.1 Diagnosis

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

The systematic review for this question was conducted by the guidance-producing centre for the guideline ‘Type 1 diabetes in adults’. There are no evidence profiles (GRADE tables) for this question because nearly all of the studies included in the evidence review were cross-sectional observational studies and thus were not able to be combined in a meta-analysis or GRADE evidence profile. All non-comparative observational studies included for this question were graded as low quality due to the inherent high risk of bias associated with these study designs. The specific methodological limitations of the included studies are summarised in the table below.

Table 27: Methodological limitations of non-comparative observational studies included for the review question about diagnosis

<table>
<thead>
<tr>
<th>Study</th>
<th>Propsective or cross-sectional study design</th>
<th>Representative population sample</th>
<th>Outcomes measured adequately</th>
<th>Appropriate statistical analysis conducted (adjusted for confounders where applicable)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZANONE 2003</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>TUNG 2008</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>VERMEULEN 2011</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>BARKER 2014</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>ANDERSSON 2013</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>SAMUELSSON 2013</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>SHIVAPRASAD 2014</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>SCHOLIN 2004a</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>BORG 2003</td>
<td>Yes</td>
<td>Partially (mixed young people and adult population)</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>BESSER 2011</td>
<td>Yes</td>
<td>Partially (mixed young</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>Study</td>
<td>Propsective or cross-sectional study design</td>
<td>Representative population sample</td>
<td>Outcomes measured adequately</td>
<td>Appropriate statistical analysis conducted (adjusted for confounders where applicable)</td>
<td>Quality</td>
</tr>
<tr>
<td>-----------------------</td>
<td>---------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>------------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>LAADHAR 2007</td>
<td>Yes</td>
<td>Partially (mixed young people and adult population)</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>BRUNOVA 2002</td>
<td>Yes</td>
<td>Partially (mixed young people and adult population)</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>OTA 2005</td>
<td>Yes</td>
<td>Partially (mostly the population of interest based on the mean age of participants)</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>SCHOLIN 2011</td>
<td>Yes</td>
<td>Partially (mixed young people and adult population)</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>SCHOLIN 2004b</td>
<td>Yes</td>
<td>Partially (mixed young people and adult population)</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>TRIDGELL 2011</td>
<td>Yes</td>
<td>Partially (mostly the population of interest based on the mean age of participants)</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>SCHOLIN 2004c</td>
<td>Yes</td>
<td>Partially (mixed young people and adult population)</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>WENZLAU 2010</td>
<td>Yes</td>
<td>Partially (mixed young people and adult population)</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>MCDONALD 2011</td>
<td>Yes</td>
<td>Partially (mixed young people and adult population)</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>ORAM 2014</td>
<td>Yes</td>
<td>Partially (mixed young people and adult population)</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>LU 2014</td>
<td>Yes</td>
<td>Partially (mixed young people and adult population)</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
</tr>
<tr>
<td>RAJALAKSHMI 2014</td>
<td>Yes</td>
<td>Partially (mixed young people and adult population)</td>
<td>Yes</td>
<td>NA</td>
<td>Low</td>
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</tbody>
</table>
### K.2 Type 1 diabetes – education

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

**Table 28: Evidence profile for effectiveness of structured education programmes in children and young people with type 1 diabetes**

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation s (risk of bias)</th>
<th>Inconsist ency</th>
<th>Indirectne ss</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>of studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Absolute (95% confidence interval)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Structured education</td>
<td>Control</td>
<td>Relative (95% confidence interval)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean HbA1c at 6 months (education only versus standard care)</td>
<td>1 (Howe 2005)</td>
<td>21</td>
<td>28</td>
<td>NA</td>
<td>MD 0.2 lower (1.21 lower to 0.81 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious1</td>
<td>No serious inconsiste ncy2</td>
<td>No serious indirectnes s3</td>
</tr>
<tr>
<td>Mean HbA1c at 6 months (education plus telephone case management versus standard care)</td>
<td>1 (Howe 2005)</td>
<td>26</td>
<td>28</td>
<td>NA</td>
<td>MD 0.4 lower (1.28 lower to 0.48 higher)</td>
<td>Low</td>
<td>RCT</td>
<td>Serious1</td>
<td>No serious inconsiste ncy2</td>
<td>No serious indirectnes s3</td>
</tr>
<tr>
<td>Mean HbA1c at 6 months (TeenCope versus Managing Diabetes)</td>
<td>1 (Grey 2013)</td>
<td>167</td>
<td>153</td>
<td>NA</td>
<td>MD 0.02 higher (0.31 lower to 0.35 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>Serious1</td>
<td>No serious inconsiste ncy2</td>
<td>No serious indirectnes s3</td>
</tr>
<tr>
<td>Effect</td>
<td>Quality</td>
<td>Design</td>
<td>Limitation(s) of Bias</td>
<td>Inconsistency</td>
<td>Indirectness</td>
<td>Imprecision</td>
<td>Other Considerations</td>
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</tr>
<tr>
<td><strong>Mean HbA&lt;sub&gt;1c&lt;/sub&gt; at 12 months (TeenCope versus Managing Diabetes)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Grey 2013)</td>
<td>167</td>
<td>153</td>
<td>NA</td>
<td>MD 0.18 lower (0.49 lower to 0.13 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Mean HbA&lt;sub&gt;1c&lt;/sub&gt; at 12 months (family-centred group education versus conventional clinical care)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Murphy 2012)</td>
<td>158</td>
<td>147</td>
<td>NA</td>
<td>MD 0.2 lower (0.55 lower to 0.15 higher)</td>
<td>Low</td>
<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious imprecision&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>HbA&lt;sub&gt;1c&lt;/sub&gt; change over 12 months (family-centred group education versus waiting list)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Murphy 2007)</td>
<td>33</td>
<td>34</td>
<td>NA</td>
<td>MD 0.01 lower (0.17 lower to 0.15 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>Mean HbA&lt;sub&gt;1c&lt;/sub&gt; at 12 months (care ambassador plus versus standard care)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Katz 2014)</td>
<td>52</td>
<td>51</td>
<td>NA</td>
<td>MD 0.1 lower (0.45 lower to 0.25 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>Mean HbA&lt;sub&gt;1c&lt;/sub&gt; at 12 months (care ambassador ultra versus standard care)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>1 (Katz 2014)</td>
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<td>51</td>
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<td>MD 0.1 higher (0.26 lower to 0.46 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>Mean HbA&lt;sub&gt;1c&lt;/sub&gt; at 12 months (CASCADE versus control)</strong></td>
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<tr>
<td>1 (Christie 2014)</td>
<td>143</td>
<td>155</td>
<td>NA</td>
<td>MD 0.1 (0.28 lower to 0.50 higher)</td>
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<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
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<td>No serious indirectness</td>
<td>Serious imprecision&lt;sup&gt;6&lt;/sup&gt;</td>
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<td><strong>Mean HbA&lt;sub&gt;1c&lt;/sub&gt; at 12 months (supportive self-care versus conventional treatment)</strong></td>
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<td>12</td>
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<td>MD 0.4 lower (not reported)&lt;sup&gt;7&lt;/sup&gt;</td>
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<td>RCT</td>
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<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Very serious imprecision&lt;sup&gt;7&lt;/sup&gt;</td>
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<tr>
<td><strong>Mean HbA&lt;sub&gt;1c&lt;/sub&gt; at 24 months (care ambassador plus versus standard care)</strong></td>
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<tr>
<td>1 (Katz 2014)</td>
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<td>51</td>
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<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious imprecision&lt;sup&gt;5&lt;/sup&gt;</td>
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<tr>
<td><strong>Mean HbA&lt;sub&gt;1c&lt;/sub&gt; at 24 months (care ambassador ultra versus standard care)</strong></td>
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<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious indirectness</td>
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</table>
### Diagnosis and management of type 1 diabetes in children and young people

**Appendix K: GRADE tables**

© 2014 National Collaborating Centre for Women’s and Children’s Health

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
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<td><strong>Structured education</strong></td>
<td><strong>Control</strong></td>
<td><strong>Number of children and young people</strong></td>
<td><strong>Effect</strong></td>
<td><strong>Quality</strong></td>
<td><strong>Design</strong></td>
<td><strong>Limitation (risk of bias)</strong></td>
<td><strong>Inconsistency</strong></td>
<td><strong>Indirectness</strong></td>
<td><strong>Imprecision</strong></td>
<td><strong>Other considerations</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Average mean HbA&lt;sub&gt;1c&lt;/sub&gt; at 24 months (care ambassador plus versus standard care)</strong></td>
<td>1 (Katz 2014)</td>
<td>52</td>
<td>51</td>
<td>NA</td>
<td>MD 0.1 lower (0.41 lower to 0.21 higher)</td>
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<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>No serious imprecision&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Average mean HbA&lt;sub&gt;1c&lt;/sub&gt; at 24 months (care ambassador ultra versus standard care)</strong></td>
<td>1 (Katz 2014)</td>
<td>50</td>
<td>51</td>
<td>NA</td>
<td>MD 0 lower (0.36 lower to 0.36 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>No serious imprecision&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Mean HbA&lt;sub&gt;1c&lt;/sub&gt; at 24 months (CASCADE versus control)</strong></td>
<td>1 (Christie 2014)</td>
<td>135</td>
<td>149</td>
<td>NA</td>
<td>MD 0.03 lower (0.36 lower to 0.41 higher)</td>
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<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>No serious imprecision&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Mean HbA&lt;sub&gt;1c&lt;/sub&gt; at 24 months (supportive self-care versus conventional treatment)</strong></td>
<td>1 (Delamater 1990)</td>
<td>9</td>
<td>12</td>
<td>NA</td>
<td>MD 0.9 lower (not reported)&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Very serious imprecision&lt;sup&gt;7&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Mean number of severe hypoglycaemic episodes (per participant) - over 12 months (Family-centred group education vs. Conventional clinical care)</strong></td>
<td>1 (Murphy 2012)</td>
<td>158</td>
<td>147</td>
<td>NA</td>
<td>MD 0.05 lower (0.21 lower to 0.11 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>No serious imprecision&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Severe hypoglycaemic episodes (1 or more episodes versus no episodes, parent- or adult-reported) over 12 months (CASCADE versus control)</strong></td>
<td>1 (Christie. 2014)</td>
<td>143</td>
<td>155</td>
<td>OR 0.76&lt;sup&gt;a&lt;/sup&gt; (0.32 lower to 2.59 higher)</td>
<td>NA</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Very serious imprecision&lt;sup&gt;4&lt;/sup&gt;</td>
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<tr>
<td><strong>Mean number of severe hypoglycaemic episodes (per participant) over 24 months (care ambassador plus psycho-education versus care ambassador only)</strong></td>
<td>1 (Svoren 2003)</td>
<td>97</td>
<td>94</td>
<td>NA</td>
<td>MD 0.17 higher (0.18 lower to 0.52 higher)</td>
<td>Low</td>
<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Serious imprecision&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Severe hypoglycaemic episodes (1 or more episodes versus no episodes, parent- or adult-reported) over 24 months (CASCADE versus control)</strong></td>
<td>1 (Christie 2014)</td>
<td>137</td>
<td>140</td>
<td>OR 0.92&lt;sup&gt;a&lt;/sup&gt; (0.32 lower to 2.59 higher)</td>
<td>NA</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Very serious imprecision&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Mean number of episodes of diabetic ketoacidosis (per participant) over 12 months (family-centred group education versus conventional clinical care)</strong></td>
<td>1 (Murphy 2012)</td>
<td>158</td>
<td>147</td>
<td>NA</td>
<td>MD 0.01 higher</td>
<td>Moderate</td>
<td>RCT</td>
<td>Serious&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision&lt;sup&gt;6&lt;/sup&gt;</td>
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## Appendix K: GRADE tables

### Adherence to diabetes treatment (percentage of positive adherence) at 6 months (education versus standard care)

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Howe 2005)</td>
<td>21 28</td>
<td>NA</td>
<td>MD 4.9 higher (10.39 lower to 20.19 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Very serious imprecision</td>
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### Children and young people’s quality of life, impact, at 6 months, higher score indicates better quality of life (family-centred group education versus conventional clinical care)

<table>
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<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
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<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Murphy 2012)</td>
<td>158 147</td>
<td>NA</td>
<td>MD 0.7 higher (3.28 lower to 4.68 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
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### Children and young people’s quality of life, worry, at 6 months, higher score indicates better quality of life (family-centred group education versus conventional clinical care)

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
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<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
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<td>1 (Murphy 2012)</td>
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<td>NA</td>
<td>MD 3 lower (5.51 lower to 0.49 higher)</td>
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<td>RCT</td>
<td>Serious</td>
<td>No serious inconsistency</td>
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<td>Serious imprecision</td>
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### Children and young people’s quality of life, parental involvement, at 6 months, higher score indicates better quality of life (family-centred group education versus conventional clinical care)

<table>
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<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Murphy 2012)</td>
<td>158 147</td>
<td>NA</td>
<td>MD 0.3 lower (1.04 lower to 0.44 higher)</td>
<td>Low</td>
<td>RCT</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious imprecision</td>
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### Children and young people’s quality of life at 6 months (TeenCope versus Managing Diabetes)

<table>
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<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Grey 2013)</td>
<td>167 153</td>
<td>NA</td>
<td>MD 4.63 higher (2.18 lower to 7.08 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Very serious imprecision</td>
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### Children and young people’s quality of life at 12 months (TeenCope versus Managing Diabetes)

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<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Grey 2013)</td>
<td>167 153</td>
<td>NA</td>
<td>MD 3.62 higher (0.98 lower to 6.26 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
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### Children and young people’s quality of life at 12 months, parent-reported (care ambassador plus versus standard care)

<table>
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<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Katz 2014)</td>
<td>52 51</td>
<td>NA</td>
<td>MD 2.7 higher (1.93 lower to 7.33 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Very serious imprecision</td>
</tr>
<tr>
<td>Number of studies</td>
<td>Number of children and young people</td>
<td>Effect</td>
<td>Quality</td>
<td>Design</td>
<td>Limitation (risk of bias)</td>
<td>Inconsistency</td>
<td>Indirectness</td>
<td>Imprecision</td>
<td>Other considerations</td>
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<tr>
<td><strong>Structured education</strong></td>
<td><strong>Control</strong></td>
<td>Relative (95% confidence interval)</td>
<td>Absolute (95% confidence interval)</td>
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<tr>
<td><strong>Children and young people’s quality of life at 12 months, child- or young person-reported (care ambassador plus versus standard care)</strong></td>
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<td>1 (Katz 2014)</td>
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<td>51</td>
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<td>MD 0.1 lower (3.07 lower to 2.87 higher)</td>
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<td>RCT</td>
<td>Serious</td>
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<td>No serious indirectness</td>
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<td><strong>Children and young people’s quality of life at 12 months, parent-reported (care ambassador ultra versus standard care)</strong></td>
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<td>1 (Katz et al. 2014)</td>
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<td>MD 4.6 higher (0.06 lower to 9.26 higher)</td>
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<td>Serious</td>
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<td>No serious indirectness</td>
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<tr>
<td><strong>Children and young people’s quality of life at 12 months, child- or young person-reported (care ambassador ultra versus standard care)</strong></td>
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<td>1 (Katz 2014)</td>
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<td>51</td>
<td>NA</td>
<td>MD 0.8 lower (3.78 lower to 2.18 higher)</td>
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<td>RCT</td>
<td>Serious</td>
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<td>No serious indirectness</td>
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<tr>
<td><strong>Children and young person’s quality of life, general module, at 12 months follow-up, young person-reported (CASCADE versus control)</strong></td>
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<tr>
<td>1 (Christie 2014)</td>
<td>148</td>
<td>159</td>
<td>NA</td>
<td>MD 1.09 lower (3.15 lower to 0.03 higher)</td>
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<td>RCT</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
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</tr>
<tr>
<td>1 (Christie 2014)</td>
<td>148</td>
<td>159</td>
<td>NA</td>
<td>MD 0.62 higher (2.35 lower to 3.04 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>Children and young people’s quality of life at 24 months, parent-reported (care ambassador plus versus standard care)</strong></td>
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</tr>
<tr>
<td>1 (Katz 2014)</td>
<td>52</td>
<td>51</td>
<td>NA</td>
<td>MD 3.3 lower (7.74 lower to 1.14 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>Children and young people’s quality of life at 24 months, child- or young person-reported (care ambassador plus versus standard care)</strong></td>
<td></td>
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</tr>
<tr>
<td>1 (Katz 2014)</td>
<td>52</td>
<td>51</td>
<td>NA</td>
<td>MD 2.1 lower (5.46 lower to 1.26 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>Children and young people’s quality of life at 24 months, parent-reported (care ambassador ultra versus standard care)</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>1 (Katz 2014)</td>
<td>50</td>
<td>51</td>
<td>NA</td>
<td>MD 0.2 higher (4.22 lower to 4.62 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
</tr>
</tbody>
</table>
### Appendix K: GRADE tables

**Number of studies** | **Number of children and young people** | **Effect** | **Quality** | **Design** | **Limitation(s) (risk of bias)** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations**
--- | --- | --- | --- | --- | --- | --- | --- | --- | ---
**Structured education** | **Control** | **Relative (95% confidence interval)** | **Absolute (95% confidence interval)** | --- | --- | --- | --- | --- | ---

**Children and young person’s quality of life at 24 months, child- or young person-reported (care ambassador ultra versus standard care)**

1 (Katz 2014) | 50 | 51 | NA | MD 2.1 lower (5.44 lower to 1.24 higher) | Very low | RCT | Serious¹ | No serious inconsistency² | No serious indirectness³ | Very serious imprecision⁴ | None

**Children and young people’s quality of life, general module, at 24 months, young person-reported (CASCADE versus control)**

1 (Christie 2014) | 144 | 151 | NA | MD 0.33 lower (2.53 lower to 1.97 higher) | Very low | RCT | Serious¹ | No serious inconsistency² | No serious indirectness³ | Very serious imprecision⁴ | None

**Children and young person’s quality of life, diabetes module, at 24 months, young person-reported (CASCADE versus control)**

1 (Christie 2014) | 144 | 151 | NA | MD 0.02 lower (3.19 lower to 2.72 higher) | Very low | RCT | Serious¹ | No serious inconsistency² | No serious indirectness³ | Very serious imprecision⁴ | None

**Children and young people’s satisfaction with treatment or intervention, follow-up time not reported (TeenCope versus Managing Diabetes)**

1 (Grey 2013) | 167 | 153 | NA | MD 0.08 lower (0.22 lower to 0.06 higher) | Moderate | RCT | Serious¹ | No serious inconsistency² | No serious indirectness³ | No serious imprecision⁴ | None

---

CASCADE Child and Adult Structured Competencies Approach to Diabetes Education, MD mean difference, NA not applicable, OR odds ratio, RCT randomised controlled trial

1 Some risk of bias due to identification of several limitations and absence of reported information

2 Single-study analysis

3 No serious indirectness

4 Confidence interval crosses three zones related to precision (see ‘Methodology for 2015 update’)

5 Confidence interval crosses two zones related to precision (see ‘Methodology for 2015 update’)

6 Confidence interval is entirely within one zone related to precision (see ‘Methodology for 2015 update’)

7Unable to assess precision using data reported in the article, 12 months HbA1 self-management mean (SD) 8.1% ± 1.5% versus conventional mean (SD) 9.3 ± 1.7, P < 0.01; 24 months HbA1 self-management mean (SD) 8.2 ± 1.5 versus conventional mean (SD) 9.8 ± 2.4, P < 0.05

### K.3 Type 1 diabetes – behavioural interventions

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

**Table 29:** Evidence profile for effectiveness of motivational interviewing versus support visits in children and young people with type 1 diabetes

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### Table 30: Evidence profile for effectiveness of motivational interviewing skills training versus standard care in children and young people with type 1 diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HbA1c at 12 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Channon 2007)</td>
<td>35</td>
<td>25</td>
<td>NA</td>
<td>MD 0.5 lower (1.43 lower to 0.43 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious</td>
</tr>
</tbody>
</table>

### Depression (wellbeing questionnaire) at 12 months (lower scores indicate better outcomes)

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Channon 2007)</td>
<td>35</td>
<td>25</td>
<td>NA</td>
<td>MD 1.77 lower (2.80 lower to 0.74 lower)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
</tr>
</tbody>
</table>

### Health-related quality of life (Diabetes Quality of Life for Youths, impact) at 12 months (lower scores indicate better outcomes)

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Channon 2007)</td>
<td>35</td>
<td>25</td>
<td>NA</td>
<td>MD 10.56 lower (17.81 lower to 3.31 lower)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
</tr>
</tbody>
</table>

---

MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk, SMD standardised mean difference

1 No apparent risk of bias in the included study
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 Confidence intervals cross two zones related to precision (see 'Methodology for 2015 update')
5 No minimally important difference for wellbeing quality of life specified by GDG
6 No minimally important difference for diabetes quality of life for youths specified by GDG

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### Table 31: Evidence profile for effectiveness of motivational interviewing versus structured education in children and young people with type 1 diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Motivational interviewing</th>
<th>Structured education</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c at 6 months</td>
<td>1 (Wang 2010)</td>
<td>21</td>
<td>23</td>
<td>NA</td>
<td>Low</td>
<td>RCT</td>
<td>No serious risk of bias1</td>
<td>No serious inconsistency2</td>
<td>Serious3</td>
<td>Serious4</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MD 1.1 higher (0.27 higher to 1.93 higher)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression (CES-D) at 6 months (lower scores indicate better outcomes)</td>
<td>1 (Wang 2010)</td>
<td>21</td>
<td>23</td>
<td>NA</td>
<td>Moderate</td>
<td>RCT</td>
<td>No serious risk of bias1</td>
<td>No serious inconsistency2</td>
<td>Serious3</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MD 0.07 higher (1.53 lower to 1.67 higher)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health-related quality of life (EDIC-QoLY, lifestyle subscale) at 6 months (lower scores indicate better outcomes)</td>
<td>1 (Wang 2010)</td>
<td>21</td>
<td>23</td>
<td>NA</td>
<td>Moderate</td>
<td>RCT</td>
<td>No serious risk of bias1</td>
<td>No serious inconsistency2</td>
<td>Serious3</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MD 0.01 lower (1.61 lower to 1.59 higher)</td>
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<td></td>
</tr>
</tbody>
</table>

MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk, SMD standardised mean difference
1 No apparent risk of bias in the included study
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 Confidence intervals entirely within one zone related to precision (see ‘Methodology for 2015 update’)
5 No minimally important difference for Diabetes Quality of Life Questionnaire specified by the GDG

### Table 32: Evidence profile for effectiveness of cognitive behavioural therapy focused on quality of life versus standard care in children and young people with type 1 diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Cognitive behavioural therapy focused on quality of life</th>
<th>Standard care</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cognitive behavioural therapy focused on quality of life</td>
<td>Standard care</td>
<td>Relative (95% confidence interval)</td>
<td>Absolute (95% confidence interval)</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
## Appendix K: GRADE tables

### 1. Evidence profile for effectiveness of cognitive behavioural therapy not specifically focused on quality of life versus standard care in children and young people with type 1 diabetes

**Table 33:** Evidence profile for effectiveness of cognitive behavioural therapy not specifically focused on quality of life versus standard care in children and young people with type 1 diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation s (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adherence to diabetes management (measured with Diabetes Self-Management Profile, child domain) at 12 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Nansel 2007)</td>
<td>40</td>
<td>41</td>
<td>NA</td>
<td>MD 0.01 lower (0.07 lower to 0.05 higher)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>Health-related quality of life (measured with Diabetes Quality of Life for Youth, impact subscale) at 15 months (higher scores indicate better outcomes)</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Nansel 2007)</td>
<td>40</td>
<td>41</td>
<td>NA</td>
<td>MD 3.67 higher (3.1 higher to 4.24 higher)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
</tr>
</tbody>
</table>

