Clinical Guideline
A Practical Approach to Management of Type 2 diabetes in Children and Young People (CYP) under 18 years

Contents

Table of Contents
Introduction .................................................................................................................................................. 4
T2DM- Diagnosis and Investigations: ........................................................................................................ 4
  Background ............................................................................................................................................ 4
  Recommendations .................................................................................................................................. 5
Glycaemic Targets for CYP with Type 2 Diabetes ....................................................................................... 6
  Background ............................................................................................................................................ 6
  Recommendations .................................................................................................................................. 6
Self-monitoring of blood glucose (SMBG): Evidence for use and frequency of SMBG in children with type 2 diabetes .............................................................................................................................. 7
  Background ............................................................................................................................................ 7
  Recommendations: ................................................................................................................................. 8
Continuous glucose monitoring (CGMS)/ Flash Glucose monitoring (FGS): Evidence for use and frequency of CGM/FGS in CYP with T2DM .............................................................................................................. 8
  Background ............................................................................................................................................ 8
  Recommendations: ................................................................................................................................. 9
Structured education for Children and Young People with Type 2 Diabetes ....................................................... 9
  Background ............................................................................................................................................ 9
  Recommendations: ................................................................................................................................. 10
Lifestyle interventions in Type 2 diabetes management in children ................................................................. 10

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Multidisciplinary team (MDT) approach: .................................................................10

Background ..............................................................................................................10
Recommendations .................................................................................................10

Weight loss............................................................................................................11

Background ............................................................................................................11
Recommendations .................................................................................................11

Dietary modifications..............................................................................................12

Recommendations .................................................................................................12

Physical activity .....................................................................................................13

Recommendations .................................................................................................13

Psychological management in childhood Type 2 diabetes ......................................14

Background ............................................................................................................14
Recommendations .................................................................................................14

Pharmacotherapy ...................................................................................................15

Background ............................................................................................................16
Recommendations .................................................................................................16

Levels of evidence ................................................................................................18

Bariatric Surgery ....................................................................................................19

Background ............................................................................................................19
Recommendations .................................................................................................19

Hypertension in youth with type 2 diabetes .............................................................20

Background ............................................................................................................20
Recommendations .................................................................................................20

Lipids in youth with type 2 diabetes .......................................................................21

Background ............................................................................................................21
Recommendations: .................................................................................................21
Appendix

Appendix 1

References

Obstructive Sleep Apnoea (OSA) in CYP with T2DM

Non-alcoholic fatty liver disease (NAFLD) in CYP with T2DM

Retinopathy in Youth-Onset T2DM

Microalbuminuria in Youth-Onset T2DM

Non-diabetic CKD should be considered in; (144, 145, 157)

Screening

Management

Recommendations

Background

Management

Recommendations (Grade B)

Screening

Definition:

Screening:

Management

Screening (All Grade B)

Recommendations

Screening:

Non-diabetic CKD should be considered in; (144, 145, 157)

Recommendations:

Obstructive Sleep Apnoea (OSA) in CYP with T2DM

Background

Recommendations (Grade B evidence)

References

Appendix 1

Adolescent Binge Eating Questionnaire (ADO-BED)

Appendix-2 PATIENT INFORMATION LEAFLET:

SGLT2 INHIBITORS AND DIABETIC KETOACIDOSIS IN TYPE-2 DIABETES

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Introduction

Type 2 diabetes (T2DM) is increasingly prevalent in children and young people (CYP) which is affected by obesity worldwide. The main risk factors for developing T2DM are excess weight, first or second degree relative with T2DM, maternal diabetes during the child’s gestation, high risk race/ethnicity and insulin resistance (signs of insulin resistance include acanthosis nigricans and presence of other metabolic conditions associated with insulin resistance such as hypertension and hyperlipidaemia, polycystic ovarian syndrome (PCOS) or small for gestational age (SGA)). T2DM in young people is an aggressive disease with increased risk of complications leading to increased morbidity and mortality during most productive years of life (1). This evidence based guideline aims to provide a practical approach in managing this condition.

T2DM- Diagnosis and Investigations:

Background

The choice of screening test is controversial with glycated haemoglobin (HbA1c) increasingly recommended over the gold standard oral glucose tolerance test despite limited evidence in CYP. HbA1c testing has advantages in not requiring a fasting sample, and because it is a predictor of vascular disease across a wider range than just the diabetic one. However, it lacks sensitivity and would miss some people with diabetes. Absolute values of HbA1c may be more useful as part of overall risk assessment than a dichotomous ‘diabetes or not diabetes’ diagnosis. The oral glucose tolerance test (OGTT) is more sensitive, but inconvenient, more costly, has imperfect reproducibility and is less popular, meaning that uptake would be lower (2, 3).

Clinical experience of the guideline development group suggests that a fasting blood glucose in addition to HbA1c may diagnose some additional patients. There needs to be a pragmatic balance between asking patients to return fasted on a different day for optimal blood tests and the opportunistic approach of obtaining a same day screening HbA1c, particularly in patients who are at risk of not reattending on another day. HbA1c should not be used in patients with haemoglobinopathies, within 3 months of transfusion or with increased red cell turnover. Iron deficiency can artificially raise HbA1c in adults, but this has not been quantified in children (4).
Identification of diabetes type can be challenging with all types having overlapping features, particularly in those with excess weight (5). Detection of diabetes antibodies identifies those at highest risk of developing autoimmune driven loss of insulin production and can aid with correct identification of diabetes subtype. There is insufficient evidence for the use of insulin or c-peptide levels at diagnosis.

Recommendations

- Asymptomatic screening is recommended if there is high body mass index (BMI > 85th centile) and 1 or more of: first or second degree family history of type 2 diabetes, high risk race/ethnicity, gestational diabetes or insulin resistance (acanthosis nigricans or presence of other metabolic conditions, such as hypertension and hyperlipidaemia, PCOS or SGA) (Grade B)
- If a diagnosis is suspected based on clinical symptoms, then a point of care random blood glucose must be performed on the same day and abnormal results discussed with the local diabetes team via locally agreed pathways. (Grade D)
- Diagnosis can be made based on fasting glucose, or 2-hour glucose concentration during an oral glucose tolerance test (OGTT) or HbA1c (Grade B)
- Any of the following are diagnostic of diabetes:
  - Fasting plasma glucose (FPG) ≥ 7.0 mmol/L (126 mg/dL)
  - Post OGTT 2-hour plasma glucose ≥11.1 mmol/L (200 mg/dL), with 1.75 g/kg (max 75 g) anhydrous glucose dissolved in water
  - Symptoms of diabetes (including polyuria, polydipsia and unexplained weight loss) and a random plasma glucose >11.1 mmol/L (200mg/dl)
  - In the absence of symptoms, hyperglycaemia detected incidentally or under conditions of acute physiologic stress may be transitory and should not be regarded as diagnostic of diabetes.
  - HbA1c ≥ 48 mmol/mol (6.5%) [Must utilise a laboratory based, DCCT aligned, National Glycohaemoglobin Standardization Program (NGSP) certified methodology that is validated for diagnosis].
- In the absence of symptoms, testing should be confirmed with a repeat test on a different day (Grade B).
OGTT need not be done routinely where HbA1c is ≥48 mmol/mol (6.5%) and should not be done where HbA1c is <6.0% (42mmol/mol). Those with HbA1c 42-48mmol/mol (6-6.5%) should be evaluated clinically and clinical judgement used to decide between a repeat HbA1c in 3-6 months or an OGTT. **(Good Practice Point)**

Those with HbA1c 42-48mmol/mol (6-6.5%) should be diagnosed with pre-diabetes, the management of this is outside the scope of this guideline.

Once diabetes is diagnosed, the type of diabetes should be diagnosed clinically based on signs and symptoms, biochemical investigations, family history and clinical progression. Monogenic diabetes must be considered, especially where the clinical picture is atypical for Type 1 or 2. Where there is diagnostic doubt, the patient should receive appropriate safety netting for the possibility of evolving type 1 diabetes (including blood ketone testing) and be re-evaluated after a short period of time. **(Good Practice Point)**

Diabetes autoantibody testing (GAD, IA2 and ZnT8) should be considered in paediatric patients with the clinical diagnosis of T2DM because of the high frequency of islet cell autoimmunity in otherwise “typical” T2DM and where there is diagnostic uncertainty for example where symptomatic or those with lean body weight. Those with diabetes antibodies are more likely to need insulin early. **(Grade B)**

**Glycaemic Targets for CYP with Type 2 Diabetes**

**Background**

Data from adult studies (6, 7) shows that intensive glucose control improved HbA1c and any diabetes-related end point but had no effect on mortality. Tight control of blood pressure reduced both diabetes-related morbidity and mortality. Unlike glycaemic control, there was a significant effect on macrovascular as well as microvascular complications, with strokes and heart failure reduced by a half.

No such robust studies exist for CYP with T2DM. The TODAY study showed that an HbA1c of 45 mmol/mol (6.3%) or more after initiation of metformin was shown to be a predictor of eventual loss of glycaemic control; for every 0.1% increase in HbA1c there was a 16% increase in risk of loss of glycaemic control, with a median time to loss of control of approximately 11 months, irrespective of treatment arm (8). In addition, TODAY study showed that high HbA1c was associated with increased risk of developing retinopathy (9).
Recommendations

- HbA1c should be measured every 3 months in CYP with T2DM (Good practice point)
- HbA1c targets should be individualised, noting the low risk of hypoglycaemia. (Grade E)
- Intensify treatment if HbA1c not below 48mmol/mol (6.5%) at 3 months. (Grade B)
- Individualise HbA1c Target after the first 3 months but aiming to keep below 48mmol/mol (6.5%) (Grade E)

Self-monitoring of blood glucose (SMBG): Evidence for use and frequency of SMBG in children with type 2 diabetes

Background
There is no high-quality evidence that SMBG in CYP with T2DM improves glycaemic control or outcomes or that more intense monitoring is better. Even in adults, the evidence is conflicting (10-13). The American Association of Clinical Endocrinologists and American College of Endocrinologists 2016 Consensus Statement asserts there is a benefit when SMBG is used as part of a coordinated and tailored care package and highlight the methodological issues with the conflicting data (10). There may be some benefit in use to adjust doses (14), better HbA1C (13) and BGL targets may be able to be set to achieve desired HbA1C goals (15).

In children, observational data from the SEARCH for Diabetes Study showed lower HbA1C was associated with increased frequency of SMBG in patients on insulin (16). A post-hoc analysis of data from the TODAY Study found adherence to twice-daily SMBG was low (59% initially, <50% by 12m) but that greater SMBG use was associated with lower HbA1C.

No association was found between SMBG and quality of life (QOL) / depression however there remains a significant financial and personal burden in monitoring without clear evidence of benefit (17).

The diagnosis in CYP is not always clear and disease progression may be more aggressive and change more rapidly. Therefore, in line with the International Society for Paediatric and Adolescent diabetes (ISPAD), American Diabetes Association (ADA) and The National institute for health and care excellence (NICE) guidelines (18-20), we recommend that SMBG is undertaken in all patients with T2DM and that frequency is tailored to the individual based on treatment-factors. This includes the risk of hypoglycaemia, how SMBG will be used to make adjustments.
to treatment and patient-factors such as availability and need for family support and the burden of disease management on the patient and/or family.

Recommendations:

- All patients should be taught SMBG and have the necessary equipment provided. (Good practice point)
- Frequency of SMBG for CYP with T2DM on basal insulin should be individualised including taking into account the risk of hypoglycaemia, glycaemic target and stage of treatment. (Good practice point)
- Those not on insulin should be encouraged to test several times a week consisting of both fasting and post-prandial levels to monitor disease progression, provide data for clinical consultations and predict glycaemic control. Testing may be more intense initially and during periods of changing blood glucose levels (e.g. illness or fasting) but may reduce when levels are stable for several weeks. (Good practice point)
- Those on multiple daily injections of insulin should undertake SMBG at least 5 times a day to adjust doses and monitor for hypoglycaemia, similar to CYP with T1DM on MDI. (Good practice point)
- Fasting, pre-prandial and post-prandial blood glucose level targets should be set to allow patients to monitor their progress. Fasting and pre-prandial levels should ideally be 3-7 mmol/l (3.9-7 mmol/l if on insulin) and post-prandial should aim to be <10 mmol/L. (Good practice point)

Continuous glucose monitoring (CGMS)/ Flash Glucose monitoring (FGS): Evidence for use and frequency of CGM/FGS in CYP with T2DM

Background

There is no good evidence available to guide the use of continuous glucose monitoring systems (CGMS) or flash glucose monitoring (FGS) in children and young people with T2DM.

The benefits of CGMS have not been widely tested in the clinical setting with conflicting results seen in adult trials (21, 22). The GLADIS study found no difference in HbA1C despite good adherence to CGM, but a reduction in time outside glucose target.
Due to the lack of consistent results in adults and the lack of any data in CYP, further research is needed to identify which patients may benefit from the use of CGMS and FGS and how they should be optimally used to maximise patient benefit and cost-effectiveness.

There may be a role for CGM/FGS in certain circumstances such as for some patients with learning difficulties, on insulin or as a short-term intervention during treatment intensification and education (19).

Link here for current (FGS) Freestyle Libre guidelines - https://www.cypdiabetesnetwork.nhs.uk/national-network/key-documents/

Recommendations:
- There is no evidence available to routinely recommend the use of CGMS or FGS in children and young people with type 2 diabetes. Individualised considerations such as learning difficulties or needle phobia may influence management. Brief periods of CGMS/FGS may be indicated during treatment intensification or education. (Good practice point)

Structured education for Children and Young People with Type 2 Diabetes

Background
Diabetes structured education programmes first started in the 1970’s. The focus has changed over time from a knowledge-based approach to one supporting self-empowerment.

There is very little evidence related to what a structured education programme for paediatric T2DM should look like and its efficacy with no programme undergoing a randomised controlled trial (RCT). Most of the evidence comes from adults with T2DM and CYP with type 1 diabetes. Meta-analysis of structured education versus informal unstructured education in improving glycaemic control found no evidence of improving control (23).

Two structured education programmes have been developed for CYP with T2DM, the TODAY Standard Diabetes Education (TSDE) and iCAN (24, 25). All families undergoing the TODAY study underwent initial education with the TSDE but it was never tested as a single intervention against standard practice.
The iCAN programme is a bespoke programme targeting children and young people with Type 2 diabetes which has been developed by a multidisciplinary team consisting of both adult and paediatric clinical teams, psychologists, commissioners and children and their carers. It has been rolled out in the form of four 2-hour workshops focussing on food, activity and emotional well-being (25).