MD mean difference, NA not applicable, RCT randomised controlled trial

1. No apparent risk of bias in the included study
### Table 34: Evidence profile for effectiveness of counselling versus standard care in children and young people with type 1 diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation s (risk of bias)</th>
<th>Inconsist ency</th>
<th>Indirectne ss</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c at 15 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Graue 2005)</td>
<td>45</td>
<td>38</td>
<td>NA</td>
<td>MD 0.44 lower (1.04 lower to 0.16 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious imprecision</td>
<td>None</td>
</tr>
<tr>
<td>Adverse events (severe hypoglycaemic episodes at 15 months)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Graue 2005)</td>
<td>7/45 (15.6%)</td>
<td>5/38 (13.2%)</td>
<td>RR 1.18 (0.41 to 3.42)</td>
<td>24 more per 1000 (from 78 fewer to 318 more)</td>
<td>Low</td>
<td>RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
<tr>
<td>Health-related quality of life (measured with Diabetes Quality of Life Questionnaire, impact subscale) at 15 months (higher scores indicates better outcomes)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Graue 2005)</td>
<td>45</td>
<td>38</td>
<td>NA</td>
<td>MD 4.3 higher (0.16 higher to 8.44 higher)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
</tbody>
</table>

**MD mean difference, NA not applicable, RCT randomised controlled trial**

1 Concern about performance bias, but this is unlikely to affect outcome
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 Confidence intervals cross two zones related to precision (see ‘Methodology for 2015 update’)
5 No minimally important difference for Diabetes Quality of Life for Youth specified by GDG
6 Confidence intervals cross three zones related to precision (see ‘Methodology for 2015 update’)

### Table 35: Evidence profile for effectiveness of multi-systemic therapy (including behavioural family systems therapy) versus standard care in children and young people with type 1 diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation s (risk of bias)</th>
<th>Inconsist ency</th>
<th>Indirectne ss</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c at 6 to 7 months’ follow-up</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Ellis 2004)</td>
<td>13</td>
<td>15</td>
<td>NR</td>
<td>MD 1.9 lower (4.24 lower to 0.44 higher)</td>
<td>Low</td>
<td>RCT</td>
<td>Serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious imprecision</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>64</td>
<td>63</td>
<td>NR</td>
<td>MD 0.77 lower</td>
<td>Moderate</td>
<td>RCT</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>Serious</td>
<td>None</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Multi-systemic therapy</th>
<th>Standard care</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation s (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Ellis 2005)</td>
<td></td>
<td></td>
<td>(1.35 to 0.19 lower)</td>
<td>risk of bias inconstistency</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**HbA1c at 6 months' follow-up**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Multi-systemic therapy</th>
<th>Standard care</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation s (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Wysocki 2001)</td>
<td>36</td>
<td>40</td>
<td>MD 0.4 lower (not reported)</td>
<td>Very low RCT</td>
<td>Very serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Very serious imprecision</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Wysocki 2007)</td>
<td>36</td>
<td>32</td>
<td>MD 0.7 lower (1.42 to 0.02 higher)</td>
<td>Low RCT</td>
<td>Serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious imprecision</td>
<td>None</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HbA1c at 12 months' follow-up**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Multi-systemic therapy</th>
<th>Standard care</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation s (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Wysocki 2001)</td>
<td>36</td>
<td>40</td>
<td>MD 0.2 lower (not reported)</td>
<td>Very low RCT</td>
<td>Very serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Very serious imprecision</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Wysocki 2007)</td>
<td>36</td>
<td>32</td>
<td>MD 0.8 lower (1.57 to 0.03 lower)</td>
<td>Low RCT</td>
<td>Serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious imprecision</td>
<td>None</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Adherence to diabetes treatment**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Multi-systemic therapy</th>
<th>Standard care</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation s (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Ellis 2004)</td>
<td>16</td>
<td>15</td>
<td>MD 0.17 higher (0.53 lower to 0.87 higher)</td>
<td>Low RCT</td>
<td>Serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious imprecision</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Ellis 2005)</td>
<td>64</td>
<td>63</td>
<td>MD 0.87 higher (0.46 to 1.28 higher)</td>
<td>Moderate RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious imprecision</td>
<td>None</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Adherence to diabetes (measured with self-care inventory) at 6 months' follow-up (higher scores indicate better adherence)**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Multi-systemic therapy</th>
<th>Standard care</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation s (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Wysocki 2001)</td>
<td>36</td>
<td>40</td>
<td>MD 4.4 higher (not reported)</td>
<td>Very low RCT</td>
<td>Very serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Very serious imprecision</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Wysocki 2007)</td>
<td>36</td>
<td>32</td>
<td>MD 6.6 higher (1.77 to 11.43 higher)</td>
<td>Moderate RCT</td>
<td>Serious risk of bias</td>
<td>No inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Adherence to diabetes (measured with self-care inventory) at 12 months' follow-up (higher scores indicate better adherence)**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Multi-systemic therapy</th>
<th>Standard care</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation s (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Wysocki 2001)</td>
<td>34</td>
<td>38</td>
<td>MD 8.7 higher (not reported)</td>
<td>Very low RCT</td>
<td>Very serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Very serious imprecision</td>
<td>None</td>
<td></td>
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</tr>
<tr>
<td>1 (Wysocki 2007)</td>
<td>36</td>
<td>32</td>
<td>MD 4 higher (1.08 lower to 9.08 higher)</td>
<td>Moderate RCT</td>
<td>Serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
MD mean difference, MID minimally important difference, NA not applicable, RCT randomised controlled trial
1 No apparent risk of bias in the included studies
2 No heterogeneity present (I^2 < 33%)
3 Population, intervention and outcome as specified in the review protocol
4 Confidence intervals cross two zones related to precision (see ‘Methodology for 2015 update’)
5 Concern about selection and performance bias, some participants received psychological support outside the study
6 Single-study analysis
7 Unable to assess precision using data reported in the article, 6 months HbA1c BFST mean (SD) 0.2% versus conventional treatment mean (SD) 0.6, not significant; 6 months self-care inventory BFST mean 1.8 versus conventional treatment mean -2.6, not significant; 12 months self-care inventory BFST mean 3.3 versus conventional treatment mean -5.4, not significant
8 Heterogeneity present (I^2 between 33% and 67%)
9 No minimally important difference for adherence specified by GDG
10 Confidence interval crosses one zone related to precision (MID -0.5 to +0.5; see ‘Methodology for 2015 update’)
11 Concern about attrition and detection bias
12 Concern about selection and performance bias (unclear reporting, lack of blinding)

**Table 36:** Evidence profile for effectiveness of family-based teamwork intervention versus standard care in children and young people with type 1 diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation s (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HbA1c at 12 months</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1 (Laffel 2003)</td>
<td>50/50 NA MD 0.5 lower (1.02 lower to 0.02 higher)</td>
<td>Moderate/RCT/No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious imprecision</td>
<td>None</td>
<td></td>
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</tr>
<tr>
<td>1 (Anderson 1999)</td>
<td>28/27 NA MD 0.2 higher (not reported)</td>
<td>Very low/RCT/Serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Very serious imprecision</td>
<td>None</td>
<td></td>
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<tr>
<td><strong>Health-related quality of life (PedsQL) at 12 months (higher scores indicate better outcomes)</strong></td>
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<tr>
<td>1 (Laffel 2003)</td>
<td>50/50 NA MD 0.4 higher (3.91 lower to 4.71 higher)</td>
<td>High/RCT/No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
<td></td>
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</tr>
</tbody>
</table>

MD mean difference, NA not applicable, RCT randomised controlled trial
1 Concern over performance bias possibly due to poor reporting, but this is unlikely to affect outcomes
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 Confidence intervals cross two zones related to precision (see ‘Methodology for 2015 update’)
5 Some risk of bias due to identification of several limitations and absence of reported information
6 Unable to assess precision using data reported in the article, 12 months HbA1c mean (SD) 8.9% ± 1.05% versus standard care mean (SD) 8.7 ± 0.63, not significant
7 No minimally important difference for PedsQL specified by GDG
### Table 37: Evidence profile for effectiveness of family-based behavioural intervention not specifically based on teamwork versus standard care in children and young people with type 1 diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Family-based behavioural intervention</th>
<th>Standard care</th>
<th>Effect</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HbA1c at 6 months</strong></td>
<td></td>
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<tr>
<td>1</td>
<td>(Wysocki 2001a)</td>
<td>37</td>
<td>40</td>
<td>NR</td>
<td>MD 0.1 lower (not reported)</td>
<td>Very low</td>
<td>RCT</td>
<td>Very serious risk of bias&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Very serious imprecision&lt;sup&gt;4&lt;/sup&gt;</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>(Wysocki 2007)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>36</td>
<td>32</td>
<td>NR</td>
<td>MD 0.3 lower (not reported)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious risk of bias&lt;sup&gt;4&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Very serious imprecision&lt;sup&gt;10&lt;/sup&gt;</td>
<td>None</td>
</tr>
<tr>
<td><strong>HbA1c at 12 months</strong></td>
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<tr>
<td>1</td>
<td>(Nansel 2009)</td>
<td>58</td>
<td>58</td>
<td>NR</td>
<td>MD 0.2 higher (0.38 lower to 0.78 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious risk of bias&lt;sup&gt;4&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Very serious imprecision&lt;sup&gt;7&lt;/sup&gt;</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>(Anderson 1999)b</td>
<td>30</td>
<td>27</td>
<td>NA</td>
<td>MD 0.0 (not reported)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious risk of bias&lt;sup&gt;4&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Very serious imprecision&lt;sup&gt;4&lt;/sup&gt;</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>(Wysocki 2001a)</td>
<td>36</td>
<td>38</td>
<td>NR</td>
<td>MD 0.8 lower (not reported)</td>
<td>Very low</td>
<td>RCT</td>
<td>Very serious risk of bias&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Very serious imprecision&lt;sup&gt;4&lt;/sup&gt;</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>(Wysocki 2007)</td>
<td>36</td>
<td>32</td>
<td>NR</td>
<td>MD 0.1 lower (not reported)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious risk of bias&lt;sup&gt;4&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Very serious imprecision&lt;sup&gt;10&lt;/sup&gt;</td>
<td>None</td>
</tr>
<tr>
<td><strong>Adherence to diabetes management (measured with Diabetes Self-Management Profile) at 12 months (higher scores indicate better outcomes)</strong></td>
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<tr>
<td>1</td>
<td>(Nansel 2009)</td>
<td>58</td>
<td>58</td>
<td>NR</td>
<td>MD 0.2 higher (3.45 lower to 3.85 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious risk of bias&lt;sup&gt;4&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Very serious imprecision&lt;sup&gt;7&lt;/sup&gt;</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>(Wysocki 2007)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>28</td>
<td>29</td>
<td>NR</td>
<td>MD 6.6 higher (1.37 to 11.83 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>Serious risk of bias&lt;sup&gt;4&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
<tr>
<td><strong>Adherence to diabetes (measured with Self-care inventory) at 6 months follow-up (higher scores indicate better adherence)</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1</td>
<td>(Wysocki 2001a)</td>
<td>37</td>
<td>40</td>
<td>NR</td>
<td>MD 2.3 higher (not reported)</td>
<td>Very low</td>
<td>RCT</td>
<td>Very serious risk of bias&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Very serious imprecision&lt;sup&gt;4&lt;/sup&gt;</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>(Wysocki 2007)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>36</td>
<td>32</td>
<td>NR</td>
<td>MD 4.2 higher (1.4 lower to 9.4 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious risk of bias&lt;sup&gt;4&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Very serious imprecision&lt;sup&gt;7&lt;/sup&gt;</td>
<td>None</td>
</tr>
<tr>
<td><strong>Adherence to diabetes (measured with Self-care inventory) at 12 months follow-up (higher scores indicate better adherence)</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1</td>
<td>(Wysocki)</td>
<td>36</td>
<td>38</td>
<td>NR</td>
<td>MD 4.2 higher (not reported)</td>
<td>Very low</td>
<td>RCT</td>
<td>Very serious</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Very serious imprecision</td>
<td>None</td>
</tr>
</tbody>
</table>
## Appendix K: GRADE tables

### Type 1 diabetes – multiple daily injections

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

**Table 38:** Evidence profile for effectiveness of multiple daily injections in improving glycaemic control in children and young people newly diagnosed with type 1 diabetes when compared with mixed insulin injections

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Abid 2001a)</td>
<td>36 (Wysocki 2007)</td>
<td>NR</td>
<td>MD 2 higher (3.26 lower to 7.26 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Very serious imprecision</td>
</tr>
</tbody>
</table>

MD mean difference NA not applicable, NR not reported, RCT randomised controlled trial

*a* Education plus support versus conventional treatment (standard care)

*b* Attention control versus standard care

1. Concern about selection and performance bias, some participants received psychological support outside the study

2. Single-study analysis

3. Population, intervention and outcome as specified in the review protocol

4. Unable to assess precision using data reported in the article, 6 months HbA1c education support mean 0.5% versus conventional therapy mean 0.6%, not significant; 12 months HbA1c education support mean 0.3% versus conventional therapy mean 1.1%, not significant; 6 months SCI education support mean -0.3 versus conventional therapy mean -2.6, not significant; 12 months SCI education support mean -1.2 versus conventional therapy mean -5.4, not significant

5. Concern about performance bias, but this is unlikely to affect outcomes

6. Serious heterogeneity present (I²-squared > 67%)

7. Confidence intervals cross two zones related to precision (see ‘Methodology for 2015 update’)

8. Some risk of bias due to identification of several limitations and absence of reported information

9. No minimally important difference for Diabetes Self-Management Profile specified by GDG

10. Unable to assess precision using data reported in the article, 6 months post-intervention HbA1c education support mean 9.3% ± 1.4% versus standard care mean 9.6% ± 1.6; 12 months post-intervention HbA1c education support mean 9.5% ± 1.5% versus standard care mean 9.6% ± 1.7;
<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitation(s) (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011)</td>
<td>(changed from 9.1 at baseline to 7.9 at 1 year)</td>
<td>CI NC</td>
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</tr>
<tr>
<td>1 (Adhikari 2009)</td>
<td>212 (changed from 11.4 ± 1.9 at baseline to 7.5 ± 1.6 at 1 year)</td>
<td>NA</td>
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<tr>
<td><strong>HbA1c (%) change from baseline after 9 months</strong></td>
<td>1 (Adhikari 2009)</td>
<td>212 (changed from 11.4 ± 1.9 at baseline to 7.2 ± 1.7 at 9 months)</td>
<td>247 (changed from 11.6 ± 1.8 at baseline to 7.9 ± 1.4 at 9 months)</td>
<td>NA</td>
<td>MD 0.7 lower (0.98 lower to 0.42 lower)</td>
<td>Very low</td>
<td>Retrospective cohort study</td>
<td>Serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
</tr>
<tr>
<td><strong>HbA1c (%) change from baseline after 6 months</strong></td>
<td>1 (Adhikari 2009)</td>
<td>212 (changed from 11.4 ± 1.9 at baseline to 6.6 ± 1.4 at 6 months)</td>
<td>247 (changed from 11.6 ± 1.8 at baseline to 7.3 ± 1.4 at 6 months)</td>
<td>NA</td>
<td>MD 0.7 lower (1.96 lower to 0.44 lower)</td>
<td>Very low</td>
<td>Retrospective cohort study</td>
<td>Serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>Serious imprecision</td>
</tr>
<tr>
<td><strong>BMI standard deviation score (SDS) change from baseline after 1 year</strong></td>
<td>1 (Abid 2011)</td>
<td>29 (changed from 0.28 at baseline to 0.56 at 1 year)</td>
<td>88 (changed from 0.41 at baseline to 0.9 at 1 year)</td>
<td>NA</td>
<td>MD 0.34 lower CI NC</td>
<td>Very low</td>
<td>Retrospective cohort study</td>
<td>Serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>Serious imprecision</td>
</tr>
</tbody>
</table>

*BMI body mass index, CI confidence interval, MD mean difference, NA not applicable, NC not calculable*

1 Multiple daily injections offered only to older children and young people
2 Comparison is between twice-daily injections and multiple daily injections
3 No estimates of precision reported
4 Participants allocated to treatment based on family or physician preference and high drop-out rate at 12 months reported in both thrice-daily injection cohort (44%) and multiple daily injections cohort (25%)
5 Comparison is between thrice-daily injections and multiple daily injections
6 Range of MD in HbA1c crosses two zones related to precision (see ‘Methodology for 2015 update’)
7 Participants allocated to treatment based on family or physician preference and high drop-out rate at 9 months in both thrice-daily injection cohort (36%) and multiple daily injections cohort (31%)
8 Participants allocated to treatment based on family or physician preference and high drop-out rate at 6 months in both thrice-daily injection cohort (26%) and multiple daily injections cohort (27%)
Table 39: Evidence profile for effectiveness of multiple daily injections in improving glycaemic control in children and young people with type 1 diabetes of at least 1 year’s duration when compared with mixed insulin injections

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Fewer than 4 injections per day</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HbA1c (%) change from baseline after 2 years</strong></td>
<td></td>
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</tr>
<tr>
<td>1 (Al-Fifi 2003)</td>
<td>24 (changed from 9.34 ± 1.55 at baseline to 9.49 ± 1.55 at 2 years)</td>
<td>57 (changed from 9.37 ± 1.8 at baseline to 9.59 ± 1.59 at 2 years)</td>
<td>NA</td>
<td>MD 0.1 lower (0.86 lower to 0.66 higher)</td>
<td>Very low</td>
<td>Retrospective cohort study</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>Serious indirectness s1,3</td>
<td>Serious imprecision s4</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td><strong>HbA1c (%) change from baseline after 1 year</strong></td>
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</tr>
<tr>
<td>1 (Al-Fifi 2003)</td>
<td>24 (changed from 9.34 ± 1.55 at baseline to 9.2 ± 1.7 at 1 year)</td>
<td>57 (changed from 9.37 ± 1.8 at baseline to 9.46 ± 1.61 at 1 year)</td>
<td>NA</td>
<td>MD 0.26 lower (1.05 lower to 0.53 higher)</td>
<td>Very low</td>
<td>Retrospective cohort study</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>Serious indirectness s1,3</td>
<td>Serious imprecision s4</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>1 (Abid 2011)</td>
<td>36 (9.2 at 1 year)</td>
<td>36 (8.9 at treatment switch)</td>
<td>NA</td>
<td>MD 0.3 higher CI NC</td>
<td>Very low</td>
<td>Interrupted time series</td>
<td>Serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness s1</td>
<td>Serious imprecision s4</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>1 (Adhikari 2009)</td>
<td>118 (8.5 ± 1.6 at 1 year)</td>
<td>198 (8.4 ± 1.5 at treatment switch)</td>
<td>NA</td>
<td>MD 0.1 higher (0.25 lower to 0.45 higher)</td>
<td>Very low</td>
<td>Interrupted time series</td>
<td>Serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness s1</td>
<td>No serious imprecision</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>1 (Alemzadeh 2003)</td>
<td>44 (8.1 ± 1.0 at 1 year)</td>
<td>44 (9.2 ± 1.1 at treatment switch)</td>
<td>NA</td>
<td>MD 1.1 lower (1.55 lower to 0.65 lower)</td>
<td>Very low</td>
<td>Interrupted time series</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness s1</td>
<td>No serious imprecision</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>1 (Karaguzel 2005)</td>
<td>25 (8.2 ± 1.5 at 1 year)</td>
<td>25 (9.3 ± 2.5 at treatment switch)</td>
<td>NA</td>
<td>MD 1.1 lower (2.27 lower to 0.07 higher)</td>
<td>Very low</td>
<td>Interrupted time series</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>Serious indirectness s1,10,11</td>
<td>Serious imprecision s4</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td><strong>HbA1c (%) change from baseline after 9 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Adhikari 2009)</td>
<td>129 (8.5 ± 1.6 at 9 months)</td>
<td>198 (8.4 ± 1.5 at treatment switch)</td>
<td>NA</td>
<td>MD 0.1 higher (0.24 lower to 0.44 higher)</td>
<td>Very low</td>
<td>Interrupted time series</td>
<td>Serious risk of bias</td>
<td>NA</td>
<td>no serious indirectness s1</td>
<td>No serious imprecision</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td><strong>HbA1c (%) change from baseline after 6 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Adhikari 2009)</td>
<td>142 (8.3 ± 1.4 at 6 months)</td>
<td>198 (8.4 ± 1.5 at treatment switch)</td>
<td>NA</td>
<td>MD 0.1 lower (0.42 lower to 0.22 higher)</td>
<td>Very low</td>
<td>Interrupted time series</td>
<td>Serious risk of bias</td>
<td>NA</td>
<td>no serious indirectness s1</td>
<td>No serious imprecision</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>
## Diagnosis and management of type 1 diabetes in children and young people

### Appendix K: GRADE tables

#### Number of children and young people

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Multiple daily injections</th>
<th>Fewer than 4 injections per day</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Bin-Abbas 2007)</td>
<td>10 (8.4 ± 0.7 at endpoint)</td>
<td>10 (8.6 ± 1.2 at treatment switch)</td>
<td>NA</td>
<td>MO 0.2 lower (1.12 lower to 0.72 higher)</td>
<td>Very low</td>
<td>Interrupted time series</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>Serious indirectness 2,4</td>
<td>Serious imprecision 4</td>
<td>None</td>
</tr>
<tr>
<td>1 (Bin-Abbas 2006)</td>
<td>10 (8.6 ± 0.5 at endpoint)</td>
<td>10 (10.6 ± 1.2 at treatment switch)</td>
<td>NA</td>
<td>MO 2.0 lower (2.86 lower to 1.14 lower)</td>
<td>Very low</td>
<td>Interrupted time series</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>Serious indirectness 3,16,17</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
<tr>
<td>1 (Karaguzel 2005)</td>
<td>25 (8.3 ± 1.6 at 6 months)</td>
<td>25 (9.3 ± 2.5 at treatment switch)</td>
<td>NA</td>
<td>MO 1.0 lower (2.19 lower to 0.19 higher)</td>
<td>Very low</td>
<td>Interrupted time series</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>Serious indirectness 3,10,11</td>
<td>Serious imprecision 4</td>
<td>None</td>
</tr>
</tbody>
</table>

#### HbA1c (%) during study period (cross-sectional observational data)

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Alexander 2001)</td>
<td>30 (9.79 ± 1.77)</td>
<td>1573 (9.04 ± 1.53)</td>
<td>NA</td>
<td>MO 0.75 higher (0.20 higher to 1.30 higher)</td>
<td>Very low</td>
<td>Cross-sectional survey</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>Serious indirectness 16,19,20</td>
<td>Serious imprecision 4</td>
</tr>
<tr>
<td>1 (de Beaufort 2007)</td>
<td>926 (8.2 ± 0.0)</td>
<td>524 (8.2 ± 0.1)</td>
<td>NA</td>
<td>MO 0.0 (0.01 lower to 0.01 higher)</td>
<td>Low</td>
<td>Cross-sectional survey</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness 2</td>
<td>No serious imprecision</td>
</tr>
<tr>
<td>1 (Dorchy 1997)</td>
<td>15 (6.6 ± 1.1)</td>
<td>129 (6.6 ± 1.2)</td>
<td>NA</td>
<td>MO 0.0 (0.64 lower to 0.64 higher)</td>
<td>Very low</td>
<td>Cross-sectional survey</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>Serious indirectness 3</td>
<td>Serious imprecision 4</td>
</tr>
<tr>
<td>1 (Vanelli 2005)</td>
<td>1911 (8.7 ± 0.2)</td>
<td>1608 (8.3 ± 0.1)</td>
<td>NA</td>
<td>MO 0.4 higher (0.39 higher to 0.41 higher)</td>
<td>Low</td>
<td>Cross-sectional survey</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness 20</td>
<td>No serious imprecision</td>
</tr>
</tbody>
</table>

#### Proportion achieving ADA age-specific HbA1c target (cross-sectional observational data)

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Mohammad 2012)</td>
<td>31/42 (73.8%)</td>
<td>192/373 (51.5%)</td>
<td>RR 1.43 (1.17 to 1.76)</td>
<td>211 more per 1000 (from 88 more to 391 more)</td>
<td>Very low</td>
<td>Cross-sectional survey</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness 25</td>
<td>Serious imprecision 6</td>
</tr>
</tbody>
</table>