Recommendations

- Individualised Structured diabetes education should be provided to CYP with T2DM and their carers at the time of diagnosis, revised soon after diagnosis then annually or more frequently dependent on individual need. (Good Practice point)

- No single structured programme is recommended, with TSDE and iCAN being examples of existing programmes. (Grade C)

Resources from TODAY (TSDE) are available for public use on their website (portal.bsc.gwu.edu/web/today). These have also been modified by the ADA as a program called Be Healthy TODAY; Be Healthy for Life (http://main.diabetes.org/dorg/PDFs/Type-2-Diabetes-in-Youth/Type-2-Diabetes-in-Youth.pdf).

Lifestyle interventions in Type 2 diabetes management in children

Multidisciplinary team (MDT) approach:

Background

Most recommendations relating to multi-disciplinary diabetes team structure and approach are based on observational studies and expert opinion (26-28).

Team members recommended include dietitians, paediatric nurses, diabetes educators, psychologists, social workers (sometimes called community/cultural workers) and medical doctors. Other MDT members include ophthalmologist, metabolic specialist (lipids albuminuria and obesity management) and dental health professionals.

The SEARCH cross-sectional study showed glycaemic control in youth under 20 years in South Carolina was associated with having any form of regular specialist support, but outcomes in primary care were not different to
The only disadvantages of an MDT cited in one study, was that some adult patients were reluctant to see multiple providers and communication between members should be key (27).

**Recommendations**

- MDT approach (including dietitian, specialist nurse and psychologist support) to T2DM management in children is key to improving outcomes. (Grade D)
- A unified approach with consistent team messaging improves outcomes. (Grade D)
- T2DM should be managed in the secondary care setting with close integration with primary care. GP primary health team members should be involved in the child’s care in line with whole family approach, and additional resources such as social prescribing, exercise prescription. (Grade D)
- Multi-agency working is important to be included in the MDT approach (such a youth support workers, family support workers, patient advocate, schools, school nurses, social workers) (Grade D)
- Telemedicine could help establish regular contact with the MDT in T2DM patients and their families (including home health monitoring, video clinics, telephone, emails and text support) whilst acknowledging that access may be challenging (including digital poverty). (Grade D)
- Collaboration with an adult diabetes MDT team is essential (ideally young adult service) to enable seamless transition and support with complex cases.

**Weight loss**

**Background**

Weight loss in adults is associated with improved glycaemic control, with clinical benefits seen from 5% loss (30, 31) with further improvements seen with increasing weight loss, such as the Direct Study (32). There is no direct evidence in young people with type 2 diabetes to recommend a target weight loss. No large RCT has aimed for sufficient energy restriction that is likely to result in 5-10% weight loss seen in adult studies.

The highest rates of glycaemic control in the TODAY study were seen by the addition of rosiglitazone to metformin rather adding lifestyle support. This was despite weight gain in the rosiglitazone and weight loss in the lifestyle group. Secondary analysis from TODAY study did show weight loss of >7% across all groups was associated with small but significant benefits in cardio metabolic risk factors (33).

Bariatric surgery is currently the only treatment modality that results in large magnitudes of weight loss (34). RCT evidence in adults demonstrates improved glycaemic control associated with the physiological changes, negative
caloric balance and subsequent weight loss seen after bariatric surgery and results in significant reduction in insulin usage (35, 36).

A retrospective study of the impact of Gastric bypass surgery in youths compared with adults identified that youth were significantly more likely than adults to have diabetes remission (86%) despite having similar weight loss (26 vs 29%) to adults.

Recommendations

- Weight reduction as part of strategy to reduce BMI should form part of diabetes management in youth with T2DM as this has been associated with better glycaemic outcomes (Grade C)
- CYP with T2DM should be offered a family based weight loss programmes based on a range of personalised diet strategies, physical activity and behavioural intervention to treat obesity. (Grade B)
- There is currently insufficient evidence in CYP to recommend specific targets for weight loss to control or reverse T2DM. Targets should be at minimum in line with accepted recommendations for the management of obesity. It is important to remember that increasing height in pre-pubertal and pubertal young people results in reduction in BMI.
  - Targets for weight should be set to reduce weight by 5% in first 3 months in pre-pubertal and pubertal CYP. (Grade D)
  - Post pubertal young people should be advised to aim for 5% weight loss in 3-6 months and 10% weight loss in the 1st year. (Grade D)
  - In the longer term CYP should be encouraged to aim to reduce BMI to below 85th centile. Professionals need to be aware this may take several years especially in post pubertal young people (Grade D).

Dietary modifications

Recommendations

- An individualised and family wide approach to dietary modification is essential. A specialised paediatric diabetes dietitian should work together with the family to identify potential diet and lifestyle changes and formulate a plan with SMART (specific, measurable, achievable, relevant, time bound) goals (37-39) (Grade B)
- Regular follow up appointments with a specialised paediatric diabetes dietitian are essential to monitor progress and review goals. Additional appointments with the specialised paediatric diabetes dietitian outside the MDT every 4-8 weeks should be considered (Good practice point)
● From the diagnosis of T2DM, families should be encouraged to follow a healthy balanced diet that is rich in wholegrains, vegetables, fruit, low fat dairy, nuts and seeds and limits fats, oils and sugary foods. (40-47) (Grade B)

● Families should be encouraged to consume balanced meals including complex carbohydrate, protein and vegetables to regulate appetite and improve satiety after a meal (48-51) (Grade B)

● Intake of sugary drinks should be limited (52-56) (Grade C)

● If there has been no significant weight loss 6 months after diagnosis while aiming to implement a healthy balanced diet, then alternative approaches can be considered. There is limited evidence in paediatrics that one particular dietary intervention is more successful than another therefore evidence has been extrapolated from adult data. One of the following approaches to promote weight loss can be considered:
  o A healthy low fat diet (limits fat to 30% of energy intake, 45-50% of energy from carbohydrates and 20-25% of energy from protein) (42, 57) (Grade B)
  o A lower carbohydrate diet (limits carbohydrate to 30% of energy intake, 45% of energy from fat and 20% of energy from protein) (58) (Grade D)
  o A low energy diet using either meal replacement products or a guided amount of calories from food at each mealtime that limits energy intake to 800kcal a day for an 8-12 week period (post pubertal, individualised, adult data). This initial phase is followed by the gradual reintroduction of a healthy balanced diet. This may be a suitable treatment option for young people who are keen to follow a structured plan. Careful consideration should be given to the appropriateness of this option and take in to account life events such as exams, learning to drive and family celebrations (43, 59-63) (Grade C)

Physical activity

Background

Physical activity (PA) is likely to have multiple beneficial effects on health beyond glycaemic control (64). The evidence-base for the use of physical activity for treatment of type 2 diabetes in children yielded limited results.
Multiple cohorts show that young people with type 2 diabetes undertake insufficient physical activity, although most rely on self-report which is a poor measure (65). Self-reports of physical activity in 578 CYP in Austria and Germany with type 2 diabetes demonstrated that 55.7% carried out no regular physical activity. A smaller cohort demonstrated youth undertaking 6.5 minutes/day of moderate/vigorous activity compared to the 60 minutes recommended (66). These cohorts show different associations between PA and diabetes control, with the first showing increased physical activity being associated with a lower HbA1c as well as lower BMI SDS and a higher HDL cholesterol and the second finding no association.