#### Number of severe hypoglycaemic episodes (ISPAD 2000 grades 2-3 or ISPAD 2009 ‘severe’)

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Al-Fifi 2003)</td>
<td>4/24 (16.7%)</td>
<td>16/57 (28.1%)</td>
<td>RR 0.59 (0.22 to 1.59)</td>
<td>115 fewer per 1000 (from 219 fewer to 166 more)</td>
<td>Very low</td>
<td>Retrospective cohort study</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>Serious indirectness 3</td>
<td>Very serious imprecision 4</td>
</tr>
<tr>
<td>1 (Alemzadeh 2003)</td>
<td>7/44 (15.9%)</td>
<td>17/44 (38.6%)</td>
<td>RR 0.41 (0.19 to 0.89)</td>
<td>228 fewer per 1000 (from 43 fewer to 313 fewer)</td>
<td>Very low</td>
<td>Interrupted time series</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness 3</td>
<td>Serious imprecision 4</td>
</tr>
</tbody>
</table>

#### Number of episodes of DKA

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Al-Fifi 2003)</td>
<td>6/24 (25%)</td>
<td>17/57 (29.8%)</td>
<td>RR 0.84 (0.38 to 1.86)</td>
<td>48 fewer per 1000 (from 0)</td>
<td>Very low</td>
<td>Retrospective study</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>Very serious imprecision 10</td>
</tr>
</tbody>
</table>
## Appendix K: GRADE tables

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Alemzadeh 2003)</td>
<td>Multiple daily injections 0/44 (0%) Fewer than 4 injections per day 2/44 (4.5%)</td>
<td>Relative (95% confidence interval) 185 fewer to 256 more</td>
<td>cohort study</td>
<td>Very low</td>
<td>Interrupted time series</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>Very serious imprecision</td>
<td></td>
</tr>
<tr>
<td>1 (Bin Abbas 2007)</td>
<td>0/10 (0%) 0/10 (0%)</td>
<td>NC</td>
<td>Very low</td>
<td>Interrupted time series</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>Serious indirectness</td>
<td>NA</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>1 (Bin Abbas 2006)</td>
<td>0/10 (0%) 0/10 (0%)</td>
<td>NC</td>
<td>Very low</td>
<td>Interrupted time series</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>Serious indirectness</td>
<td>NA</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>

ADA American Diabetes Association, CI confidence interval, DKA diabetic ketoacidosis, ISPAD International Society for Pediatric and Adolescent Diabetes, MD mean difference, NA not applicable, NC not calculable, RR relative risk

1. Participants matched for age, sex, body mass index (BMI), insulin dose and compliance
2. All participants enrolled into adolescent education programme at baseline
3. Comparison is between twice-daily injections and multiple daily injections
4. Range of MD in HbA1c crosses two zones related to precision (see 'Methodology for 2015 update')
5. Multiple daily injections offered only to older children and young people
6. No estimates of precision reported
7. Participants allocated to treatment according to family or physician preference and high drop-out rate at 12 months (40%)
8. Comparison is between thrice-daily injections and multiple daily injections
9. Comparison is between 2-3 injections per day and multiple daily injections
10. Length of time on twice-daily injections not reported
11. Participants had poor or moderate diabetes control before treatment switch
12. Participants allocated to treatment according to family or physician preference and high drop-out rate at 9 months (35%)
13. Participants allocated to treatment according to family or physician preference and high drop-out rate at 6 months (28%)
14. HbA1c measured at different time points before and after treatment switch; mean during 3 months before switch and in last month after switch (6-10 months after switch)
15. Participants had poor diabetes control (HbA1c > 8.5%) and recurrent daytime and nocturnal hypoglycaemia (> 4 episodes per month) before treatment switch
16. HbA1c measured at different time points before and after treatment switch; mean during 6 months before switch, time point/span of measurement after switch not reported; follow-up 6-9 months
17. Participants had poor diabetes control (HbA1c > 8.5%) and recurrent daytime and nocturnal hypoglycaemia (> 8 episodes per month) before treatment switch
18. Study had only 2% participants using multiple daily injections
19. Duration of diabetes of participants was < 6 months to > 5 years
20. Participants had 1, 2 or 3 injections per day or multiple daily injections
21. Study had 11% loss to follow-up, duration of diabetes longer in those providing HbA1c data
22. Participants had 2 or 3 injections per day or a basal-bolus regimen (multiple daily injections)
23. Study had only 10% participants using multiple daily injections and included children and young people with duration of diabetes 5 months to 15 years
24. ADA age-specific targets: age < 6 years, HbA1c 7.5 - 8.5%; age 6-12 years, HbA1c ≤ 8%; age 13-18 years, HbA1c ≤ 7.5%
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25 Participants had multiple daily injections, twice-daily injections, or a regimen of twice-daily intermediate-acting insulin plus 1 or more injections of regular-acting insulin (classified as < 4 injections per day)

26 RR crosses two zones related to precision (see ‘Methodology for 2015 update’)

27 Severe hypoglycaemia defined in study methods as hypoglycaemia requiring assistance or leading to coma or convulsion but figures reported are for admissions for hypoglycaemia over 2 year study period

28 RR crosses three zones related to precision (see ‘Methodology for 2015 update’)

29 Severe hypoglycaemia defined as episodes of blood glucose < 2.8 mmol/l with unconsciousness and with or without seizure

30 Outcome defined as number of admissions for DKA and length of follow-up 2 years

31 Length of follow-up 1 year

32 RR calculated by adding 0.5 to events in each arm

33 Frequency of DKA episodes measured at different times; 3 months before switch and 6-10 months after treatment switch

34 Length of follow-up 6 months

35 Frequency of DKA episodes may be measured at different times before and after treatment switch; follow-up 6-9 months after treatment switch and not reported before treatment switch

K.5 Type 1 diabetes – HbA1c targets

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

There are no evidence profiles for this review question because no studies were identified for inclusion.

K.6 Type 1 diabetes – blood glucose targets

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

There are no evidence profiles for this review question because no studies were identified for inclusion.

K.7 Type 1 diabetes – blood glucose monitoring

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

Table 40: Evidence profile for frequency of self-monitoring of blood glucose in children and young people with type 1 diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Relative effect</th>
<th>Absolute effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistenc y</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Association between frequency of SMBG and HbA1c, reported as coefficients of associations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Diagnosis and management of type 1 diabetes in children and young people

#### Appendix K: GRADE tables

**Number of studies** | **Number of children and young people** | **Relative effect** | **Absolute effect** | **Quality** | **Design** | **Limitations (risk of bias)** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations**
---|---|---|---|---|---|---|---|---|---|---
5 (de Beaufort 2013; Haller 2004; Ingerski 2011; Levine 2001; Moreland 2004) | 4,794 | NA | Increased frequency of SMBG was inversely correlated with HbA1c independent of other variables \( r = -0.17 \) (\( p < 0.0001 \)) to \( r = -0.45 \) (\( p < 0.001 \)) | Low | Observation al | No serious risk of bias\(^1\) | Not calculated\(^2\) | No serious indirectness\(^3\) | No serious imprecision\(^4\) | None

**Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 6 to 13 years, SMBG performed 3-4 times per day versus 0-2 times per day**

| 1 (Campbell 2014) | 3,272 | Adjusted OR 1.7 (0.7 to 3.9) | NA | Very Low | Observation al | No serious risk of bias\(^1\) | Not calculated\(^2\) | No serious indirectness\(^3\) | No serious imprecision\(^4\) | None

**Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 1 to 6 years, SMBG performed 3-4 times per day versus 0-2 times per day**

| 1 (Campbell 2014) | 3,272 | Adjusted OR 2.3 (1.0 to 5.1) | NA | Low | Observation al | No serious risk of bias\(^1\) | Not calculated\(^2\) | No serious indirectness\(^3\) | Serious imprecision\(^6\) | None

**Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 1 to 6 years, SMBG performed 5-9 times per day versus 0-2 times per day**

| 1 (Campbell 2014) | 3,272 | Adjusted OR 7.0 (2.9 to 17.0) | NA | Low | Observation al | No serious risk of bias\(^1\) | Not calculated\(^2\) | No serious indirectness\(^3\) | No serious imprecision\(^4\) | None

**Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 1 to 6 years, SMBG performed 3-4 times per day**

| 1 (Miller 2013) | NA | NA | Unadjusted mean HbA1c level 8.5% | Low | Observation al | No serious risk of bias\(^1\) | Not calculated\(^2\) | No serious indirectness\(^3\) | No serious imprecision\(^4\) | None

**Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 1 to 6 years, SMBG performed 5-6 times per day**

| 1 (Miller 2013) | NA | NA | Unadjusted mean HbA1c level 8.4% | Low | Observation al | No serious risk of bias\(^1\) | Not calculated\(^2\) | No serious indirectness\(^3\) | No serious imprecision\(^4\) | None

**Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 1 to 6 years, SMBG performed 7-9 times per day**

| 1 (Miller 2013) | NA | NA | Unadjusted mean HbA1c level 8.1% | Low | Observation al | No serious risk of bias\(^1\) | Not calculated\(^2\) | No serious indirectness\(^3\) | No serious imprecision\(^4\) | None

**Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 1 to 6 years, SMBG performed 10 times per day**

| 1 (Miller 2013) | NA | NA | Unadjusted mean HbA1c level 7.8% | Low | Observation al | No serious risk of bias\(^1\) | Not calculated\(^2\) | No serious indirectness\(^3\) | No serious imprecision\(^4\) | None

**Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 6 to 13 years, SMBG performed 3-4 times per day**

| 1 (Miller 2013) | NA | NA | Unadjusted mean HbA1c level 8.7% | Low | Observation al | No serious risk of bias\(^1\) | Not calculated\(^2\) | No serious indirectness\(^3\) | No serious imprecision\(^4\) | None

**Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 6 to 13 years, SMBG performed 5-6 times per day**

| 1 (Miller 2013) | NA | NA | Unadjusted | Low | Observation | No serious | Not | No serious | No serious | None

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### Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 6 to 13 years, SMBG performed ≥ 10 times per day

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Relative effect</th>
<th>Absolute effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistenc y</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Miller 2013)</td>
<td>NA</td>
<td>NA</td>
<td>Unadjusted mean HbA1c level 8.5%</td>
<td>Low</td>
<td>Observation al</td>
<td>No serious risk of bias</td>
<td>Not calculated</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
</tbody>
</table>

### Association between frequency of SMBG and HbA1c, reported as unadjusted mean HbA1c level among children aged 6 to 13 years, SMBG performed 0-3 times per day

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Relative effect</th>
<th>Absolute effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistenc y</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Miller 2013)</td>
<td>NA</td>
<td>NA</td>
<td>Unadjusted mean HbA1c level 10.3%</td>
<td>Low</td>
<td>Observation al</td>
<td>No serious risk of bias</td>
<td>Not calculated</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
</tbody>
</table>

### Change in HbA1c for 1 additional test per day

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Relative effect</th>
<th>Absolute effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistenc y</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>31,083</td>
<td>NA</td>
<td>HbA1c decreased by between 0.056 percentage points and 0.4 percentage points for each additional test</td>
<td>Low</td>
<td>Observation al</td>
<td>No serious risk of bias</td>
<td>Not calculated</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
</tbody>
</table>

### Association between frequency of SMBG and severe hypoglycaemic episodes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Relative effect</th>
<th>Absolute effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistenc y</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Ziegler 2011)</td>
<td>26,723</td>
<td>NA</td>
<td>2.38 (± 0.54) additional events per 100 patient years for every 1 additional test</td>
<td>Low</td>
<td>Observation al</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
</tbody>
</table>

CI confidence interval, MID minimally important difference, NA not applicable, OR odds ratio, r correlation coefficient, SMBG self-monitoring of blood glucose
1 No apparent risk of bias in the included studies
2 No calculation of inconsistency performed
3 Population, intervention and outcome as specified in the review protocol
4 No MID specified by the GDG
5 Confidence interval crosses three zones related to precision (see ‘Methodology for 2015 update’)
6 Confidence interval crosses two zones related to precision (see ‘Methodology for 2015 update’)
7 Single-study analysis

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

Table 41: Evidence profile for effectiveness of self-monitoring of blood glucose against continuous glucose monitoring systems in children and young people diagnosed with type 1 diabetes at least 1 year before enrolment to the study

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Change in HbA1c level – at 6 months (real-time CGMS)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (Langendam; 2012; Mauras 2012)</td>
<td>146</td>
<td>152</td>
<td>NA</td>
<td>MD 0.09 lower in CGMS group (0.24 lower to 0.07 higher)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias¹</td>
<td>No serious inconsistency²</td>
<td>No serious indirectness³</td>
<td>No serious imprecision⁴</td>
</tr>
<tr>
<td><strong>Change in HbA1c level - at 6 months (retrospective CGMS)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (Bukarara-Radujkovic 2011; Langendam 2012)</td>
<td>59</td>
<td>57</td>
<td>NA</td>
<td>MD 0.3 lower (0.67 lower to 0.07 higher)</td>
<td>Low</td>
<td>RCT</td>
<td>Serious5</td>
<td>No serious inconsistency⁶</td>
<td>No serious indirectness⁷</td>
<td>Serious⁸</td>
</tr>
<tr>
<td><strong>Mean blood glucose level – at 6 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Bukarara-Radujkovic 2011)</td>
<td>40</td>
<td>40</td>
<td>NA</td>
<td>MD 0.7 lower (1.56 lower to 0.16 higher)</td>
<td>Very low</td>
<td>RCT</td>
<td>Serious8</td>
<td>No serious inconsistency⁹</td>
<td>No serious indirectness¹⁰</td>
<td>Very serious¹⁰</td>
</tr>
<tr>
<td><strong>Severe hypoglycaemic episodes – at 6 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (Langendam 2012; Mauras 2012)</td>
<td>8/148 (5.4%)</td>
<td>13/146 (8.9%)</td>
<td>RR 0.63 (0.27 to 1.46)</td>
<td>33 fewer per 1000 (from 65 fewer to 41 more)</td>
<td>Low</td>
<td>RCT</td>
<td>No serious risk of bias¹</td>
<td>No serious inconsistency⁶</td>
<td>No serious indirectness⁷</td>
<td>No serious imprecision⁴</td>
</tr>
<tr>
<td><strong>Parental satisfaction with the intervention – change over 6 months (scale 1 to 3; higher score means greater satisfaction)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Mauras 2012)</td>
<td>69</td>
<td>68</td>
<td>NA</td>
<td>MD 0.3 higher (0.21 to 0.39)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision⁴</td>
</tr>
</tbody>
</table>
### Table 42: Evidence profile for effectiveness of self-monitoring of blood glucose against continuous glucose monitoring systems in children and young people recently diagnosed with type 1 diabetes (less than 1 year before enrolment to the study)

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Change in HbA1c level - at 6 months (real-time CGMS)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Langendam 2012)</td>
<td>76</td>
<td>78</td>
<td>NA</td>
<td>MD 0.10 lower in CGMS group (0.46 lower to 0.66 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious*</td>
<td>None</td>
</tr>
<tr>
<td><strong>Change in HbA1c level - at 12 months (real-time CGMS)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Langendam 2012)</td>
<td>76</td>
<td>78</td>
<td>NA</td>
<td>MD 0.10 higher (0.46 lower to 0.66 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious*</td>
<td>None</td>
</tr>
<tr>
<td><strong>Severe hypoglycaemic episodes – at 12 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Langendam 2012)</td>
<td>0/76 (0%)</td>
<td>4/78 (5.1%)</td>
<td>RR 0.11 (0.01 to 2.08)</td>
<td>46 fewer per 1000 (from 51 fewer to 55 more)</td>
<td>Low</td>
<td>RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Very serious*</td>
<td>None</td>
</tr>
</tbody>
</table>

CGMS continuous glucose monitoring system, CI confidence interval, MD mean difference, NA not applicable, QoL quality of life, RCT randomised controlled trial, RR relative risk, SMBG self-monitoring of blood glucose, SMD standardised mean difference

1 No apparent risk of bias in the included studies
2 Heterogeneity amongst the studies was low (I^2 = 26%)
3 Population, intervention and outcome as specified in the review protocol
4 Confidence interval is entirely within one zone related to precision (see 'Methodology for 2015 update')
5 In one of the included studies methods of randomisation and allocation concealment were unclear and the groups were not altogether comparable at baseline
6 No heterogeneity found between studies (I^2 = 0%)
7 Confidence interval crosses two zones related to precision (see 'Methodology for 2015 update')
8 Methods of randomisation and allocation concealment were unclear and the groups were not altogether comparable at baseline
9 Single-study analysis
10 Confidence interval crosses three zones related to precision (see 'Methodology for 2015 update')
11 There were statistically significant differences between the intervention and control groups at baseline in terms of age (p=0.016), diabetes duration (p=0.013), insulin dose (p=0.005) and mean blood glucose (p=0.031)
### Appendix K: GRADE tables

**Number of studies** | **Number of children and young people** | **Effect** | **Quality** | **Design** | **Limitations (risk of bias)** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations**
--- | --- | --- | --- | --- | --- | --- | --- | --- | ---
1 (Langendam 2012) | 76 | 78 | NA | MD 0.5 lower (7.64 lower to 6.64 higher) | High | RCT | No serious risk of bias \(^1\) | No serious inconsistency \(^2\) | No serious indirectness \(^3\) | No serious imprecision \(^6\) | None

#### Quality of life of parents – at 12 months (scale 1 to 100; higher score means better quality of life)

1 (Langendam 2012) | 76 | 78 | NA | MD 1.9 higher (4.13 lower to 7.93 higher) | High | RCT | No serious risk of bias \(^1\) | No serious inconsistency \(^2\) | No serious indirectness \(^3\) | No serious imprecision \(^6\) | None

**CGMS** continuous glucose monitoring system, **CI** confidence interval, **MD** mean difference, **NA** not applicable, **RCT** randomised controlled trial, **RR** relative risk, **SMBG** self-monitoring of blood glucose, **SMD** standardised mean difference

1. No apparent risk of bias in the included studies
2. Single-study analysis
3. Population, intervention and outcome as specified in the review protocol
4. Confidence interval crosses two zones related to precision (see ‘Methodology for 2015 update’)
5. Confidence interval crosses three zones related to precision (see ‘Methodology for 2015 update’)
6. Confidence interval is entirely within one zone related to precision (see ‘Methodology for 2015 update’)

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

**Table 43: Evidence profile for effectiveness of continuous glucose monitoring performed in real-time compared with continuous glucose monitoring performed intermittently in children and young people with type 1 diabetes**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HbA1c value (% - at 6 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| 1 (Battelino 2011) | 27 (changed from 6.92 ± 0.56 at baseline to 6.92 ± 0.98 at 6 months) | 26 (changed from 6.91 ± 0.67 at baseline to 7.15 ± 0.98 at 6 months) | NA | MD 0.23 lower in the real-time CGMS group (0.76 lower to 0.3 higher) | Low | RCT | No serious risk of bias \(^1\) | No serious inconsistency \(^2\) | Serious indirectness \(^3\) | Serious imprecision \(^6\) | None

**Severe hypoglycaemic episodes – at 6 months**

1 (Battelino 2011) | 0/27 (0%) | 0/26 (0%) | NC5 | NA | Moderate | RCT | No serious risk of bias \(^1\) | No serious inconsistency \(^2\) | Serious indirectness \(^3\) | NA | None

**CGMS** continuous glucose monitoring system, **MD** mean difference, **NA** not applicable, **NC** not calculable, **RCT** randomised controlled trial, **RR** relative risk,
K.8 Type 1 diabetes – blood ketone monitoring

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

Table 44: Evidence profile for effectiveness of blood ketone monitoring compared with urine ketone monitoring for the prevention of diabetic ketoacidosis

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital admission rates: incidence of acute complications as a proxy for admission rates</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Laffel 2005)</td>
<td>62</td>
<td>61</td>
<td>NA</td>
<td>MD 0.37 lower (0.74 lower to 0.00)</td>
<td>Low</td>
<td>RCT</td>
<td>Serious¹</td>
<td>No serious inconsistency²</td>
<td>Serious indirectness³</td>
<td>1</td>
</tr>
<tr>
<td>Adherence to ketone monitoring: percentage of time ketones checked on sick days</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Laffel 2005)</td>
<td>62</td>
<td>61</td>
<td>NA</td>
<td>90.8% of time for blood ketone monitoring and 61.3% of time for urine ketone monitoring*</td>
<td>Low</td>
<td>RCT</td>
<td>Serious¹</td>
<td>No serious inconsistency²</td>
<td>Serious indirectness³</td>
<td>None</td>
</tr>
</tbody>
</table>

NA not applicable, MD mean difference, RCT randomised controlled trial

1 Several limitations identified which amounted to a serious risk of bias but these did not negate the study findings
2 Single-study analysis
3 People aged 18 years and over were included in the study but this did not negate the study findings
4 The guideline development group (GDG) did not set a minimally important difference (MID) for this outcome
5 The study authors reported statistical significance of p < 0.001
**K.9 Type 1 diabetes – dietary advice**

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

**Table 45: Evidence profile for effectiveness of dietary advice based on carbohydrate counting in maintaining glycaemic control in children and young people with type 1 diabetes**

<table>
<thead>
<tr>
<th>Number of children and young people</th>
<th>Carbohydrate counting</th>
<th>Treatment as usual</th>
<th>Effect</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HbA1c value (%) - at 12 months</strong></td>
<td>2 (Enander 2012; Goksen 2014)</td>
<td>78</td>
<td>46</td>
<td>NA</td>
<td>WMD 0.38 lower (0.77 lower to 0.01 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>Serious risk of bias¹</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious*</td>
</tr>
<tr>
<td><strong>HbA1c value (%) - at 24 months</strong></td>
<td>1 (Goksen 2014)</td>
<td>52</td>
<td>32</td>
<td>NA</td>
<td>MD 0.89 lower (1.61 to 0.17 lower)</td>
<td>Moderate</td>
<td>RCT</td>
<td>Serious risk of bias¹</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious*</td>
</tr>
<tr>
<td><strong>BMI-SDS – at 12 months</strong></td>
<td>2 (Enander 2012; Goksen 2014)</td>
<td>78</td>
<td>46</td>
<td>NA</td>
<td>WMD 0.28 lower (0.68 lower to 0.12 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>No serious risk of bias²</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious*</td>
</tr>
<tr>
<td><strong>BMI-SDS – at 24 months</strong></td>
<td>1 (Goksen 2014)</td>
<td>52</td>
<td>32</td>
<td>NA</td>
<td>MD 0.14 lower (0.66 lower to 0.38 higher)</td>
<td>Moderate</td>
<td>RCT</td>
<td>Serious risk of bias¹</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious*</td>
</tr>
<tr>
<td><strong>Severe hypoglycaemic episodes (over the 12-month study)</strong></td>
<td>1 (Enander 2012)</td>
<td>0/30 (0%)</td>
<td>0/15 (0%)</td>
<td>NA*</td>
<td>MD 0.00 (NC)</td>
<td>Moderate</td>
<td>RCT</td>
<td>No serious risk of bias¹</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision²</td>
</tr>
</tbody>
</table>

BMI-SDS: body mass index standard deviation score, MD: mean difference, NA: not applicable, NC: not calculable, RCT: randomised controlled trial, RR: relative risk, WMD: weighted mean difference

---

³ Unknown as no events reported in either treatment group
¹ Moderate risk of bias in the included studies
² No apparent risk of bias in the included study
³ Single-study analysis
⁴ Population, intervention and outcome as specified in the review protocol
⁵ Confidence intervals cross two zones related to precision (see ‘Methodology for 2015 update’)
Review question: What is the effectiveness of dietetic advice using glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes?