A systematic review in 2010 (before publication of the TODAY study) did not find any high quality evidence to support the use of lifestyle modification in the goal to achieve good glycaemic control in youth with type 2 diabetes (67). All participants in the TODAY study were encouraged to increase physical activity. The addition of a lifestyle intervention in the TODAY study, in the form a family-focused intensive behavioural change programme covering nutrition and physical activity, reduced the percentage overweight but this did not translate into sustained glycaemic control and had no additional impact when compared to metformin alone.

Recommendations
● Physical activity levels recommended for CYP with T2DM are the same as for young people without T2DM across countries (UK, USA, Europe) and the suggestion is for 60 minutes per day of moderate/vigorous physical activity to improve body composition and insulin sensitivity. (Grade B)
● For CYP with T2DM, exercise may need to occur in more than one session a day or start with a lesser amount and build up as able. (Good Practice Point)

Psychological management in childhood Type 2 diabetes

Background
There is variation in the evidence relating to the prevalence of depression in CYP with T2DM. The SEARCH study reports that the young people older than 10 years of age with T2DM have a much higher risk of moderate to severe depression than young people with type 1 diabetes (18 vs. 5% in boys; 20 vs. 9% in girls, respectively). Higher mean HbA1c and frequency of ED visits were associated with depressed mood (68).

More than 25% of females and males in the SEARCH cohort of youth with type 2 diabetes reported symptoms of disordered eating behaviours, such as skipping insulin, vomiting, and using diet pills or laxatives, and these behaviours were associated with poorer glycaemic control in females (69). Binge eating rates in the TODAY cohort were high (26%) and were associated with more severe obesity, psychological symptoms of disordered eating, and symptoms of depression (70).
Psychological needs should be both screened and also implemented within everyday practice. Recently, the paediatric quality of life questionnaire initially developed for type 1 diabetes has been validated for Diabetes Module Diabetes Symptoms and Type 2-specific Diabetes Management Summary Scores for young people with T2DM and can be used to evaluate and monitor ongoing issues (71).

Approaches for mental health practitioners include personalised tailored interventions to their interests, health coaching and behaviour therapy and using peer counsellors. There is limited research into which behavioural interventions are most effective (72). They are likely to need to address cultural differences and home lifestyles in order to achieve better outcomes (73). PHQ-2 has been validated for individuals aged 12 years and older across multiple population and cultural settings (74).

Recommendations

- CYP must have on-going access to mental health professionals embedded within a diabetes team. (Good Practice point)
- All CYP should be screened for mental health regularly by a team member (at least annually, or more frequently with inadequate diabetes control) including depression and eating disorders. (Good practice point)
  - The PedsQL™ Diabetes Module is a specific module of the PedsQL™ freely available for clinical use through registration - [https://eprovide.mapi-trust.org/instruments/pediatric-quality-of-life-inventory](https://eprovide.mapi-trust.org/instruments/pediatric-quality-of-life-inventory). It effectively screens for diabetes-related quality of life. PHQ-2 is used for screening for depression.
  - There is no suitable validated eating disorder questionnaire that adequately screens for binge eating in this population. However the Adolescent Binge Eating Disorder Questionnaire ADO-BED has been validated in young people with obesity to identify those at risk of binge eating disorder. (Appendix 1)

Pharmacotherapy
Background

The choice of medication depends on the patient’s glycaemic control at presentation. For CYP diagnosed with T2DM, the ADA position statement and ISPAD guidance both recommend starting metformin with or without insulin (given patients have normal kidney function and are not acidotic) (18, 19).

Initial treatment for CYP less than 18 years of age with obesity and diabetes should take into account that the type of diabetes is relatively uncertain for the first few weeks, due to overlap in presenting symptoms and a significant number presenting with ketosis (75). Patients who present with ketosis, have symptoms of polydipsia, polyuria, and weight loss, or have HbA1c > 69.4 mmol/mol (8.5%) should be stabilised if needed with intravenous insulin and then started on subcutaneous basal insulin along with metformin, while waiting for the autoantibody results.

There is some evidence that insulin can be successfully weaned off after initially starting it. TODAY trial had a run in phase with 927 participants. 90.9% of the 927 participants who entered run-in achieved or maintained HbA1c < 8% on metformin monotherapy. 137 (12.5%) were on insulin alone and 281 (25.7%) were on both insulin and metformin. Of the 330 participants who were on insulin at screening and who completed 8 weeks of run-in, all but 36 (11%) could be weaned from insulin and some of these 11% failed run-in for other reasons (e.g., poor compliance with visits) (76). There is no evidence that continuing insulin will preserve B-cell (77).

Recommendations

Initial treatment

If HbA1c at diagnosis is > 69.4 mmol/L (8.5%):
Start long-acting basal insulin at 0.25 – 0.5 units/kg/day and escalate to a maximum of 1.5 units/kg/day (18, 78). Metformin can be started at the same time as insulin, unless acidosis is present.

Once glycaemic control is achieved (HbA1c < 48 mmol/L (6.5%) (51):
Basal insulin can be tapered over 2-6 weeks by decreasing the insulin dose by 10-30% each time the metformin is titrated up (79)

If HbA1c < 69.4 mmol/L (8.5%) and metabolically stable at diagnosis:
Metformin monotherapy should be commenced (19)
Start at doses as per BNFc and titrate up to maximum dose of 2 grams per day. Standard release preparations can be crushed and added to food. Liquid preparations are also available but should only be considered in exceptional circumstances due to cost implications. Sustained release preparations are available and should be considered if GI side effects is a concern for compliance issues (80)
Stop metformin during intercurrent illnesses to reduce risk of lactic acidosis.

Treatment Intensification

The goal of initial treatment should be to attain an HbA1c of less than 48 mmol/mol (6.5%)

If metformin is started at the onset and there is poor glycaemic control, with failure to obtain a
Target HbA1c < 48mmol/mol within 4 months of metformin monotherapy, second line treatment with Liraglutide should be considered.

If Liraglutide is not tolerated, addition of basal insulin therapy to metformin is the only subsequent treatment option currently licenced.

GLP1 agonists:
Liraglutide is currently licensed to use in CYP of 10 years of age or above and BMI >85th percentile if no improvement in glycaemic control (HbA1c >48mmol/mol or 6.5%) with metformin alone or with basal insulin therapy +/- diet and exercise. Baseline blood tests include pancreatic amylase and lipase and repeated at the first clinic review after starting the treatment and then annually.
Liraglutide is given as daily subcutaneous injections and can be started at 0.6mg daily and can be increased every 1-2 weeks (on increments of 0.6mg) up to 1.8mg daily based on fasting capillary blood glucose >6mmol/L and tolerability.
Side effects are mainly gastrointestinal (nausea and diarrhoea) or mild hypoglycaemic episodes and rarely pancreatitis though not reported in the studies (81, 82). Patients should be counselled and monitored for signs of acute pancreatitis (e.g. persistent, severe abdominal pain) and if suspected Liraglutide should be stopped. This should also be reported to the MHRA via the Yellow Card scheme.

Insulin: Since studies show that compliance with insulin could be a challenge in CYP (83, 84), single daily insulin using a long acting insulin analogue (eg. Glargine, Detemir or Degludec) is preferred. Severe insulin resistance is characteristic of T2DM in CYP going through mid-late puberty and might require higher doses of basal insulin to achieve glycaemic control. Higher concentrations of basal insulin (U-300 glargine, U-200 Degludec) may be required to avoid large volume injections that may further diminish medication adherence (19).

Once both basal insulin (up to 1.5 units/kg/day) and metformin +/-Liraglutide, cannot achieve glycaemic control, rapid acting insulin (Aspart) at meal times may be needed, based on post-prandial blood glucose readings. High doses of basal insulin increases risk of hypoglycaemia and some may need lower basal doses (e.g. 0.75 u/kg/day) together with prandial insulin to counteract this. This should be done in discussion with the Diabetes Dietician who is supporting the young person on lifestyle changes, including diet and weight management.

The main side effect of insulin treatment is hypoglycaemia and weight gain; though the incidence of hypoglycaemia is low in CYP with type 2 diabetes even with insulin treatment, patients should be educated on the management of hypoglycaemia, including the use of glucagon (18).

Other medications:
SGLT-2 inhibitors
There is not enough evidence currently to recommend the use of SGLT 2 inhibitors for paediatric use routinely. Completed RCTs only include data on Pharmacokinetics in the form of a single dose of empagliflozin, dapagliflozin, canagliflozin in children and adolescents to assess pharmacokinetic and pharmacodynamic profile of these medications and decide on the dose to be used of phase 3 clinical trials (85-88).
In all studies, results were comparable to adults pharmacokinetic and pharmacodynamic profiles therefore standard doses of the medications will be/are being tested on the RCTs. Currently, 5 ongoing RCT are assessing
safety and efficacy of SGLT-2 inhibitors in children and adolescents. There are no data on efficacy of this group of drugs in paediatric T2DM population.

For post-pubertal YP not achieving adequate control despite Metformin, +/- Liraglutide and +/- Insulin, the use of a SGLT2 inhibitor could be considered cautiously following discussion with adult diabetologists who have more experience of using it. In patients not on insulin, a c-peptide level should be assessed prior to initiation and the medication should be considered only if adequate inherent insulin production is present, to prevent euglycaemic diabetic ketoacidosis. Patients should be counselled on the symptoms of DKA and advised to seek immediate medical advice if they develop any of these. SGLT-2 inhibitor treatment should be discontinued if DKA is suspected or confirmed and should not be restarted, unless the cause of DKA is not related to the use of SGLT2 inhibitor. (appendix2)

GDG looked at the use of other drug groups such as sulphonylureas, DPP4 agonists and orlistat but felt that there wasn’t enough evidence to make a positive recommendation.

Levels of evidence

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin monotherapy is effective in achieving metabolic control in youth with T2DM at least initially after diagnosis</td>
<td>A</td>
</tr>
<tr>
<td>Initial treatment with insulin+/-metformin based on metabolic state and ketosis. Metabolically unstable CYP with diabetes being started on s/c or IV insulin</td>
<td>D</td>
</tr>
<tr>
<td>Once daily basal insulin with starting dose of 0.25-0.5 units/kg/day Evidence for HbA1c cut off 69 mmol/mol (8.5%) Maximum dose of basal insulin 1.5 units/kg</td>
<td>C</td>
</tr>
<tr>
<td>Weaning off insulin after initial treatment</td>
<td>A</td>
</tr>
<tr>
<td>Evidence for HbA1c cut off 69 mmol/mol (8.5%)</td>
<td>C</td>
</tr>
<tr>
<td>Addition of insulin if metformin monotherapy fails and Beta cell loss</td>
<td>A</td>
</tr>
<tr>
<td>Prandial insulin and dose</td>
<td>E</td>
</tr>
<tr>
<td>Liraglutide as an adjunct</td>
<td>B</td>
</tr>
</tbody>
</table>
Bariatric Surgery

Background
T2DM in CYP is a more aggressive and progressive disease with more rapid reduction in beta cell mass following diagnosis than in adult populations. The decline in beta cell mass is 3-4 x faster in young people and “failure” rates of treatment to control blood glucose are significantly higher (1, 89). Beta cell mass declines by between 20-35% per year (90-92). Diabetes control typically deteriorates within 18 months- 2 years after diagnosis (84).

Bariatric surgery in adolescents leads to successful weight loss in those with severe obesity (BMI> 35kg/m2) and demonstrates greater weight loss outcomes when compared to lifestyle and pharmacological interventions (93, 94). Bariatric surgery is the most effective current treatment available for reducing metabolic comorbidities in obesity; with remission rates of 85% for type 2 diabetes, 85% for hypertension, 75% for dyslipidaemia and 78% for musculoskeletal problems (95).

The impact on future pregnancy related complications is mixed following bariatric surgery with some problems improved and others worsened (96, 97).

Nutritional deficiencies are common post–operatively with reports of up to 70% of patients exhibiting some deficiency of micronutrients (95)

NICE guidelines currently recommend consideration of bariatric surgery for those with achieved or nearly achieved physiological maturity (i.e. tanner stage 4-5) together with BMI >40kg/m² without comorbidity and 35kg/m² with comorbidity such as type 2 diabetes (98). NHS-England are due to announce funding for new national bariatric surgery centres and will likely include clear pathways including referral criteria.

Recommendations
- Bariatric surgery in adolescents with BMI>35kg/m2 shows clear benefit in remitting T2DM. (Grade A)
- It should be considered as an option for treatment of obesity related T2DM for obese CYP who are demonstrating inadequate response to pharmacological treatments within 12-18 months to avoid reduction in beta-cell mass. (Good practice point)
- Bariatric surgery is effective in inducing remission and reducing progression in diabetic nephropathy and improving hypertension. (Grade C)
- Bariatric surgery has been demonstrated to stabilise progression of diabetic retinopathy (DR) but evidence for long term resolution of DR is currently not available. (Grade D)
- Monitoring of long-term complications post-bariatric surgery in CYPs is required for nutritional deficiencies and metabolic bone health. (Grade B). There is inadequate data to support bariatric surgery in prepubertal children with obesity related T2DM with limited data on long-term outcomes. (Good practice point)
Hypertension in youth with type 2 diabetes

Background
Blood pressure in children should be recorded not only in millimetres of mercury but as a centile for that individual’s age, sex and height. Hypertension in children under 13 years of age is defined as a systolic and/or diastolic blood pressure that is greater than the 95th centile on three or more occasions and in those over 13 as a blood pressure greater than 130/80 (99). [https://www.nhlbi.nih.gov/files/docs/guidelines/child_tbl.pdf](https://www.nhlbi.nih.gov/files/docs/guidelines/child_tbl.pdf)

In adult patients with T2DM concomitant treatment of hypertension has been shown to improve microvascular and macrovascular outcomes at least as much as improvement in glycaemic control (7). It would be reasonable to suggest a similar improvement in outcomes could be achieved in CYP.