Table 46: Evidence profile for effectiveness of dietary advice based on glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes, glycaemic index diet versus standard diet

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Glycaemic index</th>
<th>Standard diet</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postprandial hyperglycaemia</td>
<td>1 (Collier 1988)</td>
<td>7</td>
<td>7</td>
<td>Blood glucose after standard meal reduced from baseline in low glycaemic index phase (p &lt; 0.05) No significant change in blood glucose after standard meal when compared with baseline in normal diet phase.</td>
<td>Moderate RCT No Serious risk of bias¹ No Serious inconsistency² No Serious indirectness³ Serious* None</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RCT randomised controlled trial
1 No apparent risk of bias in the included study
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 Data reported only graphically with an accompanying p value, therefore unable to calculate mean difference between the intervention and comparator groups – not currently reported in table

Table 47: Evidence profile for effectiveness of dietary advice based on glycaemic index in maintaining glycaemic control in children and young people with type 1 diabetes, glycaemic index diet versus carbohydrate exchange diet

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Glycaemic index</th>
<th>Carbohydrate exchange</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c value (% change from baseline to 12 months)</td>
<td>1 (Gilbert 2001)</td>
<td>51 (changed from 8.3 ± 1.4 at baseline)</td>
<td>38 (no change, was 8.6 ± 1.4 at baseline and at 12)</td>
<td>NA</td>
<td>MD in change in values between groups 0.3 lower</td>
<td>Moderate RCT No serious risk of bias¹ No serious inconsistency No serious indirectness³ Serious* None</td>
<td></td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

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### Table

#### Number of children and young people

<table>
<thead>
<tr>
<th>Effect</th>
<th>Glycaemic Index</th>
<th>Carbohydrate exchange</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistencies</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>to 8.0 ± 1.0 at 12 months</td>
<td>(0.89 lower to 0.29 higher)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No Serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Mean number of hypoglycaemic episodes (preprandial blood glucose < 3.5 mmol/l) per month

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Glycaemic Index</th>
<th>Carbohydrate exchange</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistencies</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Gilbertson 2001)</td>
<td>51 (6.9 ± 6.8 episodes at 12 months)</td>
<td>38 (5.8 ± 5.5 episodes at 12 months)</td>
<td>NA</td>
<td>MD 1.1 more (1.46 more to 3.66 fewer)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No Serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
</tbody>
</table>

#### Mean number of hyperglycaemic episodes (preprandial blood glucose > 15 mmol/l) per month

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Glycaemic Index</th>
<th>Carbohydrate exchange</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistencies</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Gilbertson 2001)</td>
<td>51 (11.2 ± 9.8 episodes at 12 months)</td>
<td>38 (16.8 ± 11.8 episodes at 12 months)</td>
<td>NA</td>
<td>MD 5.6 fewer (10.22 to 0.98 fewer)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No Serious indirectness</td>
<td>Serious</td>
<td>None</td>
</tr>
</tbody>
</table>

#### Number adhering to treatment (up to 12 months)

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Glycaemic Index</th>
<th>Carbohydrate exchange</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistencies</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Gilbertson 2001)</td>
<td>46/55 (83.6%)</td>
<td>32/49 (65.3%)</td>
<td>RR 1.28 (1.01 to 1.62)</td>
<td>183 more per 1000 (from 7 more to 405 more)</td>
<td>Moderate</td>
<td>RCT</td>
<td>No Serious risk of bias</td>
<td>No Serious inconsistency</td>
<td>No Serious indirectness</td>
<td>Serious</td>
<td>None</td>
</tr>
</tbody>
</table>

**MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk**

1. No apparent risk of bias in the included study
2. Single-study analysis
3. Population, intervention and outcome as specified in the review protocol
4. Findings do not meet the GDG agreed minimally important difference (MID) of 0.5 percentage points for the change in HbA1c level
5. Confidence intervals cross two zones related to precision (see the 2015 methods section of the full guideline)

---

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

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

**Table 48: Evidence profile for diagnostic test accuracy of serum beta-hydroxybutyrate and end-tidal carbon dioxide as indicators of diabetic ketoacidosis**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number</th>
<th>Measure of diagnostic test accuracy (95% CI)</th>
<th>Quality</th>
<th>Quality assessment</th>
</tr>
</thead>
</table>

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<table>
<thead>
<tr>
<th>studies</th>
<th>of children and young people</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive likelihood ratio</th>
<th>Negative likelihood ratio</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum beta-hydroxybutyrate (cut-off ≥ 3 mmol/l) for detecting DKA (defined by serum bicarbonate ≤ 18 mEq/l)</td>
<td>1 (Sheikh-Ali 2008)</td>
<td>129</td>
<td>0.92 (0.87 to 0.97)</td>
<td>0.84 (0.70 to 0.91)</td>
<td>5.86 (2.96 to 11.61)</td>
<td>0.08 (0.04 to 0.18)</td>
<td>Very low</td>
<td>Retrospective</td>
<td>Serious¹</td>
<td>NA</td>
<td>No serious</td>
</tr>
<tr>
<td>Serum beta-hydroxybutyrate (cut-off ≥ 3 mmol/l) for detecting DKA (defined by venous pH of &lt; 7.3)</td>
<td>1 (Prisco 2006)</td>
<td>90</td>
<td>0.83 (NC)</td>
<td>0.68 (NC)</td>
<td>2.59 (NC)</td>
<td>0.25 (NC)</td>
<td>Moderate</td>
<td>Prospective</td>
<td>No serious</td>
<td>NA</td>
<td>No serious</td>
</tr>
<tr>
<td>Serum beta-hydroxybutyrate (cut-off ≥ 3 mmol/l) for detecting DKA (defined by blood glucose &gt; 13.9 mmol/l)</td>
<td>1 (Prisco 2006)</td>
<td>110</td>
<td>0.57 (NC)</td>
<td>0.83 (NC)</td>
<td>3.35 (NC)</td>
<td>0.52 (NC)</td>
<td>Moderate</td>
<td>Prospective</td>
<td>No serious</td>
<td>NA</td>
<td>No serious</td>
</tr>
<tr>
<td>End-tidal carbon dioxide (cut-point ≤ 29 mmHg) for detecting DKA</td>
<td>1 (Fearon 2002)</td>
<td>44</td>
<td>0.83 (0.52 to 0.98)</td>
<td>1.0 (0.88 to 1.0)</td>
<td>NC</td>
<td>0.17 (0.05 to 0.59)</td>
<td>Low</td>
<td>Prospective</td>
<td>No serious</td>
<td>NA</td>
<td>No serious</td>
</tr>
<tr>
<td>End-tidal carbon dioxide (cut-point ≤ 30 mmHg) for detecting DKA</td>
<td>1 (Gilhotra 2007)</td>
<td>63</td>
<td>0.93 (0.70 to 0.99)</td>
<td>0.91 (0.78 to 0.96)</td>
<td>10.03 (3.91 to 25.76)</td>
<td>0.07 (0.01 to 0.49)</td>
<td>Low</td>
<td>Prospective</td>
<td>No serious</td>
<td>NA</td>
<td>No serious</td>
</tr>
<tr>
<td>End-tidal carbon dioxide (cut-point &lt; 36 mmHg) for detecting DKA</td>
<td>1 (Gilhotra 2007)</td>
<td>58</td>
<td>1.0 (0.78 to 1.0)</td>
<td>0.86 (0.72 to 0.95)</td>
<td>7.17 (3.41 to 15.05)</td>
<td>0 (NC)</td>
<td>Low</td>
<td>Prospective</td>
<td>Low</td>
<td>NA</td>
<td>No serious</td>
</tr>
<tr>
<td>End-tidal carbon dioxide (cut-point &lt;36 mmHg) for detecting DKA</td>
<td>1 (Fearon 2002)</td>
<td>42</td>
<td>1.0 (0.74 to 1.0)</td>
<td>0.67 (0.47 to 0.83)</td>
<td>3.0 (1.81 to 4.98)</td>
<td>0 (NC)</td>
<td>High</td>
<td>Prospective</td>
<td>Low</td>
<td>NA</td>
<td>No serious</td>
</tr>
</tbody>
</table>

CI confidence interval, DKA diabetic ketoacidosis, NA not applicable, NC not calculable,
a Calculated by the NCC-WCH technical team from data reported in the article
b Point estimate reported only; unable to calculate 95% CI from data reported
c Point estimate reported only, CI calculated by NCC-WCH technical team from data reported in the article
d Sensitivity = 1.0 therefore negative likelihood ratio = 0, and CI not calculable
1 Highly selected population – only included participants where medical records stated ‘diabetes with ketoacidosis’
2 Confidence interval for positive likelihood ratio ranges from not useful to definitely useful
K.11 Type 1 and type 2 diabetes – diabetic ketoacidosis – assessments, monitoring and investigations

Review questions:

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

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

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

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

- blood glucose
- blood or urine ketones
- serum urea or electrolytes
Table 49: Evidence profile for comparison of blood ketone monitoring versus urine ketone monitoring during treatment of diabetic ketoacidosis

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Blood ketone monitoring</th>
<th>Urine ketone monitoring</th>
<th>Effect</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>None</td>
</tr>
<tr>
<td>1 (Vanelli 2003)</td>
<td>0/16 (0%)</td>
<td>0/17 (0%)</td>
<td>NC</td>
<td>NC</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>No serious imprecision&lt;sup&gt;4&lt;/sup&gt;</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to resolution of ketosis (proxy measure for duration of treatment)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Vanelli 2003)</td>
<td>16</td>
<td>17</td>
<td>NA</td>
<td>MD 6.5 hours fewer (from 4 to 9.4 fewer)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>No serious imprecision&lt;sup&gt;5&lt;/sup&gt;</td>
<td>None</td>
</tr>
<tr>
<td>1 (Prisco 2006)</td>
<td>99</td>
<td>NA</td>
<td>NA</td>
<td>MD 2.3 hours fewer (from 9.42 hours fewer to 4.82 hours more)</td>
<td>Very low</td>
<td>Case series</td>
<td>No serious risk of bias&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Serious imprecision&lt;sup&gt;7&lt;/sup&gt;</td>
<td>None</td>
</tr>
<tr>
<td>1 (Noyes 2007)</td>
<td>28 episodes of DKA</td>
<td>NA</td>
<td>NA</td>
<td>Median difference 11 hours fewer (range 1 hour fewer to 36 hours fewer)</td>
<td>Low</td>
<td>Case series</td>
<td>No serious risk of bias&lt;sup&gt;1&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;3&lt;/sup&gt;</td>
<td>No serious imprecision&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Yes&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

DKA diabetic ketoacidosis, MD mean difference, NA not applicable, NC not calculable, RCT randomised controlled trial

1 No apparent risk of bias
2 Single-study analysis
3 Population, intervention and outcome as specified in the review protocol
4 No events reported
5 No minimally important difference specified by the GDG
6 Population includes a majority of participants without DKA
7 Confidence interval crosses the line of no effect
8 The 25 participants experienced a total of 40 episodes of DKA during the study period; 28 of the episodes which were followed up until negative ketonuria was obtained and included in this analysis
## K.12 Type 1 and type 2 diabetes – diabetic ketoacidosis – fluids

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

There are no evidence profiles for this review question because no studies were identified for inclusion.

### Review question: At what rate should children and young people with diabetic ketoacidosis be rehydrated?

#### Table 50: Evidence profile for an increased rate of fluid administration in children and young people with diabetic ketoacidosis – case-control studies

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Effect of a per 5 ml/kg/hour increase in fluids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Glaser 2001)</td>
<td>61/183</td>
<td>RR 1.1 (0.4 to 3.0)&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>NA</td>
<td>Low</td>
<td>Retrospective case control</td>
<td>No serious bias&lt;sup&gt;1&lt;/sup&gt;</td>
<td>NA&lt;sup&gt;c&lt;/sup&gt;</td>
<td>No serious indirectness</td>
<td>Very serious&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Effect of a per 1ml/kg/hour increase in fluids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Lawrence 2005)</td>
<td>21/42</td>
<td>MD 3.96 (0.80 to 7.12)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Low</td>
<td>Prospective surveillance with retrospective case control</td>
<td>Serious&lt;sup&gt;4&lt;/sup&gt;</td>
<td>NA&lt;sup&gt;e&lt;/sup&gt;</td>
<td>No serious indirectness&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Serious&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Yes&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Effect of per tertile increases in fluids within the first 4 hours of treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Edge 2006)</td>
<td>43/169</td>
<td>OR 3.30 (0.71 to 15.27)&lt;sup&gt;g&lt;/sup&gt;</td>
<td>NA</td>
<td>Low</td>
<td>Matched case control</td>
<td>No serious bias&lt;sup&gt;3&lt;/sup&gt;</td>
<td>NA&lt;sup&gt;f&lt;/sup&gt;</td>
<td>Serious&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Very serious&lt;sup&gt;10&lt;/sup&gt;</td>
</tr>
<tr>
<td>1 (Edge 2006)</td>
<td>43/169</td>
<td>OR 6.55 (1.38 to 30.97)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>NA</td>
<td>Moderate</td>
<td>Matched case control</td>
<td>No serious bias&lt;sup&gt;3&lt;/sup&gt;</td>
<td>NA&lt;sup&gt;f&lt;/sup&gt;</td>
<td>Serious&lt;sup&gt;7&lt;/sup&gt;</td>
<td>No serious imprecision&lt;sup&gt;11&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Effect of the rate of fluid administration in the first 4 hours of treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Mahoney 1999)</td>
<td>9/186</td>
<td>MD 36.4 (8.9 to 63.9)&lt;sup&gt;i&lt;/sup&gt;</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Very serious&lt;sup&gt;12,13,14&lt;/sup&gt;</td>
<td>NA&lt;sup&gt;g&lt;/sup&gt;</td>
<td>No serious indirectness</td>
<td>No serious imprecision&lt;sup&gt;15&lt;/sup&gt;</td>
<td>None</td>
</tr>
</tbody>
</table>

CI confidence interval, DKA diabetic ketoacidosis, MD mean difference, MID minimally important difference, NA not applicable, OR odds ratio, RR risk ratio

<sup>a</sup> Study used both matched and unmatched controls; results presented are for matched controls as unmatched analyses did not include treatment-related variables

<sup>b</sup> Reported as RR by study authors based on the rare disease assumption; effect estimate actually derived from conditional multivariate logistic regression; controls were matched to cases by age, onset of diabetes, venous pH at presentation and serum glucose at presentation

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Table 51: Evidence profile for a slower rate of fluid administration compared with a faster rate of fluid administration in children and young people with diabetic ketoacidosis – randomised study

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Quality assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of mild cerebral oedema (brain swelling)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Glaser 2013)</td>
<td>10/18</td>
<td>8/18</td>
<td>NA</td>
<td>Two-tailed p-value 0.63*</td>
<td>Very low*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Randomised controlled trial pilot study</td>
<td></td>
</tr>
</tbody>
</table>

ADC apparent brain diffusion coefficient, CI confidence interval, MID minimally important difference, NA not applicable, RCT randomised controlled trial

a One group received a bolus of 0.9% saline of 20 ml/kg with two-thirds of fluid deficit replaced over the first 24 hours and the remaining third replaced over the next 24 hours (a fluid deficit of 10% was assumed); the other treatment group received a bolus of 0.9% saline of 10 ml/kg with fluid deficit replaced evenly over 48 hours (a fluid deficit of 7% was assumed)
b Calculated by the NCC-WCH technical team using the Wilcoxon rank sum test for non-parametric data using an online calculator at cs.fairfield.edu/~sawin/stats/templates/wilcoxon.xls; individual patient data were obtained from study authors as results were presented graphically in the original article
c Starting point of moderate quality as the study is a pilot study for an RCT
1 Single-study analysis

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2 ADC to detect brain swelling was used as a proxy for mild cerebral oedema
3 Not sufficiently powered to detect small differences and power calculations were not aimed at detecting between-group differences; calculations were to detect a 1.3 standard deviation change in ADC between treatment and post-recovery
4 No confidence interval was calculable as data were not normally distributed
5 MID not calculable

Table 52: Evidence profile for a slower rate of fluid administration compared with a faster rate of fluid administration in children and young people with diabetic ketoacidosis – partially randomised study

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Quality assessment</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Slower rate,a,b</td>
<td>Faster rate,a,b</td>
<td>Relative (95% CI)</td>
<td>Absolute (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to resolution of acidosis, hours</td>
<td>1 (Felner 2001)</td>
<td>30</td>
<td>60</td>
<td>NA</td>
<td>MD -4.10 (-5.88 to -2.32)</td>
<td>Very low</td>
<td>Partially randomised cohort study</td>
<td>Serious¹</td>
<td>No serious inconsistency²</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td>Change in serum sodium, mmol/l</td>
<td>1 (Felner 2001)</td>
<td>30</td>
<td>60</td>
<td>NA</td>
<td>MD 0.00 (-1.78 to 1.78)</td>
<td>Very low</td>
<td>Partially randomised cohort study</td>
<td>Very serious⁵,⁶</td>
<td>No serious inconsistency²</td>
<td>Serious⁷</td>
</tr>
<tr>
<td>Change in serum chloride, mmol/l</td>
<td>1 (Felner 2001)</td>
<td>30</td>
<td>60</td>
<td>NA</td>
<td>MD 1.95 (-0.78 to 4.68)</td>
<td>Very low</td>
<td>Partially randomised cohort study</td>
<td>Very serious⁵,⁶</td>
<td>No serious inconsistency²</td>
<td>Serious⁷</td>
</tr>
<tr>
<td>Admission to ICU¹</td>
<td>1 (Felner 2001)</td>
<td>30</td>
<td>60</td>
<td>RR 0.95 (0.48 to 1.86)</td>
<td>NA</td>
<td>Very low</td>
<td>Partially randomised cohort study</td>
<td>No serious bias</td>
<td>No serious inconsistency²</td>
<td>No serious indirectness</td>
</tr>
</tbody>
</table>

CI confidence interval, ICU intensive care unit, MD mean difference, NA not applicable
a Treatment groups were assigned based on the introduction of a new treatment protocol in 1997; for the faster rate group fluid deficit was calculated based on the percentage of dehydration (7 to 10%) by weight in kg and added to 1.5 times the required maintenance rate (50% of the fluids were administered in the first 12 hours and the remaining 50% over the next 24 hours); the slower rate group received total fluids at a rate of 2.5 times the required maintenance rate regardless of the degree of dehydration (fluids were decreased to 1 to 1.5 times the maintenance rate after 24 hours of treatment)
b The total mean volumes of fluid (l/m²/24 hours) were 5.3 ± 1.4 and 5.4 ± 1.2 for the faster rate group, depending on whether a two- or three-bag protocol was used, and 4.1 ± 1.1 for the slower rate group
c Calculated by the NCC-WCH technical team using the t-distribution due to a small sample size
d Admission to ICU was defined according to symptoms and signs including altered level of consciousness, severe acidosis (pH < 7.00), haemodynamic instability, or very young age (< 3 years)
1 Resolution of acidosis was not defined
2 Single-study analysis
3 Confidence interval crosses two zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 3.70 calculated by the NCC-WCH technical team using sample means and standard deviations
4 The study authors conducted retrospective analyses on non-randomised participants to compare groups 1A and 1B due to subtle differences in the treatment protocols (three-versus two-bag rehydration); no statistically significant differences were observed therefore data were pooled by the NCC-WCH technical team
5 The amount of sodium chloride varied slightly between treatment groups (0.45% for the faster rate group and 0.675% for the slower rate group)
Review question: What is the optimal fluid composition (including glucose, potassium and bicarbonate additives) for rehydrating children and young people with diabetic ketoacidosis?

Table 53: Evidence profile for comparison of 75 mEq/l concentration of sodium with 100 mEq/l concentration of sodium for the treatment of diabetic ketoacidosis in children and young people with type 1 diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma sodium (corrected)</strong></td>
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<td><strong>Baseline</strong></td>
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<tr>
<td>1 (Savas-Erdeve 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD 0.7 (-3.1 to 4.5)*</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious indirectness</td>
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<tr>
<td><strong>4 hours’ follow-up</strong></td>
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<tr>
<td>1 (Savas-Erdeve 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD 0.6 (-3.0 to 4.2)*</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious indirectness</td>
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<td><strong>8 hours’ follow-up</strong></td>
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<tr>
<td>1 (Savas-Erdeve 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD -1.5 (-5.3 to 2.3)*</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious indirectness</td>
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<tr>
<td><strong>16 hours’ follow-up</strong></td>
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<tr>
<td>1 (Savas-Erdeve 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD -0.2 (-2.7 to 2.3)*</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious indirectness</td>
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<tr>
<td><strong>24 hours’ follow-up</strong></td>
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<tr>
<td>1 (Savas-Erdeve 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD -0.6 (-3.1 to 1.9)*</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious indirectness</td>
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<tr>
<td><strong>Plasma carbon dioxide</strong></td>
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<tr>
<td>1 (Savas-Erdeve 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD -0.9 (-4.8 to 3.0)*</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious indirectness</td>
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<tr>
<td><strong>4 hours’ follow-up</strong></td>
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<tr>
<td>1 (Savas-Erdeve 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD -0.2</td>
<td>Very</td>
<td>Retrospective</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious</td>
</tr>
<tr>
<td>Number of studies</td>
<td>Number of children and young people</td>
<td>Effect</td>
<td>Quality</td>
<td>Design</td>
<td>Risk of bias</td>
<td>Inconsistency</td>
<td>Indirectness</td>
<td>Imprecision</td>
<td>Other considerations</td>
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<tr>
<td></td>
<td>Intervention (75 mEq/l)</td>
<td>Comparator (100 mEq/l)</td>
<td>Relative (95% CI)</td>
<td>Absolute (95% CI)</td>
<td>Design</td>
<td>Quality assessment</td>
<td></td>
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<tr>
<td>Erdeve 2011</td>
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<td></td>
<td></td>
<td>low</td>
<td>chart review</td>
<td>indirectness</td>
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<tr>
<td><strong>8 hours’ follow-up</strong></td>
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<tr>
<td>1 (Savas-Erdeve 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD -0.8 (-5.5 to 3.9)</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>16 hours’ follow-up</strong></td>
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<tr>
<td>1 (Savas-Erdeve 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD 0.4 (-3.5 to 4.3)</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>24 hours’ follow-up</strong></td>
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<tr>
<td>1 (Savas-Erdeve 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD -1.2 (-5.9 to 3.5)</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>pH</strong></td>
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<td>Baseline</td>
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<tr>
<td>1 (Savas-Erdeve 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD -0.10 (-0.21 to 0.01)</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious indirectness</td>
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<tr>
<td><strong>4 hours’ follow-up</strong></td>
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<tr>
<td>1 (Savas-Erdeve et al., 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD 0.00 (-0.07 to 0.07)</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>8 hours’ follow-up</strong></td>
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<tr>
<td>1 (Savas-Erdeve et al., 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD -0.06 (-0.13 to 0.01)</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>16 hours’ follow-up</strong></td>
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<tr>
<td>1 (Savas-Erdeve 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD 0.0 (-0.7 to 0.7)</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious indirectness</td>
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<tr>
<td><strong>24 hours’ follow-up</strong></td>
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<tr>
<td>1 (Savas-Erdeve 2011)</td>
<td>19/32</td>
<td>13/32</td>
<td>NA</td>
<td>MD 0.0 (-0.7 to 0.7)</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious¹</td>
<td>NA²</td>
<td>No serious indirectness</td>
</tr>
</tbody>
</table>

ANOVA analysis of variance, CI confidence interval, MD mean difference, MID minimally important difference, NA not applicable

a Calculated by the NCC-WCH technical team using confidence intervals based on the t-distribution due to a small sample size

1 Analysis used ANOVA however there is no mention of potential confounders being accounted for in the analysis
2 Single-study analysis
3 Confidence interval crosses all three zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 2.48 calculated by the NCC-WCH technical team using sample means and standard deviations
4 Confidence interval crosses all three zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 2.37 calculated by the NCC-WCH technical team using sample means and standard deviations

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5. Confidence interval crosses more than one zone related to precision (see ‘Methodology for 2015 update’) based on an MID of 2.42 calculated by the NCC-WCH technical team using sample means and standard deviations.

6. Confidence interval spans all three zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 1.57 calculated by the NCC-WCH technical team using sample means and standard deviations.

7. Confidence interval crosses all three zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 1.49 calculated by the NCC-WCH technical team using sample means and standard deviations.

8. Confidence interval crosses all three zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 2.59 calculated by the NCC-WCH technical team using sample means and standard deviations.

9. Confidence interval crosses all three zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 3.03 calculated by the NCC-WCH technical team using sample means and standard deviations.

10. Confidence interval crosses all three zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 3.08 calculated by the NCC-WCH technical team using sample means and standard deviations.

11. Confidence interval crosses all three zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 2.63 calculated by the NCC-WCH technical team using sample means and standard deviations.

12. Confidence interval crosses all three zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 3.19 calculated by the NCC-WCH technical team using sample means and standard deviations.

13. Confidence interval crosses all three zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 0.09 calculated by the NCC-WCH technical team using sample means and standard deviations.

14. Confidence interval crosses all three zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 0.05 calculated by the NCC-WCH technical team using sample means and standard deviations.

15. Confidence interval crosses all three zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 0.46 calculated by the NCC-WCH technical team using sample means and standard deviations.

16. Confidence interval crosses all three zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 0.46 calculated by the NCC-WCH technical team using sample means and standard deviations.

### Table 54: Evidence profile for comparison of bicarbonate with no bicarbonate for the treatment of diabetic ketoacidosis in children and young people

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Comparator (no bicarbonate)</th>
<th>Relative (95% CI)</th>
<th>Absolute (95% CI)</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of hospitalisation, hours</td>
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<tr>
<td>1 (Green 1998)</td>
<td>57/106 Mean duration 85 (75 to 95) 49/106 Mean duration 69 (58 to 60) NA</td>
<td>Adjusted R2 0.23, p-value 0.0714 Very low</td>
<td>Retrospective case series</td>
<td>Serious(^1) NA(^2) Serious(^3) No serious imprecision(^4) Yes(^5)(^6)</td>
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<tr>
<td>1 (Marr 1981) &amp; 45 &amp; 33 &amp; NA &amp; MD 1.75 (0.04 to 3.46) Very low &amp; Retrospective chart review &amp; Serious(^1) NA(^2) Serious(^3) Serious(^5) Yes(^5)</td>
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<tr>
<td>Risk of cerebral oedema</td>
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<tr>
<td>1 (Lawrence 2005) &amp; 4/17 cases 1/34 controls &amp; 13/17 cases 33/34 controls OR 10.15 (1.03 to 99.57) NA &amp; Very low &amp; Surveillance and retrospective case control &amp; Serious(^1) NA(^2) No serious indirectness Serious(^1) Ye(^3)</td>
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<tr>
<td>Number of studies</td>
<td>Number of children and young people</td>
<td>Effect</td>
<td>Quality</td>
<td>Design</td>
<td>Risk of bias</td>
<td>Inconsistency</td>
<td>Indirectness</td>
<td>Imprecision</td>
<td>Other considerations</td>
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</tr>
<tr>
<td>1 (Edge 2006)</td>
<td>5/43 cases 6/169 controls</td>
<td>OR 3.70 (1.02 to 13.10)</td>
<td>NA</td>
<td>Very low</td>
<td>Matched case control</td>
<td>No serious bias</td>
<td>NA²</td>
<td>No serious indirectness</td>
<td>Serious¹¹</td>
</tr>
</tbody>
</table>

Risk of cerebral oedema adjusted for baseline acidosis

1 (Edge 2006) 5/43 cases 6/169 controls OR 1.50 (0.39 to 5.76)\(^f\) NA Very low Matched case control No serious bias Na\(^{12}\) NA" No serious indirectness Very serious¹⁴ None

Duration of acidosis, hours

1 (Marr 1981)\(^c\) 45 33 NA MD -2.70 (-5.20 to -0.20)\(^d\) Very low Retrospective chart review Very serious\(^5,14\) NA² Serious⁸ Serious¹⁵ Yes⁵

CI confidence interval. DKA diabetic ketoacidosis. MD mean difference. MID minimally important difference. NA not applicable. OR odds ratio. RR relative risk.
a R² represents the correlation between duration of hospitalisation and the administration of bicarbonate.
b Adjusted for calendar year, pH, base deficit, creatinine and haemoglobin because treatment groups were not comparable at baseline for these variables.
c Comparison of children and young people who received sodium as either sodium bicarbonate, or sodium bicarbonate plus saline, or sodium bicarbonate and saline and lactic Ringers, or sodium bicarbonate and lactic Ringers with children and young people who received saline alone, lactate Ringers, or lactate Ringers with saline.
d Calculated by the NCC-WCH technical team.
e Crude effect estimate calculated by the NCC-WCH technical team.
f The OR was also adjusted for age, sex and whether diabetes was newly diagnosed.
g Missing data were present for 124 out of 486 admissions reviewed for inclusion and these admissions were, therefore, excluded from analyses; high risk of bias.
h Single-study analysis.
i Only severe cases of DKA were included in the study; generalisability is reduced.
j MID not calculable.
k Diabetes type not reported.
l Data from matched analyses were not used by the NCC-WCH technical team due to the high percentage of missing data (41%) generated by the matching process (49 participants per group, reduced to 29 participants per group after matching).
m No baseline characteristics were reported; selection bias is likely.

8 Treatments were grouped according to data extracted from medical records and combined by the NCC-WCH technical team to derive comparisons which best matched the review protocol.
9 Confidence interval crosses more than one zone related to precision (see ‘Methodology for 2015 update’) based on an MID of 2.41 calculated by the NCC-WCH technical team using sample means and standard deviations.
10 Results are from only 17 of 21 cases and 34 of 42 controls; loss of information is likely to have caused bias.
11 Confidence interval crosses two zones related to precision (see ‘Methodology for 2015 update’).
12 Retrospective review of case reports led to matching being ineffective and therefore broken for analysis as controls were unavailable for a large proportion of cases within matched sets.
13 Confidence interval crosses all three zones related to precision (see ‘Methodology for 2015 update’).
14 Acidosis was not defined.
15 Confidence interval crosses more than one zone related to precision (see ‘Methodology for 2015 update’) based on an MID of 3.48 calculated by the NCC-WCH technical team using sample means and standard deviations.
### Table 55: Evidence profile for the use of bicarbonate in treating diabetic ketoacidosis in children and young people with type 1 diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment with bicarbonate</td>
<td></td>
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<tr>
<td>1 (Glaser 2001)</td>
<td>61 cases (cerebral oedema)</td>
<td>183 controls (no cerebral oedema)</td>
<td>RR 4.2 (1.5 to 12.1)</td>
<td>Moderate&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Retrospective case control</td>
<td>No serious bias</td>
<td>NA&lt;sup&gt;b&lt;/sup&gt;</td>
<td>No serious indirectness</td>
<td>No serious imprecision&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reported as RR by study authors based on the rare disease assumption; effect estimate actually derived from conditional multivariate logistic regression; controls were matched to cases by age, onset of diabetes, venous pH at presentation and serum glucose at presentation

<sup>b</sup> Quality upgraded due to a large effect size

1 Single-study analysis

2 Confidence interval is entirely in one zone related to precision (see ‘Methodology for 2015 update’)

### Table 56: Evidence profile for comparison of phosphate with no phosphate for the treatment of diabetic ketoacidosis in children and young people

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum calcium</td>
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<tr>
<td>1 (Becker 1983)</td>
<td>13 intervention (phosphate)</td>
<td>9 comparator (no phosphate)</td>
<td>MD -1.1 (-1.7 to -0.5)</td>
<td>Very low</td>
<td>Partially randomised prospective cohort</td>
<td>Very serious&lt;sup&gt;1,2,3,4&lt;/sup&gt;</td>
<td>NA&lt;sup&gt;5&lt;/sup&gt;</td>
<td>No serious indirectness</td>
<td>No serious imprecision&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Calculated by the NCC-WCH technical team using confidence intervals based on the t-distribution due to a small sample size

<sup>b</sup> The intervention group received potassium replacement as mono- or di-basic phosphate salts versus controls who received no phosphate

1 Controls were not allocated using randomisation; randomisation method for the treatment groups is not described

2 Controls were less severe cases and received substantially different treatment compared with the two randomised treatment groups

3 Groups were not comparable at baseline

4 Data were presented graphically in the original article; numerical data were reported only for values at 12 hours’ follow-up because results were significant for phosphate versus controls; high risk of reporting bias

5 Single-study analysis

6 Confidence interval crosses all three zones related to precision (see ‘Methodology for 2015 update’) based on an MID of 0.29 calculated by the NCC-WCH technical team using sample means and standard deviations

7 Diabetes type is not reported
### K.13 Type 1 and type 2 diabetes – diabetic ketoacidosis – intravenous osmotic agents

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

**Table 57:** Effectiveness of intravenous osmotic agents in the treatment of cerebral oedema associated with diabetic ketoacidosis in children and young people with type 1 diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Quality assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mannitol</td>
<td>Hypertonic saline</td>
<td>Relative (95% CI)</td>
<td>Absolute (95% CI)</td>
<td>Risk of bias</td>
</tr>
<tr>
<td>1 (DeCourcey 2013)</td>
<td>NA</td>
<td>NA</td>
<td>2.71 (1.01 to 7.26)</td>
<td>NA</td>
<td>Very low</td>
</tr>
</tbody>
</table>

**Healthcare utilisation: brain imaging with CT scan (%)**

1 (DeCourcey 2013)
525/1202 (43.7) 109/299 (36.5) NA NA Very low Retrospective cohort Serious¹ NA² Serious indirectness³ Very serious imprecision⁴ None

**Healthcare utilisation: mechanical ventilation (%)**

1 (DeCourcey 2013)
184/1202 (15.3) 43/299 (14.4) NA NA Very low Retrospective cohort Serious¹ NA² Serious indirectness³ Very serious imprecision⁴ None

**Healthcare utilisation: intensive care unit admission (%)**

1 (DeCourcey 2013)
784/1202 (65.2) 269/299 (90) NA NA Very low Retrospective cohort Serious¹ NA² Serious indirectness³ Very serious imprecision⁴ None

CI confidence interval, NA not applicable

1 More participants in the hypertonic saline group were admitted to intensive care unit (ICU) than those in the mannitol group
2 Single-study analysis
3 Upper age limit is slightly higher than the guideline population and a small number of participants (< 1.5% total) who may not have had cerebral oedema associated with diabetic ketoacidosis (DKA) were included in the analysis
4 Confidence interval crosses three zones related to precision (see ‘Methodology for 2015 update’)
5 Adjusted for discharge year, hospital clustering, gender, mechanical ventilation, brain imaging with CT scan, ICD-9 code (diabetes with hyperosmolar state (250.2) or diabetes with coma (250.3))
6 Treatment group with both hypertonic saline and mannitol was excluded from further analysis as participants treated with both agents would have been switched to the alternative agent once the initial therapy failed and the study database did not allow for the order of therapy intervention to be determined
K.14 **Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin**

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

Table 58: Evidence profile for the effect of insulin administered within 1 hour of fluid replacement compared to insulin administered at least 1 hour after fluid administration on the risk of cerebral oedema

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of patients</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases (cerebral oedema)</td>
<td>Controls (no cerebral oedema)</td>
<td>Relative (95% CI)</td>
<td>Absolute (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Association between timing of insulin therapy and risk of cerebral oedema</td>
<td>1 (Edge 2006)</td>
<td>43</td>
<td>169</td>
<td>Adjusted OR: 4.7 (1.5 to 13.9)&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>NA</td>
<td>Moderate</td>
<td>Matched case control</td>
<td>No serious bias&lt;sup&gt;1,2,3&lt;/sup&gt;</td>
<td>Not relevant</td>
</tr>
<tr>
<td>Association between timing of insulin therapy and risk of cerebral oedema, adjusted for baseline biochemical measures to account for severity of acidosis</td>
<td>1 (Edge 2006)</td>
<td>43</td>
<td>169</td>
<td>Adjusted OR: 12.7 (1.41 to 114.5)&lt;sup&gt;a,b,c&lt;/sup&gt;</td>
<td>NA</td>
<td>Moderate</td>
<td>Matched case control</td>
<td>No serious bias&lt;sup&gt;1,2,3&lt;/sup&gt;</td>
<td>Not relevant</td>
</tr>
</tbody>
</table>

CI confidence interval, OR odds ratio, NA not applicable

- <sup>a</sup> OR is for participants who received insulin therapy within 1 hour of fluid replacement compared to those who did not
- <sup>b</sup> Adjusted for matching variables: age, sex and whether diabetes was newly diagnosed as well as baseline acidosis
- <sup>c</sup> Baseline biochemical measures included in the multivariate model included: plasma glucose, potassium, urea, sodium and paCO2
- <sup>1</sup> Retrospective review of case reports led to matching being ineffective and therefore broken for analysis as controls were unavailable for a large proportion of cases within matched sets
- <sup>2</sup> Whether controls were clearly established as not being cases was not reported
- <sup>3</sup> Standardisation of exposure measurement was not clear
- <sup>4</sup> Large effect size
- <sup>5</sup> Wide CI suggests imprecision but CI is entirely within one zone related to precision (see ‘Methodology for 2015 update’) therefore not downgraded
### Review question: How should the dosage of insulin be calculated for children and young people with diabetic ketoacidosis?

Table 59: Comparison of insulin dosage of 0.025 U/kg/hour or 0.05 U/kg/hour with a dosage of 0.1 U/kg/hour in children and young people with type 1 diabetes and DKA

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Change in blood glucose from admission (low dosage 0.05 U/kg/hour)</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Children of all ages</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Al Hanshi 2011)</td>
<td>N = 33 Median difference: -17 mmol/l (IQR: -26 to -12)</td>
<td>N = 34 Median difference: -21 mmol/l (IQR: -52 to -15)</td>
<td>NA</td>
<td>P-value = 0.004, adjusted R = 0.62</td>
<td>Very low</td>
<td>Retrospective cohort</td>
<td>Serious</td>
<td>NA</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>Incidence of hypoglycaemia (low dosage 0.025 U/kg/hour)</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1 (Puttha 2010)</td>
<td>N = 41 MD: 11.3 mmol/l (8.6 to 13.9)</td>
<td>N = 52 MD: 11.8 mmol/l (8.4 to 15.2)</td>
<td>NA</td>
<td>MD: -0.50 (-4.75 to 3.75)</td>
<td>Very low</td>
<td>Retrospective cohort</td>
<td>Very serious</td>
<td>NA</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>Incidence of hypokalaemia (low dosage 0.025 U/kg/hour)</strong></td>
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</tr>
<tr>
<td>1 (Kapellen 2012)</td>
<td>N = 33 MD: 0.13 (0.09 to 0.18)</td>
<td>N = 52 MD: 0.11 (0.07 to 0.15)</td>
<td>NA</td>
<td>MD: 0.02 (-0.04 to 0.08)</td>
<td>Very low</td>
<td>Retrospective cohort</td>
<td>Very serious</td>
<td>NA</td>
<td>No serious indirectness</td>
</tr>
</tbody>
</table>

Subgroup analysis: children aged less than 5 years

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Change in blood glucose from admission (low dosage 0.05 U/kg/hour)</strong></td>
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<tr>
<td><strong>Children of all ages</strong></td>
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<td>1 (Al Hanshi 2011)</td>
<td>N = 33 Median difference: -17 mmol/l (IQR: -26 to -12)</td>
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<td>NA</td>
<td>P-value = 0.004, adjusted R = 0.62</td>
<td>Very low</td>
<td>Retrospective cohort</td>
<td>Serious</td>
<td>NA</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>Incidence of hypoglycaemia (low dosage 0.05 U/kg/hour)</strong></td>
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<tr>
<td>1 (Puttha 2010)</td>
<td>N = 41 MD: 11.3 mmol/l (8.6 to 13.9)</td>
<td>N = 52 MD: 11.8 mmol/l (8.4 to 15.2)</td>
<td>NA</td>
<td>MD: -0.50 (-4.75 to 3.75)</td>
<td>Very low</td>
<td>Retrospective cohort</td>
<td>Very serious</td>
<td>NA</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>Incidence of hypokalaemia (low dosage 0.025 U/kg/hour)</strong></td>
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<tr>
<td>1 (Kapellen 2012)</td>
<td>N = 33 MD: 0.13 (0.09 to 0.18)</td>
<td>N = 52 MD: 0.11 (0.07 to 0.15)</td>
<td>NA</td>
<td>MD: 0.02 (-0.04 to 0.08)</td>
<td>Very low</td>
<td>Retrospective cohort</td>
<td>Very serious</td>
<td>NA</td>
<td>No serious indirectness</td>
</tr>
</tbody>
</table>

Subgroup analysis: children aged less than 5 years

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Change in blood glucose from admission (low dosage 0.05 U/kg/hour)</strong></td>
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<tr>
<td><strong>Children of all ages</strong></td>
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<td></td>
<td></td>
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<td>1 (Al Hanshi 2011)</td>
<td>N = 33 Median difference: -17 mmol/l (IQR: -26 to -12)</td>
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<td>NA</td>
<td>P-value = 0.004, adjusted R = 0.62</td>
<td>Very low</td>
<td>Retrospective cohort</td>
<td>Serious</td>
<td>NA</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>Incidence of hypoglycaemia (low dosage 0.05 U/kg/hour)</strong></td>
<td></td>
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<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>1 (Puttha 2010)</td>
<td>N = 41 MD: 11.3 mmol/l (8.6 to 13.9)</td>
<td>N = 52 MD: 11.8 mmol/l (8.4 to 15.2)</td>
<td>NA</td>
<td>MD: -0.50 (-4.75 to 3.75)</td>
<td>Very low</td>
<td>Retrospective cohort</td>
<td>Very serious</td>
<td>NA</td>
<td>No serious indirectness</td>
</tr>
<tr>
<td><strong>Incidence of hypokalaemia (low dosage 0.025 U/kg/hour)</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1 (Kapellen 2012)</td>
<td>N = 33 MD: 0.13 (0.09 to 0.18)</td>
<td>N = 52 MD: 0.11 (0.07 to 0.15)</td>
<td>NA</td>
<td>MD: 0.02 (-0.04 to 0.08)</td>
<td>Very low</td>
<td>Retrospective cohort</td>
<td>Very serious</td>
<td>NA</td>
<td>No serious indirectness</td>
</tr>
</tbody>
</table>
### Appendix K: GRADE tables

#### Type 1 and type 2 diabetes – diabetic ketoacidosis – anticoagulant prophylaxis

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

There are no evidence profiles for this review question because no studies were identified for inclusion.
### Type 1 diabetes – retinopathy

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

#### Table 60: Evidence profile for prevalence of retinopathy according to age

<table>
<thead>
<tr>
<th>Age</th>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Range of prevalence, % (median, %)</th>
<th>Quality</th>
<th>Design</th>
<th>Quality assessment</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 9 years</td>
<td>8</td>
<td>NC</td>
<td>0.0 to 9.0 (4.5)</td>
<td>Moderate</td>
<td>Cross sectional and prospective cohort</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA¹</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Age 9 years</td>
<td>8</td>
<td>NC</td>
<td>0.0 to 9.0 (4.5)</td>
<td>Moderate</td>
<td>Cross sectional and prospective cohort</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA¹</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Age 10 years</td>
<td>9</td>
<td>NC</td>
<td>0.0 to 15.0 (6.7)</td>
<td>Low</td>
<td>Cross sectional and prospective cohort</td>
<td>No serious risk of bias</td>
<td>Serious inconsistency²</td>
<td>No serious indirectness</td>
<td>NA¹</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Age 11 years</td>
<td>8</td>
<td>NC</td>
<td>0.0 to 15.0 (6.4)</td>
<td>Low</td>
<td>Cross sectional and prospective cohort</td>
<td>No serious risk of bias</td>
<td>Serious inconsistency²</td>
<td>No serious indirectness</td>
<td>NA¹</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Age 12 years</td>
<td>9</td>
<td>NC</td>
<td>1.0 to 19.0 (7.7)</td>
<td>Low</td>
<td>Cross sectional and prospective cohort</td>
<td>No serious risk of bias</td>
<td>Serious inconsistency²</td>
<td>No serious indirectness</td>
<td>NA¹</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Age 13 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>
### Table 61: Evidence profile for prevalence of retinopathy according to duration of diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Range of prevalence, % (median, %)</th>
<th>Quality</th>
<th>Design</th>
<th>Quality assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Risk of bias</td>
</tr>
<tr>
<td>Age 14 years</td>
<td>8</td>
<td>NC</td>
<td>1.0 to 25.0 (13.0)</td>
<td>Low(^a)</td>
<td>Cross sectional and prospective cohort</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>NC</td>
<td>5.8 to 44.0 (13.0)</td>
<td>Very low(^a)</td>
<td>Cross sectional and prospective cohort</td>
</tr>
<tr>
<td>Age 15 years</td>
<td>8</td>
<td>NC</td>
<td>5.8 to 54.0 (28.7)</td>
<td>Very low(^a)</td>
<td>Cross sectional and prospective cohort</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>NC</td>
<td>11.0 to 54.0 (42.8)</td>
<td>Very low(^a)</td>
<td>Cross sectional and prospective cohort</td>
</tr>
<tr>
<td>Age 16 years</td>
<td>5</td>
<td>NC</td>
<td>17.7 to 54.0 (45.7)</td>
<td>Very low(^a)</td>
<td>Cross sectional and prospective cohort</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>NC</td>
<td>17.7 to 60.0 (48.0)</td>
<td>Very low(^a)</td>
<td>Cross sectional and prospective cohort</td>
</tr>
</tbody>
</table>

NA not applicable, NC not calculable

\(^a\) Serious inconsistency between point estimates

\(^b\) Very serious inconsistency between point estimates

1 Unable to comment on imprecision as no confidence intervals reported for ranges

2 Serious inconsistency as range of point estimates varies between 10 and 20 percentage points

3 Very serious inconsistency as range of point estimates varies by more than 20 percentage points

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<table>
<thead>
<tr>
<th>Duration</th>
<th>children and young people</th>
<th>prevalence, % (median, %)</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2 years</td>
<td>6 (Frank 1982, Massin 2007, Kernell 1997, Flack 1996, Lobefalo 1997, Murphy 1990)</td>
<td>NC</td>
<td>1.0 to 21.0 (7.9)</td>
<td>Low</td>
<td>Cross sectional and prospective cohort</td>
<td>No serious risk of bias</td>
<td>Serious inconsistency</td>
</tr>
<tr>
<td>2 years</td>
<td>6 (Frank 1982, Massin 2007, Cho 2011, Flack 1996, Lobefalo 1997, Murphy 1990)</td>
<td>NC</td>
<td>1.0 to 21.0 (10.9)</td>
<td>Low</td>
<td>Cross sectional and prospective cohort</td>
<td>No serious risk of bias</td>
<td>Serious inconsistency</td>
</tr>
<tr>
<td>3 years</td>
<td>7 (Frank 1982, Massin 2007, Cho 2011, Flack 1996, Lobefalo 1997, Murphy 1990, Cerutti 1989)</td>
<td>NC</td>
<td>1.0 to 23.0 (10.5)</td>
<td>Very low</td>
<td>Cross sectional and prospective cohort</td>
<td>No serious risk of bias</td>
<td>Very serious inconsistency</td>
</tr>
<tr>
<td>4 years</td>
<td>7 (Frank 1982, Massin 2007, Cho 2011, Flack 1996, Lobefalo 1997, Murphy 1990, Cerutti 1989)</td>
<td>NC</td>
<td>1.0 to 23.0 (10.5)</td>
<td>Very low</td>
<td>Cross sectional and prospective cohort</td>
<td>No serious risk of bias</td>
<td>Very serious inconsistency</td>
</tr>
<tr>
<td>7 years</td>
<td>6 (Massin 2007, Flack 1996, Lobefalo 1997, Frank 1982, Cerutti 1989, Murphy 1990)</td>
<td>NC</td>
<td>6.2 to 50.0 (22.9)</td>
<td>Very low</td>
<td>Cross sectional and prospective cohort</td>
<td>No serious risk of bias</td>
<td>Very serious inconsistency</td>
</tr>
<tr>
<td>9 years</td>
<td>6 (Massin 2007, Lobefalo 1997, Frank)</td>
<td>NC</td>
<td>6.2 to 59.0 (37.0)</td>
<td>Very low</td>
<td>Cross sectional and prospective</td>
<td>No serious</td>
<td>Very serious inconsistency</td>
</tr>
</tbody>
</table>
## Diagnosis and management of type 1 diabetes in children and young people