Recommendations
- Blood pressure should be measured, using an appropriately sized cuff, at every clinic appointment – at least four times per year. (grade D)
- Blood pressure readings should be interpreted using a paediatric blood pressure centile chart. (Grade B)
- Hypertension is defined as systolic or diastolic pressure equal or greater than the 95th centile for age and sex on 3 separate occasions. If there is any concern about transient, stress related, high blood pressure readings (white coat syndrome) ambulatory blood pressure monitoring should be considered. (Grade B)
- BMI is a risk factor for developing hypertension and should be measured at every clinic appointment. (Grade B)
- Once a diagnosis of hypertension has been made initial treatment should focus on weight reduction, exercise and reducing salt in-take (100). (Grade C)
- If after 6 months blood pressure is still above the 95th centile for age, consider starting an ACE inhibitor (101) – the teratogenic risks of ACE inhibitors should be discussed with female adolescents and steps advised to mitigate against these risks, before starting treatment.
  - ACE inhibitors are particularly beneficial in young people with diabetes due to their renoprotective effect. Take advice from adult diabetologist/ paediatric nephrologist regarding other options.
  - For Afrocarribean population, consideration should be given to other causes of hypertension (refer to hypertension guidelines) but it is likely to be due to metabolic syndrome (Grade B)
  - The more common side effects of ACE inhibitors – abnormalities in sodium and potassium can be mitigated against by monitoring electrolytes with a blood test before starting treatment and at 4-6 weeks afterwards. (Grade D)
Hypotension – consider a test dose with pre and post blood pressure monitoring on a paediatric assessment unit before starting regular treatment. (Grade D)

- The aim of treatment should be to reduce blood pressure to less than the 90th centile for age, height and gender. (Grade B)
- If ACE inhibitors are not tolerated (the most common side effect, is a dry cough) angiotensin receptor blocker should be used (100). (Grade D)
- If, despite treatment, blood pressure is not lowered below the 90th centile referral to a tertiary hypertension service would be appropriate (100). (Grade D)

Lipids in youth with type 2 diabetes

Background

The dyslipidemia characteristic of obesity, insulin resistance and T2DM is hypertriglyceridemia and decreased HDL-C levels. Dyslipidemia is an important modifiable cardiovascular disease (CVD) risk factor. Earlier identification and control of dyslipidaemia reduces the risk of atherosclerosis in early adult life. Treatment of children with familial hypercholesterolaemia show reduction in subclinical atherosclerosis. (17).

- Optimal goals for lipid levels are (102):
  - LDL-C < 2.6 mmol/L (100 mg/dL)
  - HDL-C > 0.91 mmol/L (35 mg/dL)
  - Triglycerides <1.7 mmol/L (150 mg/dl)
  - Non HDL-C <3.6 mmol/L (140 mg/dL)

The American heart association (AHA), ADA (standards published in 2020: Diabetes Care) and ISPAD (2018) have provided evidence based recommendations for screening and management of dyslipidaemia (100, 102-104).

Recommendations:

Screening

- Lipid testing should be performed when initial glycaemic control has been achieved or after 3 months of treatment, and annually thereafter (Grade B)
The initial screening lipid profile does not need to be a fasted sample. Use non HDL-C level for initial screening (Grade A)

Management
If abnormal profile, initial treatment is by diet modification and improved glycaemic control (Grade A) (102)

- Limit calories from total fat to 25–30%
- Limit saturated fat to <7%
- Limit cholesterol to <200 mg/day
- Avoid trans fats
- For elevated LDL, aim for about 10% calories from monounsaturated fats.
- For elevated triglycerides, decrease simple sugar intake and increase dietary n-3 fatty acids in addition to the above changes.

A repeat lipid profile should be performed at 6 months following the dietary intervention and weight management (fasted) (Grade B)

Pharmacology
- If repeat LDL-C remains >3.4 mmol/L (130 mg/dl), treatment with a statin should be commenced. The ideal treatment target is to reduce the LDL-C to <2.6 mmol/L (100 mg/dL) (Grade B) (105-107).
- Statins can be used in children over the age of 10 years with T2DM (Grade A).
  - High intensity statins are recommended for the treatment and prevention of cardiovascular disease in patients with T2DM. Atorvastatin and Rosuvastatin are recommended as they can achieve high intensity LDL-C lowering effect (>40%) at lower doses than other statins. They can be prescribed in CYP 10-17 years old (BNFc). (Grade A)
  - Statins should be started at the lowest available dosage (Atorvostatin 10 mg daily, Rosuvastain 5 mg daily) and increased based on response and side effects.
  - If LDL-C target levels are not achieved with at least 3 months of compliant use the dose should be increased by 1 increment (usually 10mg). The dose can be increased by a further increment after a further 3 months or a second agent could be added under the guidance of a lipid specialist (eg bile acid sequestrant or cholesterol absorption inhibitor). (Grade B)
  - Liver enzymes should be measured before treatment, and repeated within 3 months and at 12 months of starting treatment.
  - Statins should be used with caution in patients at increased risk of muscle toxicity, including those with a personal or family history of muscular disorders, previous history of muscular toxicity, a high alcohol intake, renal impairment or hypothyroidism. Creatinine kinase concentration should be measured in children before treatment and if unexplained muscle pain occurs.
  - Hypothyroidism should be treated before starting statin treatment. (NICE, BNFc) (Grade B)
Statins are teratogenic and contraindicated in pregnancy – caution with use in adolescent girls (Grade B)

- If fasting triglycerides are >5.6 mmol/L (400mg/dl) or >11.3 mmol/L (>1000mg/dl) non-fasting, there is a risk of developing pancreatitis. (Grade C).
- Fibrates can be carefully considered in children over the age of 10 years for significant hypertriglyceridaemia in collaboration with lipid experts taking into account risk of rhabdomyolysis and lack of licence in children. (Grade A)
- There are no good RCT to support the use of omega 3 or fish oils in children or adolescents (108). Studies have shown benefit in adults in reducing Triglyceride levels (Grade A)

Other
- Recommend smoking cessation (Grade B)

Non-alcoholic fatty liver disease (NAFLD) in CYP with T2DM

Background
NAFLD is a histopathological spectrum of liver disease, from early benign steatosis to non-alcoholic steatohepatitis (NASH). Histologically, NAFLD is characterised by steatosis affecting more than 5% of hepatocytes.

In adults NAFLD contributes to the development of T2DM, cardiovascular disease and chronic kidney disease and also T2DM is one of the strongest clinical predictors of the progression of NAFLD to NASH and cirrhosis (109).

Hepatic steatosis is present in 25% to 50% of adolescents with T2DM and more advanced stages of disease are increasingly common. Disease starting in early childhood can be rapidly progressive. Screening for NAFLD in childhood T2D is therefore important. (110-112). Screening for NAFLD in childhood T2D is therefore important.

Management
The European and North American Societies for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN and NASPGHAN) have published clinical guidance for the diagnosis of paediatric NAFLD (113, 114).

There are no consistent recommendations for screening for NAFLD. All NASPAGHAN and ESPAGHAN both recommend using LFT to screen those with obesity. Additionally, ESPAGHAN recommends liver ultrasound in all those with obesity whilst NICE NAFLD guidelines limit ultrasound screening to those with obesity and signs of insulin resistance such as type 2 diabetes (115).

Frequency and of method of rescreening remains undetermined. NICE recommends rescreening every 3 years with ultrasound scan if initial scan is normal.
In CYP, biomarkers of NAFLD (ALT, AST) improve following weight loss and lifestyle modifications (general healthy eating and exercise). The amount of weight loss necessary is not clear. Studies have shown limited benefit from low fructose, low fat and low glycaemic index diets and low free sugar diets. Currently, there is no evidence to recommend one nutritional intervention over another (114, 116-118).