### Appendix K: GRADE tables

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<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Range of prevalence, % (median, %)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1982, Goldstein 1993, Murphy 1990, Flack 1996</td>
<td>cohort</td>
<td></td>
<td>risk of bias</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Duration 10 years</strong></td>
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<tr>
<td><strong>Duration 11 years</strong></td>
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<tr>
<td><strong>Duration 12 years</strong></td>
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<tr>
<td><strong>Duration 13 years</strong></td>
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<tr>
<td>6 (Massin 2007, Lobefalo 1997, Flack 1996, Cerutti 1989, Frank 1982, Murphy 1990)</td>
<td>NC</td>
<td>13.0 to 75.0 (57.3)</td>
<td>Very low</td>
<td>Cross sectional and prospective cohort</td>
<td>No serious risk of bias</td>
<td>Very serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA^2</td>
<td>None</td>
</tr>
<tr>
<td><strong>Duration 14 years</strong></td>
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<tr>
<td>6 (Massin 2007, Lobefalo 1997, Joner 1992, Flack 1996, Cerutti 1989, Murphy 1990)</td>
<td>NC</td>
<td>13.0 to 75.0 (53.1)</td>
<td>Very low</td>
<td>Cross sectional and prospective cohort</td>
<td>No serious risk of bias</td>
<td>Very serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA^2</td>
<td>None</td>
</tr>
<tr>
<td><strong>Duration 15 years</strong></td>
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<tr>
<td><strong>Duration 16 years</strong></td>
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<tr>
<td>6 (Massin 2007, Lobefalo 1997, Flack 1996, Cerutti 1989, Frank 1982, Murphy 1990)</td>
<td>NC</td>
<td>13.0 to 75.0 (57.3)</td>
<td>Very low</td>
<td>Cross sectional and prospective cohort</td>
<td>No serious risk of bias</td>
<td>Very serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA^2</td>
<td>None</td>
</tr>
<tr>
<td><strong>Duration 17 years</strong></td>
<td></td>
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</tr>
<tr>
<td>5 (Massin 2007,</td>
<td>NC</td>
<td>13.0 to 75.0</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>No</td>
<td>Very serious</td>
<td>No serious</td>
<td>NA^2</td>
<td>None</td>
</tr>
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</table>
### Table 62: Evidence profile for incidence of retinopathy

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Incidence per hundred person years</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any sustained retinopathy</strong></td>
<td></td>
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<tr>
<td>1 (DCCT Research Group 1994)</td>
<td>55</td>
<td>18</td>
<td>High</td>
<td>Randomised controlled trial</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Intensive treatment group; no participant had retinopathy at baseline</td>
</tr>
<tr>
<td>1 (DCCT Research Group 1994)</td>
<td>70</td>
<td>23</td>
<td>High</td>
<td>Randomised controlled trial</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Conventional treatment group; no participant had retinopathy at baseline</td>
</tr>
<tr>
<td><strong>≥ 3 step worsening of retinopathy</strong></td>
<td></td>
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</tr>
<tr>
<td>1 (DCCT Research Group 1994)</td>
<td>55</td>
<td>3.2</td>
<td>High</td>
<td>Randomised controlled trial</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Intensive treatment group; no participant had retinopathy at baseline</td>
</tr>
<tr>
<td>1 (DCCT Research Group 1994)</td>
<td>70</td>
<td>6.3</td>
<td>High</td>
<td>Randomised controlled trial</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Conventional treatment group; no participant had retinopathy at baseline</td>
</tr>
<tr>
<td><strong>Any retinopathy</strong></td>
<td></td>
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</tr>
<tr>
<td>1 (Cheung 2008)</td>
<td>645</td>
<td>14.8</td>
<td>Moderate</td>
<td>Prospective cohort study</td>
<td>No serious</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>No participant had retinopathy at</td>
</tr>
</tbody>
</table>

NA not applicable, NC not calculable

- **a** Serious inconsistency between point estimates
- **b** Very serious inconsistency between point estimates
- **1** Serious inconsistency as range of point estimates varies between 10 and 20 percentage points
- **2** Unable to comment on imprecision as no confidence intervals reported for ranges
- **3** Very serious inconsistency as range of point estimates varies by more than 20 percentage points
### Diagnosis and management of type 1 diabetes in children and young people

#### Appendix K: GRADE tables

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Incidence per hundred person years</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Flack 1996)</td>
<td>182</td>
<td>7</td>
<td>Moderate</td>
<td>Prospective cohort study</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Incidence estimated by subtracting prevalence at start of study from prevalence at end of study.</td>
</tr>
<tr>
<td><strong>Any retinopathy in age group 0 to 9 years</strong></td>
<td></td>
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</tr>
<tr>
<td>1 (Klein 1989)</td>
<td>26</td>
<td>3.85</td>
<td>Moderate</td>
<td>Prospective cohort study</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>No participant had retinopathy at baseline</td>
</tr>
<tr>
<td>1 (Klein 1997)</td>
<td>14</td>
<td>0</td>
<td>Moderate</td>
<td>Prospective cohort study</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>No participant had retinopathy at baseline</td>
</tr>
<tr>
<td><strong>Any retinopathy in age group 10 to 12 years</strong></td>
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<tr>
<td>1 (Klein 1989)</td>
<td>42</td>
<td>13.7</td>
<td>Moderate</td>
<td>Prospective cohort study</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>No participant had retinopathy at baseline</td>
</tr>
<tr>
<td><strong>Any retinopathy in age group 13 – 14 years</strong></td>
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<tr>
<td>1 (Klein 1989)</td>
<td>25</td>
<td>12</td>
<td>Moderate</td>
<td>Prospective cohort study</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>No participant had retinopathy at baseline</td>
</tr>
<tr>
<td><strong>Any retinopathy in age group 10 to 14 years</strong></td>
<td></td>
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<tr>
<td>1 (Klein 1997)</td>
<td>47</td>
<td>1.08</td>
<td>Moderate</td>
<td>Prospective cohort study</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>No participant had retinopathy at baseline</td>
</tr>
</tbody>
</table>

*DCCT Diabetes Control and Complications Trial, NA not applicable*
K.17 Type 1 diabetes – nephropathy

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

Table 63: Evidence profile for prevalence of low-level albuminuria by age (albumin:creatinine ratio ranging from > 3.39 mg/mmol to > 3.5 mg/mmol in males, and from > 3.39 mg/mmol to > 4.0 mg/mmol in females, in at least 2 out of 3 urine collections)

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Range of prevalence, % (median, %)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age &lt; 10 years</strong></td>
<td></td>
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<tr>
<td>5 (Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Yoo 2004)</td>
<td>NC</td>
<td>0 to 66.7 (0)</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>Very serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA*</td>
<td>None</td>
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<tr>
<td><strong>Age 10 years</strong></td>
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<tr>
<td>8 (Bognetti 1997; Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Gallego 2006; Galler 2012; Yoo 2004)</td>
<td>NC</td>
<td>0 to 9 (0)</td>
<td>Very low</td>
<td>Cross sectional and prospective cohort</td>
<td>Very serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA*</td>
<td>None</td>
</tr>
<tr>
<td><strong>Age 11 years</strong></td>
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<tr>
<td>5 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002)</td>
<td>NC</td>
<td>0 to 10 (2.4)</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>Very serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA*</td>
<td>None</td>
</tr>
<tr>
<td><strong>Age 12 years</strong></td>
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<tr>
<td>6 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen et al. 2004)</td>
<td>NC</td>
<td>0 to 15.4 (2.2)</td>
<td>Very low</td>
<td>Cross sectional and prospective cohort</td>
<td>Very serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA*</td>
<td>None</td>
</tr>
<tr>
<td><strong>Age 13 years</strong></td>
<td></td>
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</tr>
<tr>
<td>6 (Cho 2011; Daniels 2013;</td>
<td>NC</td>
<td>0 to 67 (5)</td>
<td>Very low</td>
<td>Cross sectional and prospective cohort</td>
<td>Very serious risk of</td>
<td>Very serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA*</td>
<td>None</td>
</tr>
<tr>
<td>Number of studies</td>
<td>Number of children and young people</td>
<td>Range of prevalence, % (median, %)</td>
<td>Quality</td>
<td>Design</td>
<td>Quality assessment</td>
<td>Inconsistency</td>
<td>Indirectness</td>
<td>Imprecision</td>
<td>Other considerations</td>
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<tr>
<td>Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen 2004</td>
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<tr>
<td><strong>Age 14 years</strong></td>
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</tr>
<tr>
<td>6 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen 2004)</td>
<td>NC</td>
<td>0 to 67 (4.7)</td>
<td>Very low</td>
<td>Cross sectional and prospective cohort</td>
<td>Very serious risk of bias</td>
<td>Very serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA*</td>
<td>None</td>
</tr>
<tr>
<td><strong>Age 15 years</strong></td>
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</tr>
<tr>
<td>7 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Galler 2012; Olsen 2004)</td>
<td>NC</td>
<td>0 to 75 (5)</td>
<td>Very low</td>
<td>Cross sectional and prospective</td>
<td>Very serious risk of bias</td>
<td>Very serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA*</td>
<td>None</td>
</tr>
<tr>
<td><strong>Age 16 years</strong></td>
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<tr>
<td>6 (Cho 2011; Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen 2004)</td>
<td>NC</td>
<td>3 to 75 (9.9)</td>
<td>Very low</td>
<td>Cross sectional and prospective cohort</td>
<td>Very serious risk of bias</td>
<td>Very serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA*</td>
<td>None</td>
</tr>
<tr>
<td><strong>Age 17 years</strong></td>
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<tr>
<td>5 (Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen 2004)</td>
<td>NC</td>
<td>5 to 67 (14)</td>
<td>Very low</td>
<td>Cross sectional and prospective cohort</td>
<td>Very serious risk of bias</td>
<td>Very serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA*</td>
<td>None</td>
</tr>
<tr>
<td><strong>Age 18 years</strong></td>
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<tr>
<td>5 (Daniels 2013; Donaghue 1999; Dunger 2014; dos Santos 2002; Olsen 2004)</td>
<td>NC</td>
<td>5 to 67 (14)</td>
<td>Very low</td>
<td>Cross sectional and prospective cohort</td>
<td>Very serious risk of bias</td>
<td>Very serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA*</td>
<td>None</td>
</tr>
</tbody>
</table>

NA not applicable, NC not calculable
1. Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for in the majority of studies
2. Small sample size (28 participants) in 1 study (dos Santos 2002)
3. Reasons for losses to follow-up (ranging from 11% to 69%) not reported in most studies
4. Not applicable as no confidence intervals were reported
5. Range of prevalence estimates varied between 0% and 67% (prevalence of 67% calculated by NCC-WCH from a study of only 28 patients)
6. Range of prevalence estimates varied between 0% and 75% (prevalence of 75% calculated by NCC-WCH from a study of only 28 patients)
7. Range of prevalence estimates varied between 3% and 75% (prevalence of 75% calculated by NCC-WCH from a study of only 28 patients)
8. Range of prevalence estimates varied between 5% and 67% (prevalence of 67% calculated by NCC-WCH from a study of only 28 patients)

Table 64: Evidence profile for prevalence of low-level albuminuria by age (albumin:creatinine ratio > 4.59 in males, and > 5.24 mg/mmol in females, in at least 2 out of 3 urine collections)

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Range of prevalence, % (median, %)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age ≤ 10 years</strong></td>
<td></td>
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<tr>
<td>1 (Karavanaki 1999)</td>
<td>NC 0 to 0 (0)</td>
<td>Low Prospective cohort</td>
<td>Serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA*</td>
<td>None</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NA not applicable, NC not calculable
1. Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for in the study
2. Not applicable as no confidence intervals were reported

Table 65: Evidence profile for prevalence of low-level albuminuria by duration of diabetes (albumin:creatinine ratio ranging from > 3.39 mg/mmol to > 3.5 mg/mmol in males, and from > 3.39 mg/mmol to > 4.0 mg/mmol in females, in at least 2 out of 3 urine collections)

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Range of prevalence, % (median, %)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration &lt; 2 years</strong></td>
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</tr>
<tr>
<td>5 (Donaghue 1999; dos Santos 2002; Dunger 2014; Nicoloff 2001; Yoo 2004)</td>
<td>NC 0 to 0 (0)</td>
<td>Very low Cross sectional and prospective</td>
<td>Very serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA*</td>
<td>None</td>
<td></td>
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</tr>
</tbody>
</table>

| **Duration 2 years** |                                   |                                   |         |        |             |               |              |             |                     |
| 5 (Donaghue 1999; dos Santos 2002; Dunger 2014; Nicoloff 2001; Yoo 2004) | NC 0 to 16.7 (1) | Very low Cross sectional and prospective | Very serious risk of bias | No serious inconsistency | No serious indirectness | NA* | None |

<p>| <strong>Duration 3 years</strong> |                                   |                                   |         |        |             |               |              |             |                     |
| 4 | NC 0 to 2 | Very low Cross sectional | Very serious | No serious | No serious | NA* | None |</p>
<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Range of prevalence, % (median, %)</th>
<th>Quality</th>
<th>Design and prospective</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Donaghue 1999; Dos Santos 2002; Dunger 2014; Nicoloff 2001)</td>
<td>(0)</td>
<td></td>
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<tr>
<td><strong>Duration 4 years</strong></td>
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</tr>
<tr>
<td>5</td>
<td>(Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Nicoloff 2001)</td>
<td>NC</td>
<td>0 to 16.7 (2)</td>
<td>Very low</td>
<td>Cross sectional and prospective</td>
<td>Very serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA*</td>
</tr>
<tr>
<td><strong>Duration 5 years</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>6</td>
<td>(Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005; Nicoloff 2001)</td>
<td>NC</td>
<td>0 to 25 (2.8)</td>
<td>Very low</td>
<td>Cross sectional and prospective</td>
<td>Very serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA*</td>
</tr>
<tr>
<td><strong>Duration 6 years</strong></td>
<td></td>
<td></td>
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<tr>
<td>6</td>
<td>(Bognetti 1997; Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005)</td>
<td>NC</td>
<td>0 to 50 (4.4)</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>Very serious risk of bias</td>
<td>Very serious inconsistency*</td>
<td>No serious indirectness</td>
<td>NA*</td>
</tr>
<tr>
<td><strong>Duration 7 years</strong></td>
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</tr>
<tr>
<td>5</td>
<td>(Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005)</td>
<td>NC</td>
<td>1.9 to 26.1 (5)</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>Very serious risk of bias</td>
<td>Very serious inconsistency*</td>
<td>No serious indirectness</td>
<td>NA*</td>
</tr>
<tr>
<td><strong>Duration 8 years</strong></td>
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<tr>
<td>5</td>
<td>(Daniels 2013; Donaghue 1999; dos Santos 2002; Kong 2005)</td>
<td>NC</td>
<td>1.9 to 22.2 (5)</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>Very serious risk of bias</td>
<td>Very serious inconsistency*</td>
<td>No serious indirectness</td>
<td>NA*</td>
</tr>
<tr>
<td><strong>Duration 9 years</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>5</td>
<td>(Daniels 2013; Donaghue 1999; dos Santos 2002; Kong 2005)</td>
<td>NC</td>
<td>1.9 to 29 (5)</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>Very serious risk of bias</td>
<td>Very serious inconsistency*</td>
<td>No serious indirectness</td>
<td>NA*</td>
</tr>
</tbody>
</table>
### Number of studies, Number of children and young people, Range of prevalence, % (median, %), Quality, Design, Quality assessment

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Range of prevalence, % (median, %)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration 10 years</strong></td>
<td></td>
<td></td>
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<tr>
<td>5 (Daniels 2013; Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005)</td>
<td>NC</td>
<td>1.9 to 31.8 (6.9)</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>Very serious risk of bias(^ {1,2,3})</td>
<td>Very serious inconsistency(^ {7})</td>
<td>No serious indirectness</td>
<td>NA(^ {4})</td>
<td>None</td>
</tr>
<tr>
<td><strong>Duration 11 years</strong></td>
<td></td>
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<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>4 (Donaghue 1999; dos Santos 2002; Dunger 2014; Kong 2005)</td>
<td>NC</td>
<td>1 to 28.3 (20.2)</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>Very serious risk of bias(^ {1,2,3})</td>
<td>Very serious inconsistency(^ {8})</td>
<td>No serious indirectness</td>
<td>NA(^ {4})</td>
<td>None</td>
</tr>
<tr>
<td><strong>Duration 12 years</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2 (Dunger 2014; Kong 2005)</td>
<td>NC</td>
<td>1 to 16.3 (8.66)</td>
<td>Low</td>
<td>Cross sectional</td>
<td>Serious risk of bias(^ {7})</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA(^ {4})</td>
<td>None</td>
</tr>
<tr>
<td><strong>Duration 13 years</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>2 (Dunger 2014; Kong 2005)</td>
<td>NC</td>
<td>1 to 31.9 (16.5)</td>
<td>Low</td>
<td>Cross sectional</td>
<td>Serious risk of bias(^ {7})</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA(^ {4})</td>
<td>None</td>
</tr>
<tr>
<td><strong>Duration 14 years</strong></td>
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<tr>
<td>2 (Dunger 2014; Kong 2005)</td>
<td>NC</td>
<td>1 to 35.9 (18.5)</td>
<td>Low</td>
<td>Cross sectional</td>
<td>Serious risk of bias(^ {7})</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA(^ {4})</td>
<td>None</td>
</tr>
<tr>
<td><strong>Duration 15 years</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>2 (Dunger 2014; Kong 2005)</td>
<td>NC</td>
<td>1 to 20 (10.5)</td>
<td>Low</td>
<td>Cross sectional</td>
<td>Serious risk of bias(^ {7})</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA(^ {4})</td>
<td>None</td>
</tr>
</tbody>
</table>

NA not applicable, NC not calculable

1. Unclear whether important confounders for low-level oaluminuria prevalence estimates were accounted for in the majority of studies
2. Small sample size (28 participants) in 1 study (dos Santos 2002)
3. Reasons for losses to follow-up (ranging from 11% to 69%) not reported in most studies
4. Not applicable as no confidence intervals were reported
5. Range of prevalence estimates varied between 0% and 50% (prevalence of 50% calculated by NCC-WCH technical team from a study of only 28 participants)
6. Range of prevalence estimates varied between 1.87% and 20% (prevalence of 20% calculated by NCC-WCH technical team from a study of only 28 participants)
7. Range of prevalence estimates varied between 1.87% and 28.6% (prevalence of 28.6% calculated by NCC-WCH technical team from a study of only 28 participants)
8. Range of prevalence estimates varied between 1.02% and 80% (prevalence of 80% calculated by NCC-WCH technical team from a study of only 28 participants)
### Table 66: Evidence profile for incidence of low-level albuminuria by duration of diabetes (albumin:creatinine ratio > 3.5 mg/mmol in males, and > 4.0 mg/mmol in females, in at least 2 out of 3 urine collections)

<table>
<thead>
<tr>
<th>Duration</th>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Range of incidence, % (median, %)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 year</td>
<td>1 (Rudberg 1993)</td>
<td>NC</td>
<td>8 (NA)</td>
<td>Low</td>
<td>Prospective</td>
<td>Serious risk of bias¹</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA²</td>
<td>None</td>
</tr>
<tr>
<td>1 year</td>
<td>1 (Rudberg 1993)</td>
<td>NC</td>
<td>8 (NA)</td>
<td>Low</td>
<td>Prospective</td>
<td>Serious risk of bias¹</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA²</td>
<td>None</td>
</tr>
<tr>
<td>2 years</td>
<td>1 (Rudberg 1993)</td>
<td>NC</td>
<td>8 (NA)</td>
<td>Low</td>
<td>Prospective</td>
<td>Serious risk of bias¹</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA²</td>
<td>None</td>
</tr>
<tr>
<td>3 years</td>
<td>1 (Rudberg 1993)</td>
<td>NC</td>
<td>8 (NA)</td>
<td>Low</td>
<td>Prospective</td>
<td>Serious risk of bias¹</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA²</td>
<td>None</td>
</tr>
<tr>
<td>4 years</td>
<td>1 (Rudberg 1993)</td>
<td>NC</td>
<td>8 (NA)</td>
<td>Low</td>
<td>Prospective</td>
<td>Serious risk of bias¹</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA²</td>
<td>None</td>
</tr>
<tr>
<td>5 years</td>
<td>1 (Rudberg 1993)</td>
<td>NC</td>
<td>14 (NA)</td>
<td>Low</td>
<td>Prospective</td>
<td>Serious risk of bias¹</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA²</td>
<td>None</td>
</tr>
<tr>
<td>6 years</td>
<td>1 (Rudberg 1993)</td>
<td>NC</td>
<td>14 (NA)</td>
<td>Low</td>
<td>Prospective</td>
<td>Serious risk of bias¹</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA²</td>
<td>None</td>
</tr>
<tr>
<td>7 years</td>
<td>1 (Rudberg 1993)</td>
<td>NC</td>
<td>14 (NA)</td>
<td>Low</td>
<td>Prospective</td>
<td>Serious risk of bias¹</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA²</td>
<td>None</td>
</tr>
<tr>
<td>8 years</td>
<td>1 (Rudberg 1993)</td>
<td>NC</td>
<td>14 (NA)</td>
<td>Low</td>
<td>Prospective</td>
<td>Serious risk of bias¹</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA²</td>
<td>None</td>
</tr>
<tr>
<td>9 years</td>
<td>1 (Rudberg 1993)</td>
<td>NC</td>
<td>14 (NA)</td>
<td>Low</td>
<td>Prospective</td>
<td>Serious risk of bias¹</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA²</td>
<td>None</td>
</tr>
</tbody>
</table>

NA not applicable, NC not calculable

1. Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for
2. Not applicable as no confidence intervals were reported

K.18 Type 2 diabetes – education

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

There are no evidence profiles for this review question because no studies were identified for inclusion.

K.19 Type 2 diabetes – behavioural interventions

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

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

There are no evidence profiles for these review questions because no studies were identified for inclusion.