Management of insulin resistance and dyslipidaemia are important. Treating CYP with OSA has been shown to improve NAFLD severity (119). Optimising vitamin D levels may minimise fibrosis (120). Psychological support (as part of multidisciplinary management) may help to improve clinical outcomes (121).

There is currently no specific pharmacological treatment for paediatric NAFLD. The efficacy of several medications: metformin, vitamin E, antioxidants, fatty acid supplements and probiotics have been investigated in CYP in RCT but no clear established benefit on histologic outcomes or sustained reduction in ALT. In adults, Pioglitazone has been recommended for advanced liver fibrosis (115, 122-130).

If liver enzymes remain over 3 times the upper limit of normal despite lifestyle modifications and optimising glycaemic control, referral to a gastroenterologist (or liver specialist) is recommended for further assessment, investigations and management (113, 114). Liver biopsy remains the gold standard investigation however other modalities are being used by specialist centres including elastography (eg fibroscan) to risk stratify those with NAFLD. There is insufficient evidence to recommend other tools such as the Fibrosis-4 or ELF scores at this time.

Recommendations

- Initial screening with liver ultrasound and ALT at diagnosis. ALT should be undertaken annually as part of annual review. Ultrasound should be repeated every 3 years if initial scan normal (Grade B)
- Investigate for NAFLD/NASH and other causes of liver disease if persistently raised ALT (>2x ULN) as ALT not specific for NAFLD (Grade C)
- Consider referral to paediatric hepatology/gastroenterology if ALT levels >3x ULN despite dietary modifications and improved glycaemic control (ESPGHAN/NASPGHAN) (Good practice point)
- Management of NAFLD should follow separate NAFLD guidelines. General dietary and lifestyle advice aiming to achieve weight reduction is important however there are currently no specific dietary recommendations shown to reverse or slow progression of NAFLD (Grade A)
- Management of extrahepatic co-morbidities known to accelerate NAFLD i.e. insulin resistance and dyslipidaemia is important however there are no currently recommended pharmacological treatments specifically for treating NAFLD in children (Grade B)
- Assessment and treatment of comorbidity (Obstructive Sleep Apnoea, Vit D deficiency) (Good practice point)
- Psychological support important (Good practice point)
Retinopathy in Youth-Onset T2DM

Background
Diabetic retinopathy (DR) is a major microvascular complication of diabetes, mainly associated with long duration diabetes (131-133). DR is a major cause of visual loss in the UK and if left untreated can lead to blindness (134). In the UK, at 20 years post diagnosis nearly all adults with type 1 diabetes and 60% of adults with T2DM have some degree of retinopathy (135). For people of working age, DR is one of the leading causes of visual impairment in the UK; DR also increases the risk of cataract and glaucoma compared with the general population (136, 137).

Screening
The UK Department of Health recommends that screening for DR should be undertaken in England from the age of 12 years, regardless of disease duration. Similarly, ISPAD has recommended DR screening should start from age 11 years with 2-5 years diabetes duration. The youngest European reported patient to develop pre-proliferative retinopathy was in a Swedish study aged 11.8 years and in puberty (138). A retrospective analysis of 143 patients aged 12 years or younger who attended diabetic eye screening for the first time in the Birmingham, Solihull and Black Country Diabetic Eye Screening Programme was performed. The results from the 2016 audit by the Midlands Diabetic Eye Screening Programme showed that no patient younger than the age of 12 had sight-threatening DR (STDR), but background DR was identified (134). Scanlon et al demonstrated screening in Great Britain for DR earlier than 12 years of age is not necessary (139).

Recommendations (All Grade B)
- Diabetic retinopathy screening should start from the age of 12 and annually thereafter, in line with consensus advice.
- Improvement in glycaemic control remains the cornerstone of primary prevention and also mitigates progression once retinopathy has developed.
- Adult literature recommends treatment of hypertension and dyslipidaemia in the presence of diabetic retinopathy.
- As in Type 1, sudden Intensification of glycaemic treatment with a rapid reduction in HbA1c may lead to a rapid progression of retinopathy.
Microalbuminuria in Youth-Onset T2DM

Background
Kidney disease is a well-recognized and important complication of diabetes and diabetic kidney disease (DKD) is one of the most common causes of chronic kidney disease. Chronic kidney disease (CKD) is characterised by low estimated glomerular filtration rate (eGFR) and high albuminuria persistent for > 3 months (140), and is associated with adverse outcomes. Albuminuria is strongly associated with the progression of CKD as well as cardiovascular disease (CVD) (141).

Definition:
Based on National Health and Nutrition Examination Survey III (NHANES III), the definition of microalbuminuria was determined to be 30-300 mg/g 24 h collection; 20-200 mg/min in an overnight collection or 30-300 mg/g creatinine (3-30 mg/mmol) in a first morning urine sample (142, 143).

There has been a trend to no longer refer to categorical nomenclature of “microalbuminuria” (3–30 mg/mmol creatinine) and “macroalbuminuria” (>30 mg/mmol creatinine) but to use moderately increased albumin creatinine ratio (ACR) and severely increased ACR respectively, instead.

Albuminuria is an independent risk factor for the development of CKD and GFR loss and for cardiovascular morbidity and mortality (145-147).

Screening:
Measurement of albumin-to-creatinine ratio (ACR) in a spot urine sample, is now the preferred screening strategy in all patients and gives a quantitative result that correlates with the 24-hour urine values (mg/day) over a wide range of protein excretion (148, 149). Detection of urinary albumin concentration in a first-morning urine sample by a semi quantitative test (Micral) is the easiest and most cost-effective screening procedure to identify albuminuric subjects in an outpatient T2DM population (150).

Microalbuminuria should be confirmed with urine ACR >3mg/mmol on a random untimed urine with a subsequent early morning urine sample (142), as an elevated ACR can be affected by orthostatic proteinuria, marked hyperglycaemia, exercise, smoking, menstruation, recent intercourse and sample contamination (18, 19).

An abnormal reading of spot urine ACR should be confirmed on two of three consecutive tests obtained on different days within a 3- to 6-month period (47). This has been recommended in various international consensus guidelines including, NKF, NKDEP, ADA and ISPAD (18, 140, 145, 151).
Albuminuria occurs more commonly in type 2 diabetes, as compared to type 1, and this difference has been suggested to be independent of differences in body mass index and hypertension (152).

In addition to optimizing glycaemia, control of hypertension is important to prevent and slow the progression of nephropathy. Therapeutic options include the use of ACE inhibitors or angiotensin receptor blockers. (19, 153-156). There are No RCTs using renin-angiotensin suppression (ACE inhibitors or Angiotensin receptor blockers) or SGLT inhibitors in youth-onset T2DM (age < 18 years) with microalbuminuria found.

Please see the section on management of Hypertension of this guideline.

We recommend referral to specialist renal/kidney care services for CYP with CKD in the following circumstances (1B) (ref Kidney disease improving global outcomes (KDIGO)) (19, 140)

- GFR < 30 ml/min/1.73 m² and/or consistent finding of significant albuminuria (> 300mg/g [> 30mg/mmol] or albumin excretion rate (AER) > 300 mg/24 hours. (KDIGO) (ADA)
- Significant haematuria. (ADA)
- Renal structural abnormality on ultrasound. (ADA)
- When there is uncertainty of aetiology/Non-diabetic CKD (ADA) (KDIGO)

Non-diabetic CKD should be considered in; (144, 145, 157)
1. The absence of albuminuria in persons with a reduced eGFR;
2. Presence of retinopathy in patients with albuminuria >30mg/mmol creatinine.