K.20 Type 2 diabetes – dietary advice

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

Table 67: Evidence profile for comparison of a very low calorie diet with usual care in morbidly obese African-American children and young people with type 2 diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Quality assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention</td>
<td>Comparator</td>
<td>Relative (95% confidence interval)</td>
<td>Absolute (95% confidence interval)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Change in BMI by end of diet (approximately 2 months after baseline)</td>
<td>1 (Willi 2004)</td>
<td>15</td>
<td>15</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Change in BMI by 6 months' follow-up</td>
<td>1</td>
<td>15</td>
<td>15</td>
<td>NA</td>
</tr>
<tr>
<td>Number of studies</td>
<td>Intervention</td>
<td>Comparator</td>
<td>Effect</td>
<td>Quality</td>
<td>Design</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------</td>
<td>------------</td>
<td>--------</td>
<td>---------</td>
<td>--------</td>
</tr>
<tr>
<td>1 (Willi 2004)</td>
<td>15</td>
<td>15</td>
<td>NA</td>
<td>MD: -12.7 (-18.1 to -7.2)</td>
<td>Very low</td>
</tr>
<tr>
<td><strong>Change in BMI by 12 months’ follow-up</strong></td>
<td></td>
<td></td>
<td></td>
<td>MD: -9.5 (-16.2 to 2.8)</td>
<td>Very low</td>
</tr>
<tr>
<td>1 (Willi 2004)</td>
<td>15</td>
<td>15</td>
<td>NA</td>
<td>MD: -9.1 (-16.8 to -1.4)</td>
<td>Very low</td>
</tr>
<tr>
<td><strong>Change in BMI by 24 months’ follow-up</strong></td>
<td></td>
<td></td>
<td></td>
<td>MD: -9.1 (-17.8 to -0.3)</td>
<td>Very low</td>
</tr>
<tr>
<td>1 (Willi 2004)</td>
<td>15</td>
<td>15</td>
<td>NA</td>
<td>MD: -1.6 (-3.5 to 0.3)</td>
<td>Very low</td>
</tr>
<tr>
<td><strong>HbA1c levels at end of diet (approximately 2 months after baseline)</strong></td>
<td></td>
<td></td>
<td></td>
<td>MD: -0.9 (-3.1 to 1.4)</td>
<td>Very low</td>
</tr>
<tr>
<td>1 (Willi 2004)</td>
<td>15</td>
<td>15</td>
<td>NA</td>
<td>MD: -0.5 (-2.7 to 1.7)</td>
<td>Very low</td>
</tr>
<tr>
<td><strong>HbA1c levels at 24 months after baseline</strong></td>
<td></td>
<td></td>
<td></td>
<td>MD: -0.4 (-2.7 to 1.9)</td>
<td>Very low</td>
</tr>
</tbody>
</table>

**BMI** body mass index, CI confidence interval, NA not applicable, MD mean difference, SDS standard deviation score, SE standard error

a Point estimate and SE derived from graphs by NCC-WCH technical team

b CI calculated using t-distribution due to small sample size

1 No randomisation used to allocate the intervention

2 Usual care for controls is unclear; likely to differ from intervention group by more than just diet as intervention group was withdrawn from oral anti-diabetic medication before treatment
K.21 Type 2 diabetes – weight loss

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

Table 68: Evidence profile for effectiveness of weight loss in children and young people with type 2 diabetes who are overweight or obese in improving glycaemic control

<table>
<thead>
<tr>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>RCT</td>
<td>No serious risk of bias¹</td>
<td>No serious inconsistency²</td>
<td>Serious indirectness³</td>
<td>No serious imprecision⁴</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>RCT</td>
<td>No serious risk of bias¹</td>
<td>No serious inconsistency²</td>
<td>Serious indirectness³</td>
<td>NA⁶</td>
<td>None</td>
</tr>
</tbody>
</table>

CI confidence interval, NA not applicable, RR relative risk, RCT randomised controlled trial, TODAY Treatment Options for type 2 Diabetes in Adolescents and Youth

a The study defined treatment failure as a persistently elevated glycated haemoglobin level of 8% or higher over a period of 6 months or persistent metabolic decompensation (defined as either the inability to wean the participant from insulin within 3 months of its initiation for decompensation or the occurrence of a second episode of decompensation within 3 months of discontinuation of insulin)

1 The evaluation identified no serious risk of bias
2 Single-study analysis
3 The outcomes reported in the study were not strictly pertinent to the requirements of the protocol
K.22 Type 2 diabetes – metformin

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

Table 69: Evidence profile for effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with placebo

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Effect</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HbA1c value (% at endpoint)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1 (Jones 2002)</td>
<td>36</td>
<td>36</td>
<td>NA</td>
<td>MD between the groups at endpoint 1.1 lower (1.19 lower to 1.01 lower)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias¹</td>
<td>No serious inconsistency²</td>
<td>No serious indirectness³</td>
</tr>
<tr>
<td><strong>Number needing rescue medication</strong></td>
<td></td>
<td></td>
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<tr>
<td>1 (Jones 2002)</td>
<td>4/42 (9.5%)</td>
<td>26/40 (65%)</td>
<td>RR 0.15 (0.06 to 0.4)</td>
<td>552 fewer per 1000 (from 390 fewer to 611 fewer)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias¹</td>
<td>No serious inconsistency²</td>
<td>No serious indirectness³</td>
</tr>
<tr>
<td><strong>Number reporting any adverse event (including number with DKA)</strong></td>
<td></td>
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</tr>
<tr>
<td>1 (Jones 2002)</td>
<td>29/42 (69%)</td>
<td>24/40 (60%)</td>
<td>RR 1.15 (0.83 to 1.59)</td>
<td>90 more per 1000 (from 102 fewer to 354 more)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias¹</td>
<td>No serious inconsistency²</td>
<td>No serious indirectness³</td>
</tr>
<tr>
<td><strong>Number of dropouts</strong></td>
<td></td>
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</tr>
<tr>
<td>1 (Jones 2002)</td>
<td>6/42 (14.3%)</td>
<td>4/40 (10%)</td>
<td>RR 1.43 (0.42 to 3.91)</td>
<td>43 more per 1000 (from 58 fewer to 291 more)</td>
<td>High</td>
<td>RCT</td>
<td>No serious risk of bias¹</td>
<td>No serious inconsistency²</td>
<td>No serious indirectness³</td>
</tr>
<tr>
<td><strong>FPG concentration (change from baseline, mmol/l)</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Jones 2002)</td>
<td>36</td>
<td>36</td>
<td>NA</td>
<td>MD between</td>
<td>High</td>
<td>RCT</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
</tr>
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</table>
Appendix K: GRADE tables

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Metformin</th>
<th>Placebo</th>
<th>Relative (95% confidence interval)</th>
<th>Absolute (95% confidence interval)</th>
<th>Quality</th>
<th>Design</th>
<th>Limitations (risk of bias)</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
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</thead>
<tbody>
<tr>
<td>2002)</td>
<td></td>
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</tbody>
</table>

DKA diabetic ketoacidosis, FPG fasting plasma glucose, MD mean difference, NA not applicable, RCT randomised controlled trial, RR relative risk

K.23 Type 2 diabetes – HbA1c targets

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

There are no evidence profiles for this review question because no studies were identified for inclusion.

K.24 Type 2 diabetes – hypertension

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

Table 70: Evidence profile for prevalence of hypertension by age

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age of 13.2 years at diagnosis</td>
<td>Hypertension (blood pressure values &gt; 95th percentile)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Reinhr 2008)</td>
<td>51</td>
<td>44.0% (30.1 to 57.9)</td>
<td>Very low</td>
<td>Prospective chart review</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>Serious</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
</tbody>
</table>

Aged 10 to 15 years at diagnosis
Diagnosis and management of type 1 diabetes in children and young people

Appendix K: GRADE tables

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Quality assessment</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (systolic blood pressure &gt; 130mmHg and diastolic blood pressure &gt; 85mmHg)</td>
<td>1 (Urakami 2009)</td>
<td>112</td>
<td>11.6% (5.6 to 17.6)*</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>No serious bias</td>
<td>No serious inconsistency</td>
<td>Very serious</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
</tbody>
</table>

CI confidence interval, IQR interquartile range

*Calculated by the NCC-WCH technical team.

1 Data were analysed only for participants with complete follow up (51/129, 39.5%); the study authors stated that the 78 participants who dropped out did not differ significantly at baseline from those who were successfully followed up

2 Single-study analysis

3 Prevalence estimates do not relate to a specific age; only the median age was reported (13.2 years, IQR 12.1 to 14.7)

4 Prevalence estimates do not relate to a specific age; only the mean age was reported (12.9 years ± 1.5)

5 Hypertension was defined based on absolute values and not percentiles

6 The study population comprised Japanese participants therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited

Table 71: Evidence profile for prevalence of hypertension by duration of diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Quality assessment</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Within 1 year of diagnosis</td>
<td>Hypertension (systolic or diastolic &gt; 95th percentile)</td>
<td>1 (Rodriguez 2010)</td>
<td>176</td>
<td>18.2% (12.5 to 23.9)*</td>
<td>Very low</td>
<td>Prospective multi-centre study</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
</tr>
</tbody>
</table>

| Within 2 years of diagnosis | Hypertension (blood pressure values > 90th percentile) | 1 (Copeland 2011) | 704 | 26.3% (23.0 to 29.6)* | Low | Analysis of baseline data from a randomised controlled trial | No serious bias | No serious inconsistency | Serious | No serious imprecision | None |

| Hypertension (blood pressure values > 95th percentile) | 1 (Copeland 2011) | 704 | 13.6% (11.1 to 16.1)* | Low | Analysis of baseline data from a randomised controlled trial | No serious bias | No serious inconsistency | Serious | No serious imprecision | None |

| Two years after diagnosis | Hypertension (blood pressure values > 95th percentile) | 1 (Reinehr 2008) | 51 | 32.0% (18.9 to 45.1)* | Very low | Prospective chart review | Serious | No serious inconsistency | No serious indirectness | No serious imprecision | None |
### Within 3 years of diagnosis

**Hypertension (blood pressure values ≥ 95th percentile)**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Ettinger 2005)</td>
<td>26</td>
<td>58.0% (38.0 to 78.0)%</td>
<td>Very low</td>
<td>Prospective chart review</td>
<td>No serious bias</td>
<td>No serious inconsistency</td>
<td>Very serious&lt;sup&gt;a&lt;/sup&gt;</td>
<td>No serious imprecision</td>
<td>Yes&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

**Within 4 years of diagnosis**

**Hypertension (systolic and diastolic > 95th percentile)**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Eppens 2006)</td>
<td>265</td>
<td>8.0% (4.7 to 11.3)%</td>
<td>Very low</td>
<td>Cross-sectional survey</td>
<td>Very serious&lt;sup&gt;6,9&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Very serious&lt;sup&gt;3,10&lt;/sup&gt;</td>
<td>No serious imprecision</td>
<td>Yes&lt;sup&gt;11&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

**Hypertension (systolic > 95th percentile)**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Hotu 2004)</td>
<td>3</td>
<td>28.0% (5.6 to 50.4)%</td>
<td>Very low</td>
<td>Cross-sectional survey</td>
<td>No serious bias</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Very serious&lt;sup&gt;3,12,13&lt;/sup&gt;</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
</tbody>
</table>

**Between 1 and 5 years after diagnosis**

**Hypertension (systolic or diastolic > 95th percentile)**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Rodriguez 2010)</td>
<td>219</td>
<td>27.9% (22.0 to 33.8)%</td>
<td>Very low</td>
<td>Prospective multi-centre study</td>
<td>Serious&lt;sup&gt;14&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
</tbody>
</table>

**More than 5 years after diagnosis**

**Hypertension (systolic or diastolic > 95th percentile)**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Rodriguez 2010)</td>
<td>15</td>
<td>26.7% (2.3 to 51.1)%</td>
<td>Very low</td>
<td>Prospective multi-centre study</td>
<td>Very serious&lt;sup&gt;15&lt;/sup&gt;</td>
<td>No serious inconsistency&lt;sup&gt;2&lt;/sup&gt;</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
</tbody>
</table>

CI confidence interval, RCT randomised controlled trial

<sup>a</sup> Calculated by the NCC-WCH technical team

1 Data for this outcome were available for only 176 (42.9%) of the 410 participants in the study
2 Single-study analysis
3 Prevalence estimates do not relate to specific times after diagnosis
4 Starting point of moderate for quality rating as baseline analysis of an RCT
5 Data were analysed only for participants with complete follow up (51/129, 39.5%); the study authors stated that the 78 participants who dropped out did not differ significantly at baseline from those who were successfully followed up
6 The population comprised non-Hispanic black or Hispanic Latino participants therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited
7 Children and young people who were taking anti-hypertensive medication were eligible for inclusion
8 Participants with missing data were excluded from analysis however the number of missing values was not reported
9 Hypertension was screened for in only 80% of participants
10 The majority of the population comprised Western Pacific Islanders therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited
11 The minimum duration of diabetes of study participants was 12 months
12 The study population comprised Maori and Pacific Islanders therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited
13 The study population comprised young people aged 18 and 19 years (age range 11 to 19 years); it is unclear at what time point after diagnosis the prevalence estimate for hypertension is based on therefore some participants may be above the age range specified in the protocol for this review
14 Data for this outcome were available for only 219 (53.4%) of the 410 participants in the study
15 Data for this outcome were available for only 15 (3.7%) of the 410 participants in the study
K.25 Type 2 diabetes – dyslipidaemia

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

Table 72: Evidence profile for prevalence of dyslipidaemia by age

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Quality assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Risk of bias</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Inconsistency</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Indirectness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Imprecision</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other considerations</td>
</tr>
<tr>
<td><strong>Median age of 13.2 years at diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevalence of dyslipidaemiaa</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Reinehr 2008)</td>
<td>51</td>
<td>65.0% (51.6 to 78.4)b</td>
<td>Very low</td>
<td>Prospective chart review</td>
<td>Very Serious1,2</td>
</tr>
<tr>
<td><strong>Aged between 10 and 15 years at diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides &gt; 150mg/dl (1.7mmol/l)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Urakami 2009)</td>
<td>112</td>
<td>33.0% (24.2 to 41.8)b</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>No serious bias</td>
</tr>
<tr>
<td>High density lipoproteins &lt; 40mg/dl (1.0mmol/l)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Urakami 2009)</td>
<td>112</td>
<td>21.4% (13.7 to 29.1)b</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>No serious bias</td>
</tr>
</tbody>
</table>

CI confidence interval, HDL high-density lipoprotein, IQR interquartile range, LDL low-density lipoprotein, RCT randomised controlled trial

a Dyslipidaemia was defined using the following cut-offs: total cholesterol > 5.1mmol/l (200mg/dl), LDL > 3.3mmol/l (130mg/dl), HDL < 0.9mmol (35mg/dl) or triglycerides > 1.7mmol/l (150mg/dl)

b Calculated by the NCC-WCH technical team

c Based on the age range for inclusion in the study as the actual age range of participants was not reported

1 Data were analysed only for participants with complete follow-up (51/129, 39.5%); the study authors stated that the 78 participants who dropped out did not differ significantly at baseline from those who were successfully followed up

2 The study did not report whether or not total cholesterol, LDL, HDL, and triglycerides were measured using fasting samples, and this would affect the accuracy of LDL and triglyceride measurements

3 Single-study analysis

4 Prevalence estimates do not relate to a specific age; only the median age was reported (13.2 years, IQR 12.1 to 14.7)

5 Prevalence estimates do not relate to a specific age; only the mean age was reported (12.9 years ± 1.5)

6 The population comprised Japanese participants therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited

Table 73: Evidence profile for prevalence of dyslipidaemia by duration of diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Quality assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Risk of bias</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Inconsistency</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Indirectness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Imprecision</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other considerations</td>
</tr>
<tr>
<td><strong>At 1 year after diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevalence of LDL &gt; 130mg/dl (3.4mmol/l)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Le 2013)</td>
<td>86</td>
<td>12.5% (5.4 to 19.6)b</td>
<td>Very low</td>
<td>Retrospective chart review</td>
<td>Serious bias1</td>
</tr>
<tr>
<td>Prevalence of HDL &lt; 35mg/dl (0.9mmol/l)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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### Within 2 years of diagnosis

**Low density lipoproteins ≥ 160mg/dl (4.1mmol/l)**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Copeland 2011)</td>
<td>704</td>
<td>0.4% (0.00 to 0.87)*</td>
<td>Low</td>
<td>Analysis of baseline data from a randomised controlled trial</td>
<td>No serious bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td></td>
</tr>
</tbody>
</table>

**High density lipoproteins < 50mg/dl (1.3mmol/l, females) or < 40mg/dl (1.0mmol/l, males)**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Copeland 2011)</td>
<td>704</td>
<td>79.8% (76.8 to 82.8)*</td>
<td>Low</td>
<td>Analysis of baseline data from a randomised controlled trial</td>
<td>No serious bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td></td>
</tr>
</tbody>
</table>

**Triglycerides ≥ 200mg/dl (2.3mmol/l)**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Copeland 2011)</td>
<td>704</td>
<td>10.2% (8.0 to 12.4)*</td>
<td>Low</td>
<td>Analysis of baseline data from a randomised controlled trial</td>
<td>No serious bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td></td>
</tr>
</tbody>
</table>

### At 2 years after diagnosis

**Prevalence of dyslipidaemia**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Reinehr 2008)</td>
<td>51</td>
<td>69.0% (56.0 to 82.0)*</td>
<td>Very low</td>
<td>Prospective chart review</td>
<td>Very serious</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td></td>
</tr>
</tbody>
</table>

### Within 3 years of diagnosis

**Dyslipidaemia (not defined)**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Ettinger 2005)</td>
<td>26</td>
<td>69.2% (50.5 to 87.9)*</td>
<td>Very low</td>
<td>Prospective chart review</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>Very serious</td>
<td>No serious imprecision</td>
<td></td>
</tr>
</tbody>
</table>

### Within 4 years of diagnosis

**Total cholesterol ≥ 6mmol/l**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Eppens 2006)</td>
<td>331</td>
<td>12.0% (8.5 to 15.5)*</td>
<td>Very low</td>
<td>Cross-sectional survey</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>Very serious</td>
<td>No serious imprecision</td>
<td>Yes*</td>
</tr>
</tbody>
</table>

**Low density lipoproteins > 4mmol/l**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Eppens 2006)</td>
<td>331</td>
<td>12.0% (8.5 to 15.5)*</td>
<td>Very low</td>
<td>Cross-sectional survey</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>Very serious</td>
<td>No serious imprecision</td>
<td>Yes*</td>
</tr>
</tbody>
</table>

**High density lipoproteins < 0.9mmol/l**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Eppens 2006)</td>
<td>331</td>
<td>10.0% (6.8 to 13.2)*</td>
<td>Very low</td>
<td>Cross-sectional survey</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>Very serious</td>
<td>No serious imprecision</td>
<td>Yes*</td>
</tr>
</tbody>
</table>

**Triglycerides ≥ 2.2mmol/l**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Eppens 2006)</td>
<td>331</td>
<td>16.0% (12.1 to 19.9)*</td>
<td>Very low</td>
<td>Cross-sectional survey</td>
<td>Serious</td>
<td>No serious inconsistency</td>
<td>Very serious</td>
<td>No serious imprecision</td>
<td>Yes*</td>
</tr>
</tbody>
</table>

**Total cholesterol:high density lipoproteins molar ratio > 4.5 molar units**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Hotu 2004)</td>
<td>13</td>
<td>85.0% (63.4 to 1.00)*</td>
<td>Very low</td>
<td>Cross-sectional survey</td>
<td>Very serious</td>
<td>No serious inconsistency</td>
<td>Very serious</td>
<td>No serious imprecision</td>
<td>Yes*</td>
</tr>
</tbody>
</table>

CI confidence interval, HDL high-density lipoprotein, IQR interquartile range, LDL low-density lipoprotein, RCT randomised controlled trial

* Calculated by the NCC-WCH technical team

b Starting point of moderate for quality rating as baseline analysis of an RCT
Dyslipidaemia was defined using the following cut-offs: total cholesterol > 5.1mmol/l (200mg/dl), LDL > 3.3mmol/l (130mg/dl), HDL < 0.9mmol (35mg/dl) or triglycerides > 1.7mmol/l (150mg/dl).

1. Due to the retrospective study design, the study could not guarantee the fasting status of lipid measures, which would affect the accuracy of LDL and triglycerides.
2. Single-study analysis
3. Prevalence estimates do not relate to specific times after diagnosis
4. Data were analysed only for participants with complete follow-up (51/129, 39.5%); the study authors stated that the 78 participants who dropped out did not differ significantly at baseline from those who were successfully followed up
5. The study did not report whether or not total cholesterol, LDL, HDL, and triglycerides were measured using fasting samples and this would affect the accuracy of LDL and triglyceride measurements.
6. Dyslipidaemia was not defined
7. The population comprised non-Hispanic black or Hispanic Latino participants therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited
8. Participants with missing data were excluded from analysis however the number of missing values was not reported
9. The majority of the population comprised Western Pacific Islanders therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited
10. The minimum duration of diabetes of study participants was 12 months (this item was not included in evidence grading)
11. Dyslipidaemia was measured in only 72.0% (13/18) of study participants
12. The study population comprised Maori and Pacific Islanders therefore generalisability with respect to children and young people with type 2 diabetes in the UK is limited
13. The study population comprised young people aged 18 and 19 years (age range 11 to 19 years); it is unclear at what time point after diagnosis the prevalence estimate for dyslipidaemia is based on and, therefore, some participants may be above the age range specified in the protocol for this review.

K.26 Type 2 diabetes – retinopathy

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

Table 74: Evidence profile for prevalence of retinopathy according to age

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 to 16 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Levitsky 2013)</td>
<td>140</td>
<td>5.7 (2.5 to 11.0)*</td>
<td>Moderate</td>
<td>Randomised controlled trial</td>
<td>No serious risk of bias</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
<tr>
<td>17 to 18 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Levitsky 2013)</td>
<td>137</td>
<td>12.4 (7.4 to 19.1)*</td>
<td>Moderate</td>
<td>Randomised controlled trial</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
<tr>
<td>10.8 to 17.8 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Shield 2009)</td>
<td>55</td>
<td>0.0 (0.0 to 6.5)*</td>
<td>Lowc</td>
<td>Prospective cohort</td>
<td>Serious risk of bias1</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>None</td>
</tr>
</tbody>
</table>

CI confidence interval, NA not applicable, RCT randomised controlled trial

* 95% CI calculated by NCC-WCH technical team from data reported in the article
**Diagnosis and management of type 1 diabetes in children and young people**

**Appendix K: GRADE tables**

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**Table 75: Evidence profile for prevalence of retinopathy according to duration of diabetes**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Prevalence, % (95% CI)</th>
<th>Quality</th>
<th>Design</th>
<th>Quality assessment</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 months</td>
<td>1 (Shield 2009)</td>
<td>0.0 (0.0 to 6.5) a</td>
<td>Low b</td>
<td>Prospective cohort</td>
<td>Serious risk of bias</td>
<td>NA</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 to 49 months</td>
<td>1 (Levitsky 2013)</td>
<td>5.3 (2.5 to 9.8) a</td>
<td>Low c,d</td>
<td>Randomised controlled trial</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>Serious indirectness</td>
<td>No serious imprecision</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 to 66 months</td>
<td>1 (Levitsky 2013)</td>
<td>13.4 (8.7 to 19.4) a</td>
<td>Low c,d</td>
<td>Randomised controlled trial</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>Serious indirectness</td>
<td>No serious imprecision</td>
<td></td>
<td></td>
</tr>
<tr>
<td>67 to 101 months</td>
<td>1 (Levitsky 2013)</td>
<td>22.3 (16.3 to 29.2) a</td>
<td>Low c,d</td>
<td>Randomised controlled trial</td>
<td>No serious risk of bias</td>
<td>NA</td>
<td>Serious indirectness</td>
<td>No serious imprecision</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI confidence interval, NA not applicable, RCT randomised controlled trial
a 95% CI calculated by NCC-WCH technical team from data reported in the article
b Serious risk of bias
c Although the study design was an RCT, data obtained were cross-sectional and observational in nature
d Serious indirectness
1 Study design included postal survey of clinicians therefore at risk of selection bias

---

**K.27 Type 2 diabetes – nephropathy**

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

**Table 76: Evidence profile for prevalence of low-level albuminuria by age in children and young people with type 2 diabetes**

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Range of prevalence, % (median, %)</th>
<th>Quality</th>
<th>Design</th>
<th>Quality assessment</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;11</td>
<td>1 (Yoo. 2004)</td>
<td>NC 0 (NA)</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>Very serious risk of bias</td>
<td>NA</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA d</td>
<td>None</td>
</tr>
</tbody>
</table>

CI confidence interval, NA not applicable, RCT randomised controlled trial
d Serious risk of bias
c Although the study design was an RCT, data obtained were cross-sectional and observational in nature

---

b Although the study design was an RCT, data obtained were cross-sectional and observational in nature
c Serious risk of bias
1 Study design included postal survey of clinicians therefore at risk of selection bias
**Low-level albuminuria defined as albumin:creatinine ratio (ACR) > 3.5 mg/mmol in males and ACR > 4.0 mg/mmol in females in at least 2 out of 3 urine collections**

NC not calculable, NA not applicable

1 Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for in the study

2 Small sample sizes (22 participants) for type 2 diabetes

3 Not applicable as confidence intervals were not reported

### Table 77: Evidence profile for prevalence of low-level albuminuria by duration of diabetes in children and young people with type 2 diabetes

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of children and young people</th>
<th>Range of prevalence, % (median, %)</th>
<th>Quality</th>
<th>Design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration &lt; 2 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 (Farah 2006; Lynch 2013; Yoo 2004)</td>
<td>NC</td>
<td>0 to 29.6 (6.3)</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>Very serious risk of bias(^1,2)</td>
<td>Very serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA(^*)</td>
<td>None</td>
</tr>
<tr>
<td>Duration 2 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Farah 2006)</td>
<td>NC</td>
<td>29.6 (NA)</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>Very serious risk of bias(^1,2)</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA(^*)</td>
<td>None</td>
</tr>
<tr>
<td>Duration 3 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Farah 2006)</td>
<td>NC</td>
<td>32.3 (NA)</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>Very serious risk of bias(^1,2)</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA(^*)</td>
<td>None</td>
</tr>
<tr>
<td>Duration 4 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Farah 2006)</td>
<td>NC</td>
<td>32.3 (NA)</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>Very serious risk of bias(^1,2)</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA(^*)</td>
<td>None</td>
</tr>
<tr>
<td>Duration 5 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (Farah 2006)</td>
<td>NC</td>
<td>32.3 (NA)</td>
<td>Very low</td>
<td>Cross sectional</td>
<td>Very serious risk of bias(^1,2)</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>NA(^*)</td>
<td>None</td>
</tr>
</tbody>
</table>

Low-level albuminuria defined as albumin:creatinine ratio (ACR) > 3.5 mg/mmol in males and ACR > 4.0 mg/mmol in females in at least 2 out of 3 urine collections

NC not calculable, NA not applicable

1 Unclear whether important confounders for low-level albuminuria prevalence estimates were accounted for in studies

2 Small sample sizes in studies for type 2 diabetes (40 participants in Farah 2006 and 22 in Yoo 2004)

3 Prevalence estimates ranged from 0% to 29.6%

4 Not applicable as confidence intervals were not reported
Appendix L: Research recommendations

L.1 2015 recommendations for research

L.1.1 Type 1 diabetes – education

L.1.1.1 What is the clinical and cost effectiveness of a programme of structured education from diagnosis for children and young people with type 1 diabetes?