Recommendations:

- Monitoring for albuminuria should commence at the time of diagnosis and annually thereafter by using the early morning spot urine (EMU) for albumin to creatinine ratio (ACR). (Grade B)
- An elevated urine ACR of above 3mg/mmol, should be confirmed by repeating the test on 2 further occasions on different days within a 3- to 6-month period. (Grade B)
- For moderately elevated albuminuria (Urine ACR 3-30mg/mmol), a multidisciplinary team approach should be applied to improve glycaemic control along with targeting other risk factors (smoking, obesity and hypertension) for albuminuria to improve the outcome. (Grade B)
- Use an ACE-inhibitor (ACE-I) or angiotensin receptor blocker (ARB), in non-pregnant patients with type 2 diabetes in the following circumstances: (Grade B)
  - For those with moderately increased albuminuria (3-30mg/mmol)
  - For those with severely increased albuminuria (>30mg/mmol)
- Referral to specialist renal/Kidney care services is recommended for children and young person (CYP) with chronic kidney disease (CKD) in the following circumstances (see guidance above) (Grade B)
Obstructive Sleep Apnoea (OSA) in CYP with T2DM

Background

Obstructive sleep apnoea (OSA) is a disorder characterized by repetitive episodes of upper-airway obstruction during sleep, which result in intermittent hypoxemia and transient arousals leading to sleep fragmentation and poor sleep quality. Obesity, male sex, and advancing age are the strongest risk factors for OSA (158, 159). It affects an estimated 1-2% of normal children (160, 161). OSA is common in obese youth, but the prevalence in paediatric type 2 diabetes has not been well documented (18). Sleep disturbance and OSA are increasingly recognised as being associated with obesity, insulin resistance in adults and children and type 2 diabetes in adults as well as risk for future cardiovascular disease (162-168).

Both ISPAD and Australasian Clinical Practice Guidelines suggest evaluating symptoms of obstructive sleep apnoea using questions about snoring, sleep quality, morning headaches, daytime sleepiness, stop breathing episodes, nocturia and enuresis at every visit after diagnosis (18). Questionnaires alone do not provide a high enough sensitivity/specificity to diagnose OSA (170, 171). The gold standard diagnostic test is overnight laboratory PSG, which allows for the quantification of episodes of apnoea and hypopnoea per hour of sleep, yielding an apnoea–hypopnea index (AHI). A diagnosis of OSA is made when the AHI of 5 and over (164). Treatment of OSA with continuous airway pressure has been associated with improvement in the glycaemic profile, decreased A1C and improvement in insulin sensitivity as well as inflammation in some but not in all studies (172-176).

Recommendations (Grade B evidence)

- The gold standard diagnostic test is overnight laboratory PSG, which allows for the quantification of episodes of apnoea and hypopnoea per hour of sleep.
- Clinical signs and symptoms are not always specific. A validated sleep questionnaire may be helpful. Clinicians should have high index of suspicion for SA.
- If symptoms and home sleep monitoring devices are suggestive, the diagnosis of OSA should be made by formal polysomnography and referral to sleep specialist for further management.
References

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Appendix 1

Adolescent Binge Eating Questionnaire (ADO-BED)

A 10-item questionnaire (Adolescent Binge Eating Scale) developed for the prediction of binge eating disorder (BED) diagnosis in adolescents seen for obesity.

- Ages: 12-18 years
- Languages: English
- Sensitivity/specificity: 83%/96%
- Scoring: A positive response to questions 1 or 2 plus more than 6 positive responses to questions 3-10 identifies those at high risk for BED; a score of 3 or fewer indicates a low likelihood of BED.

Free to download at [Adolescent Binge Eating Scale (ADO-BED) Questionnaire](268 KB).

ADO-BED Questionnaire

A simple questionnaire developed to identify obese adolescents at risk for binge eating disorder from (177) [Chamay-Weber: 2017].

1. Do you sometimes have a strong craving to eat although you are not really hungry or you have recently eaten? Yes/No

2. In this situation, do you sometimes find yourself starting to eat and then being unable to stop? For example, have you in the past wanted to eat a few biscuits and been unable to stop until the pack was empty? Yes/No

3. In these moments when you find yourself eating although you are not hungry or when you can't stop eating
   a) Do you sometimes feel the need to be alone, to isolate yourself to eat? Yes/No
   b) Do you sometimes have the feeling of being very detached, not really in the moment, as if you were eating while day-dreaming? Yes/No
   c) Do you sometimes eat because you feel unsettled, unwell, sad, angry or bored? Yes/No
   d) Do you sometimes feel you eat too much or that you eat more than others? Yes/No
   e) Do you sometimes have regrets or feel ashamed after you've eaten? Yes/No

4. How often do you experience not being able to stop eating or do you find yourself eating without being hungry?
   At least once a month/2-3 times a month/2-3 times per week every day

5. Since when have you experienced this?
6. When you are in these situations do you sometimes need to take action to eliminate what you have just eaten (exercise, skip the next meal, self-induce vomiting...) Yes / No

Referral to psychologist for further assessment and consideration of onward referral to children’s mental health/eating disorder services.
Appendix-2 PATIENT INFORMATION LEAFLET:

SGLT2 INHIBITORS AND DIABETIC KETOACIDOSIS IN TYPE-2 DIABETES

Why have I been given this leaflet?

You are taking, or about to take, one of the following drugs for improving your diabetes management:

- empagliflozin (Jardiance)
- canagliflozin (Invokana)
- dapagliflozin (Forxiga)

What do I need to know about these drugs?

These medications have been given to you to help you improve your weight and your blood sugar levels. However, people taking this drug can develop an unusual complication of diabetes, called euglycaemic diabetic ketoacidosis. This happens when too much acid builds up in the blood and can happen even when your blood glucose level is normal. If not identified early, this can be dangerous. However, this is a VERY RARE complication.

What should I look out for?

If you are taking one of these tablets, please look out for these symptoms:

- nausea and/or vomiting,
- fast breathing,
- abdominal pains,
- unusual drowsiness or
- fever.

If you have any of these symptoms, please measure your blood ketones, if you have a blood ketone meter at home. If your levels are over 0.6, please contact your diabetes team immediately, even if your blood sugars are near normal. If you cannot get hold of your diabetes team, please call NHS Direct at 111 for more advice. Inform them that you are worried about “Diabetic keto-acid-osis”

If you do not have a blood ketone meter at home, please contact your diabetes team or 111, as above.

STOP YOUR MEDICATION TILL FURTHER MEDICAL ADVICE

What can cause this problem?

This problem can develop at any time. You need to be especially careful:

- If you develop an infection (like a chest or urine infection) or undergo surgery.
If you are planning to have an operation or any other procedure which involves fasting overnight, please discuss this medication with your doctor or nurse – you may need to stop your tablets.

If I feel unwell, what will my doctor or nurse do?

You will have a finger prick blood test to test for the amount of sugar and ketones (a breakdown product of fat) in the blood. If the levels of ketones are high, you may need to attend the hospital to be treated. In the meantime, please ensure you are keeping yourself well hydrated. Please continue to take your insulin, if you usually take insulin.