Why is this important

The GDG has recommended education from diagnosis for children and young people with type 1 diabetes but not specified that this should be 'structured' because there is no evidence to support structured education delivered at diagnosis. Future research should compare a structured education programme delivered from diagnosis with a non-structured education programme delivered from diagnosis (usual care). Important outcomes will include achieving the target HbA1c after 1 year and satisfaction of the child or young person and their family members or carers (as appropriate).

L.1.1.2 What is the impact of training in teaching skills for healthcare professionals on the effectiveness of education for children and young people with type 1 diabetes?

Why this is important

The GDG has recommended that children and young people with type 1 diabetes should be offered education, but has not specified that the education should be delivered by healthcare professionals trained in its delivery. Future research should use randomised controlled trials to compare diabetes education delivered by healthcare professionals who have received training in teaching skills and those who have not. Different approaches to training (such as participating in training in schools) should be considered as part of the research. Important outcomes will include the child or young person achieving their target HbA1c, satisfaction of the child or young person and their family members or carers (as appropriate), and satisfaction among healthcare professionals delivering the education.

L.1.1.3 What is the effectiveness of education programmes in which young people with type 1 diabetes provide training for their peers?

Why this is important

Training delivered by peers is effective both in healthcare and in other settings. This research should evaluate the engagement of the child or young person with type 1 diabetes and their family members or carers (as appropriate), and outcomes for the child or young person. Outcomes could include their success in achieving their target HbA1c level, engagement with diabetes care and management (for example, attendance at clinic), and satisfaction with the education programme. The impact on the young person delivering the training should also be evaluated (this could cover the impact on their diabetes care and the psychosocial impact of providing training for their peers). The research should be conducted using quantitative, qualitative and mixed methods.

This is a rephrasing of a 2004 research recommendation to comply with current NICE format and style as it was selected a key research recommendation by the GDG for the 2015 update. The justification for the selection is summarised in the table below.
### Potential criterion | Explanation
---|---
Importance to patients or the population | This is of importance because there is evidence of the effectiveness of peer-delivered education in other healthcare and wider settings
Relevance to NICE guidance | Relevant to a future update of this guideline
Relevance to the NHS | Relevant to a future update of this guideline and potential reduction in costs associated with long-term complications
National priorities | Not applicable
Current evidence base | Lack of evidence specific to peer-delivered education in children and young people with diabetes
Equality | Research would need to take account of accessibility to and effectiveness of education for people with protected characteristics such as different age and ethnic groups
Feasibility | Feasible
Other comments | None

### L.1.2 Type 1 diabetes – blood glucose targets

#### L.1.2.1 What is the optimal upper limit and timing for blood glucose measurements after meals for children and young people with type 1 diabetes to achieve an HbA1c level of 48 mmol/mol (6.5%) without unacceptable hypoglycaemia?

**Why this is important**

Setting an upper limit for blood glucose measurements 1–2 hours after meals of less than 8 mmol/litre (rather than the 9 mmol/litre recommended in this guideline) could potentially lead to an improvement in blood glucose control without an unacceptable risk of hypoglycaemia. The evidence reviewed for the guideline did not allow a precise evaluation of the upper limit for the target range, or the timing of blood glucose testing relative to meals. Future research should investigate the HbA1c levels of children and young people with type 1 diabetes who aim for blood glucose measurements after meals slightly lower (to ensure their safety) than 9 mmol/litre, to help decide whether lowering the upper limit is effective in improving long-term blood glucose control. Outcomes include the child or young person’s satisfaction with treatment, their HbA1c levels, rates of hypoglycaemia, and the views of their family members or carers (as appropriate), and quality of life.

This was selected a key research recommendation by the GDG for the 2015 update. The justification for the selection is summarised in the table below.

### Potential criterion | Explanation
---|---
Importance to patients or the population | This is of importance because it is of interest to know whether it is safe and acceptable to refine the target range for postprandial blood glucose measurements
Relevance to NICE guidance | Relevant to a future update of this guideline
Relevance to the NHS | Relevant to a future update of this guideline and potential reduction in costs associated with long-term complications
National priorities | Not applicable
Current evidence base | Further evidence is needed
Equality | Not applicable
Feasibility | Feasible
Other comments | None
L.1.3 Type 1 diabetes – intermittent continuous glucose monitoring compared with real-time continuous glucose monitoring

L.1.3.1 What is the clinical and cost effectiveness of real-time continuous glucose monitoring systems compared to 5 or more capillary blood glucose tests per day in children aged 5 years or younger with type 1 diabetes who use insulin pump therapy?

Why this is important

The GDG’s recommendation was to consider ongoing real-time continuous glucose monitoring systems (CGMS) for neonates, infants and pre-school children with type 1 diabetes. This weak recommendation reflected a lack of evidence of effectiveness of CGMS in such children (only a few studies having been conducted in this age group). The GDG considered use of CGMS in this age group to be important because of the risk of adverse neurodevelopmental consequences of type 1 diabetes and parental anxiety (particularly in those with pre-school children). Further research in the form of a multi-centre randomised controlled trial comparing CGMS with 5 or more capillary blood glucose tests per day is needed to achieve a large enough sample size. Important outcomes include HbA1c levels, incidence of hypoglycaemia, satisfaction of the child and their family members or carers (as appropriate), and quality of life. Future research should ideally monitor neurodevelopmental consequences but this would require studies with long-term follow up.

L.1.4 Type 1 diabetes – dietary advice

L.1.4.1 What is the impact of educating children and young people with type 1 diabetes and their family members or carers (as appropriate) about their glycaemic index from diagnosis?

Why this is important

Very little evidence on the effectiveness of dietary advice based on glycaemic index was identified for inclusion in the guideline review, and the evidence that was identified related mostly to twice-daily insulin regimens. Research is needed to evaluate the effectiveness of teaching children and young people with type 1 diabetes and their family members or carers (as appropriate) about glycaemic index in the context of modern, intensive insulin treatment regimens (insulin pump therapy or multiple daily injections). Important outcomes include success in achieving the target HbA1c level, blood glucose levels after meals, frequency of hypoglycaemia, quality of life, food choices, and the frequency and timing of insulin administration to lower blood glucose levels after meals.

This was selected a key research recommendation by the GDG for the 2015 update. The justification for the selection is summarised in the table below.

<table>
<thead>
<tr>
<th>Potential criterion</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Importance to patients or the population</td>
<td>This is of importance because there is very little evidence of effectiveness of dietic advice based on glycaemic index from diagnosis in terms of improving glycaemic control</td>
</tr>
<tr>
<td>Relevance to NICE guidance</td>
<td>Relevant to a future update of this guideline</td>
</tr>
<tr>
<td>Relevance to the NHS</td>
<td>Relevant to a future update of this guideline and potential reduction in costs associated with long-term complications</td>
</tr>
<tr>
<td>National priorities</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Current evidence base</td>
<td>Lack of evidence currently other than in relation to cardiovascular health and no evidence in relation to modern intensive insulin treatment regimens</td>
</tr>
<tr>
<td>Equality</td>
<td>Research would need to take account of accessibility to and</td>
</tr>
</tbody>
</table>
L.1.5  Type 1 and type 2 diabetes – diabetic ketoacidosis – insulin

L.1.5.1  What is the optimal dosage of intravenous insulin for managing diabetic ketoacidosis (DKA) in children and young people?

Why this is important

The evidence reviewed for the guideline did not allow evaluation of the comparative effectiveness and safety of specific dosages of intravenous insulin, such as 0.025, 0.05 and 0.1 units/kg/hour. The only relevant studies conducted to date have been small retrospective cohort studies with fewer than 100 participants. A large, multi-centre randomised controlled trial is needed to undertake a comparative study of different dosages. This is because DKA is relatively uncommon and cerebral oedema (a potential adverse consequence of DKA) is rare, and there is a concern that larger dosages are associated with an increased risk of cerebral oedema. Important outcomes include rate of DKA resolution, incidence of hypoglycaemia and incidence of cerebral oedema.

This was selected a key research recommendation by the GDG for the 2015 update. The justification for the selection is summarised in the table below.

<table>
<thead>
<tr>
<th>Potential criterion</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Importance to patients or the population</td>
<td>The GDG was able to make a recommendation about dosages of 0.05-0.1 units/kg/hour and further research would allow refinement of the recommendations</td>
</tr>
<tr>
<td>Relevance to NICE guidance</td>
<td>Relevant to a future update of this guideline</td>
</tr>
<tr>
<td>Relevance to the NHS</td>
<td>Relevant to a future update of this guideline and potential reduction in costs from avoiding prolonged hospitalisation and improving patient safety</td>
</tr>
<tr>
<td>National priorities</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Current evidence base</td>
<td>Limited evidence was identified and there were no randomised controlled trials</td>
</tr>
<tr>
<td>Equality</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Feasibility</td>
<td>Feasible with a large multi-centre randomised controlled trial</td>
</tr>
<tr>
<td>Other comments</td>
<td>None</td>
</tr>
</tbody>
</table>

L.1.6  Type 2 diabetes – behavioural interventions

L.1.6.1  What is the clinical and cost effectiveness of behavioural interventions for children and young people with type 2 diabetes?

Why this is important

The GDG has recommended that children and young people with type 2 diabetes and their family members or carers (as appropriate) should have access to mental health services, and this could include access to behavioural interventions. However, the evidence reviewed for the guideline was insufficient to recommend any specific behavioural intervention (no evidence at all related to behavioural interventions in children and young people with type 2
diabetes was identified for inclusion in the guideline review). The GDG recognised that for children and young people with type 2 diabetes and their family members or carers (as appropriate) lack of engagement with services (for example, non-attendance at clinic) is an important factor. Research is, therefore, needed to evaluate the effectiveness of any of the behavioural interventions prioritised by the GDG for consideration: family therapy (including behavioural family systems therapy); cognitive behavioural therapy; motivational interviewing; counselling; mentoring; and peer support. In particular, family therapy is a priority for evaluation given the social and cultural impact of type 2 diabetes in children and young people. Other behavioural interventions that are socially and culturally relevant and appropriate for children and young people with type 2 diabetes should also be evaluated. Initial research should be piloted at a local level and include process evaluation to assess cultural factors which may affect the application of interventions. Research ultimately needs to consist of multicentre, regional or national randomised controlled trials because type 2 diabetes in children and young people is still relatively rare. Any large-scale research study should include consideration of clinical and cost effectiveness.

L.1.7 Type 2 diabetes – weight loss

L.1.7.1 What is the correlation between changes in body mass index standard deviation scores and absolute HbA1c measurements or changes in HbA1c in children and young people with type 2 diabetes?

Why this is important

The GDG did not identify any evidence in children and young people with type 2 diabetes to indicate a correlation between weight loss or changes in body mass index standard deviation scores (BMISDS) and HbA1c. However, this form of correlation would be expected in children and young people and has already been demonstrated in adults. Studies in children and young people with type 2 diabetes are, therefore, needed. Such studies are likely to be observational in design and a prospective, register-based follow-up study covering all children and young people with type 2 diabetes in the UK would be ideal because type 2 diabetes is a relatively rarer condition in this age group. Changes in BMISDS and HbA1c over time would be of interest in such a study.

L.1.8 Type 2 diabetes – metformin

L.1.8.1 What is the long-term comparative clinical and cost effectiveness of different metformin preparations for treating type 2 diabetes in children and young people?

Why this is important

There is high-quality evidence for the clinical and cost effectiveness of metformin as a treatment for type 2 diabetes from diagnosis in children and young people. However, all of the relevant evidence relates to administration in tablet form and using a standard dosage, despite alternative preparations (including extended-release tablets and oral solutions) being available and having potential advantages to the standard preparation. Gastrointestinal disorders (for example, nausea, vomiting, diarrhoea, abdominal pain and loss of appetite) are very common with metformin, especially at the start of treatment, and may be reduced or avoided with alternative preparations. Extended-release tablets and oral solutions may also be easier to swallow, as standard formulation metformin consists of large tablets. Further research would preferably consist of randomised controlled trials. Outcomes should include blood glucose control (preferably using measurement of HbA1c levels) and the child or young person’s satisfaction with and adherence to treatment.

This was selected a key research recommendation by the GDG for the 2015 update. The justification for the selection is summarised in the table below.
### Potential criterion | Explanation
--- | ---
Importance to patients or the population | This is of importance because there are existing and emerging non-insulin agents (for example, metformin) which could be combined with insulin with potential benefit
Relevance to NICE guidance | Relevant to a future update of this guideline
Relevance to the NHS | Relevant to a future update of this guideline and potential reduction in costs associated with long-term complications
National priorities | Not applicable
Current evidence base | Not yet addressed in a NICE guideline
Equality | Not applicable
Feasibility | Feasible
Other comments | None

#### L.2 2004 recommendations for research that remain relevant in the 2015 update

| Type 1 diabetes | Comments |
--- | ---
**Education** | Further research is needed to evaluate the effectiveness of education programmes in which young people with type 1 diabetes provide training for their peers. This research recommendation was retained by the GDG but re-expressed to conform to current NICE format and style (it was also selected as a key research recommendation – see above)

**Insulin regimens** | Research is needed to compare the effectiveness of continuous subcutaneous insulin infusion (or insulin pump therapy) and multiple daily injection regimens in children and young people with type 1 diabetes.

**Insulin preparations** | Research is needed to evaluate the effectiveness of long-acting insulin analogues in children and young people with type 1 diabetes.

**Methods of delivering insulin** | Further research is required to evaluate the effectiveness of insulin delivery systems in children and young people with type 1 diabetes. Research is needed to compare the effectiveness of insulin delivery modes (for example, dermal, nasal, oral and pulmonary) in children and young people with type 1 diabetes. The GDG for the 2015 update noted that this research recommendation was still relevant because there is a new product to evaluate

**Non-insulin agents (oral antidiabetic drugs)** | What is the clinical and cost effectiveness of non-insulin agents (for example, metformin) combined with insulin treatment in children and young people with type 1 diabetes? This research recommendation replaces the following from the 2004 guideline. Further research is needed to evaluate the effectiveness of (for example, metformin) combined with insulin treatment in children and young people with type 1 diabetes. The GDG’s view was this remained an important area for research, and that non-insulin agents other than metformin could be
## Research recommendations

<table>
<thead>
<tr>
<th>Type 1 diabetes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>investigated as part of the research. The GDG summarised the importance of the proposed research as follows. There are existing and emerging non-insulin agents which have potential for improving control in type 1 diabetes in children and young people (for example, metformin). Research comparing treatment with such agents combined with insulin and treatment with insulin alone should be conducted in the form of randomised controlled trials. Important outcomes to measure will include achieving HbA1c targets, tolerability and satisfaction with treatment.</td>
</tr>
<tr>
<td>Monitoring glycaemic control</td>
<td>Research is needed to investigate the clinical implications of alternative site monitoring (for example, the arm as opposed to the finger) in children and young people with type 1 diabetes.</td>
</tr>
<tr>
<td>Screening for complications and associated conditions</td>
<td>Further research is needed to evaluate the effectiveness of screening for cardiovascular risk factors in children and young people with type 1 diabetes.</td>
</tr>
<tr>
<td>Cognitive disorders</td>
<td>Further research is needed to evaluate the effects of persistent hypoglycaemia and recurrent diabetic ketoacidosis on neurocognitive function</td>
</tr>
<tr>
<td>Adolescence</td>
<td>Further studies are needed to evaluate the effectiveness of behavioural and social interventions on anxiety and depression, eating disorders, behavioural and conduct disorders, and adherence to therapy in children and young people with type 1 diabetes, especially in adolescence, from diagnosis and in established diabetes.</td>
</tr>
<tr>
<td>Communication between organisations</td>
<td>Further research is needed to evaluate the effects of low blood glucose levels on learning, attendance at school and educational attainment</td>
</tr>
<tr>
<td>Transition from paediatric to adult care</td>
<td>Further research is needed to investigate young people’s experiences of transition from paediatric to adult services for people with type 1 diabetes.</td>
</tr>
</tbody>
</table>

### L.3 2004 recommendations for research that were deleted as part of the 2015 update

<table>
<thead>
<tr>
<th>Type 1 diabetes</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education</td>
<td>This research has been done and the intervention was ineffective. The GDG has, therefore, deleted this research</td>
</tr>
<tr>
<td>Type 1 diabetes</td>
<td>Explanation</td>
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<td>covering all aspects of care in children and young people with type 1 diabetes, their families and other carers.</td>
<td>recommendation as part of the update</td>
</tr>
<tr>
<td>Further research is needed to determine the most effective way of training healthcare professionals to provide education about type 1 diabetes in children and young people.</td>
<td>This research recommendation was replaced by a new research recommendation related to training of healthcare professionals as part of the update</td>
</tr>
<tr>
<td>Insulin regimens</td>
<td>Research is needed to compare the effectiveness of multiple daily injection regimens with twice-daily injection regimens in children and young people with type 1 diabetes.</td>
</tr>
<tr>
<td>Insulin preparations</td>
<td>Further research is needed to evaluate the effectiveness of once-daily injection regimens in children and young people with type 1 diabetes, and especially in pre-school children.</td>
</tr>
<tr>
<td>Monitoring glycaemic control</td>
<td>Research is needed to evaluate the clinical effectiveness of the routine use of invasive and non-invasive continuous glucose monitoring systems for optimising glycaemic control in children and young people with type 1 diabetes.</td>
</tr>
<tr>
<td>Diet</td>
<td>Further research is needed to evaluate the effectiveness of training in flexible, intensive insulin management to enable children and young people with type 1 diabetes to adjust insulin doses to match carbohydrate intake.</td>
</tr>
<tr>
<td>Diabetic ketoacidosis</td>
<td>Further research is needed to evaluate the role of blood ketone monitoring in preventing diabetic ketoacidosis in children and young people with type 1 diabetes.</td>
</tr>
<tr>
<td></td>
<td>Further research is needed to investigate the effectiveness of different concentrations of rehydration fluid, the rate of rehydration, the use of albumin infusion and the dose of insulin infusion in the management of diabetic ketoacidosis in children and young people.</td>
</tr>
</tbody>
</table>

**Appendix M: Young people’s consultation day**

A young people’s consultation day was organised for this guideline in collaboration with the NCB. The objective of the consultation day was to elicit the views of young people with type 1 diabetes and their carers in relation to topics considered in the guideline. Fourteen young women aged 13 to 17 years, seven young men aged 13 to 18 years, and 20 adults (14
mothers, five fathers and one older sister) participated in the consultation day. The main conclusions were\textsuperscript{38} [evidence level IV]

- Young people wanted to be treated as ‘normal’ individuals growing towards adulthood.
- Young people wanted to be well informed about diabetes and to be involved in decisions affecting their care as they became more mature and independent.
- Young people and their parents wanted health care to be accessible, supportive and age-banded.
- Young people and their parents wanted consistent, accessible and up-to-date information about living with type 1 diabetes.
- Young people and their parents wanted schools to have consistent, but flexible, policies that offered support to young people with type 1 diabetes without treating them differently from their peers.

More specific points identified by the NCB are summarised below and in the relevant sections of the guideline.\textsuperscript{38} [evidence level IV]

- Young people with type 1 diabetes felt that healthcare professionals should be skilled in gaining the confidence of young people by educating them about diabetes in accessible language, treated them as individuals and with respect, and ensuring that they are given the opportunity to contribute to decisions about their diabetes care – see Section 3.2 (diabetes care teams).
- Young people with type 1 diabetes and their parents felt they should have 24-hour access to a named specialist nurse with whom they could speak confidentially and whom they could contact between clinic appointments – see Section 3.2 (diabetes care teams).
- Some young women with type 1 diabetes stated a preference for a female doctor who they felt they would be more comfortable with than a male doctor – see Section 3.2 (diabetes care teams).
- Young people with type 1 diabetes and their parents felt that it was important to see the same members of the diabetes care team wherever possible – see Section 3.2 (diabetes care teams).
- Young people with type 1 diabetes liked age-banded clinics – see Sections 3.2 (diabetes care teams) and 7.2 (transition from paediatric to adult care).
- Young people with type 1 diabetes were happy to miss school in order to attend clinic appointments, but their parents would prefer clinic appointments to be available outside school hours – see Section 3.2 (diabetes care teams).
- Parents suggested that clinic appointments should be flexible enough to take into account school terms and timetables and examination schedules – see Section 3.2 (diabetes care teams).
- Parents of young people with type 1 diabetes felt that there should be easy access to psychology services and suggested that paediatric diabetes care teams should include a psychologist – see Sections 3.2 (diabetes care teams) and 6.7 (psychosocial support).
- At the time of diagnosis some young people with type 1 diabetes felt they were given too much information at one time – see Section 3.4 (essential education at diagnosis).
- Young people with type 1 diabetes wanted information aimed at them rather than just at their parents although they understood that their parents also needed to know how to manage type 1 diabetes – see Section 3.4 (essential education at diagnosis).
- Young people with type 1 diabetes wanted insulin regimens that were flexible and allowed for a measure of spontaneity, and they wanted to be informed about the types of insulin that are available and given up-to-date information on insulin delivery devices and blood glucose testing monitors – see Section 4.2 (insulin regimens).
- Parents suggested annual updates from staff on the new products available – see Section 4.2 (insulin regimens).
It was mentioned that some young people with type 1 diabetes may find four injections/day too many but they wanted to be involved in the discussion about how best to fit diabetes treatment into their chosen lifestyle while maintaining optimal metabolic control – see Section 4.2 (insulin regimens).

Young people with type 1 diabetes and their parents wanted consistent, accessible up-to-date information on many aspects of living with type 1 diabetes, including information on what happens when you have type 1 diabetes, healthy eating, what to expect at clinic visits, types of insulin, injecting insulin and injection sites, hypoglycaemia and what to do if it occurs, complications of diabetes, how to drink alcohol safely, travelling abroad and leisure activities, becoming more independent, leaving home, implications for future careers, and new products and research – see Sections 4.2 (insulin regimens) and 4.1 (universal principles of education).

Parents felt that education should be delivered through one-to-one or group education sessions with a specialist nurse, whereas young people with type 1 diabetes were more positive about accessing information through leaflets, CD-ROMs, videos and websites – see Section 4.1 (universal principles of education).

Young people with type 1 diabetes, in particular young women, were sensitive about body weight and wanted weighing to be carried out in a private room – see Section 5.5 (screening for complications and associated conditions).

Young people with type 1 diabetes valued meeting other young people with type 1 diabetes and might benefit from formalised arrangements for meeting each other – see Section 7.1 (support groups).

Some parents suggested that age of transfer of young people with type 1 diabetes from paediatric to adult services should be standardised and that clinics should be jointly run by paediatric and adult services to provide continuity of care – see Section 7.2 (transition from paediatric to adult care).

Other parents thought that individual young people with type 1 diabetes should be involved in the decision about when transfer should occur – see Section 7.2 (transition from paediatric to adult care).

Appendix N: Superseded text from 2004 guideline

This appendix is presented in a separate document.