Screening, assessment and management of type 2 diabetes mellitus in children and adolescents: Australasian Paediatric Endocrine Group guidelines

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Abstract

Introduction: The incidence of type 2 diabetes mellitus has increased in children and adolescents due largely to the obesity epidemic, particularly in high risk ethnic groups. β-Cell function declines faster and diabetes complications develop earlier in paediatric type 2 diabetes compared with adult-onset type 2 diabetes. There are no consensus guidelines in Australasia for assessment and management of type 2 diabetes in paediatric populations and health professionals have had to refer to adult guidelines. Recent international paediatric guidelines did not address adaptations to care for patients from Indigenous backgrounds.

Main recommendations: This guideline provides advice on paediatric type 2 diabetes in relation to screening, diagnosis, diabetes education, monitoring including targets, multicomponent healthy lifestyle, pharmacotherapy, assessment and management of complications and comorbidities, and transition. There is also a dedicated section on considerations of care for children and adolescents from Indigenous background in Australia and New Zealand.

Changes in management as a result of the guidelines: Published international guidelines currently exist, but the challenges and specifics to care for children and adolescents with type 2 diabetes which should apply to Australasia have not been addressed to date. These include:

- recommendations regarding care of children and adolescents from Indigenous backgrounds in Australia and New Zealand including screening and management;
- tighter diabetes targets (glycated haemoglobin, ≤ 48 mmol/mol [≤ 6.5%]) for all children and adolescents;
- considering the use of newer medications approved for adults with type 2 diabetes under the guidance of a paediatric endocrinologist; and
- the need to transition adolescents with type 2 diabetes to a diabetes multidisciplinary care team including an adult endocrinologist for their ongoing care.

In Australasia, the incidence of paediatric type 2 diabetes has increased in parallel to paediatric obesity, especially in high risk ethnic groups. Between 1990 and 2012 in Western Australia, the incidence increased from 4.5 to 31.1 per 100 000 person-years in Indigenous children, and from 0 to 1.4 per 100 000 person-years in non-Indigenous children.[1] The overall annual incidence of type 2 diabetes in people under 15 years of age was 1.5 per 100 000 person-years, with higher rates in Pacific Islanders (5.9 per 100 000 person-years) and Māori people (4.1 per 100 000 person-years).[2]

Glycaemic control in type 2 diabetes during adolescence deteriorates faster than in adults due to greater insulin resistance and β-cell dysfunction.[3] Complication rates occur earlier and are higher, with increased mortality rates, in paediatric type 2 diabetes compared with type 1 diabetes mellitus.[4,5]

Recent international guidelines were developed for paediatric type 2 diabetes[6,7] without addressing specifics for Australasia, including high risk ethnic groups. To date, there have been no management guidelines in Australasia for paediatric type 2 diabetes. This manuscript aims to provide guidelines for clinical practice based on available evidence for health care in the assessment and management of paediatric type 2 diabetes in Australasia.

The guidelines are targeted to children and adolescents younger than 18 years who are at risk of developing type 2 diabetes or who have been diagnosed with this disease in Australasia. They do not cover the management of acute complications of type 2 diabetes (eg, diabetes ketoacidosis and hyperglycaemic hyperosmolar state).

These guidelines are directed to all health care personnel and service providers responsible for the assessment and management of paediatric type 2 diabetes at all levels of care (eg, general practitioners, paediatricians, paediatric endocrinologists, allied health care professionals).

Methods

The Australasian Paediatric Endocrine Group (APEG) supported the establishment of a type 2 diabetes guideline development group, which included a multidisciplinary group of health care professionals (Supporting Information, table 1). The group members agreed on the scope and structure of the guidelines and were allocated specific writing sections based on areas of expertise. Previous paediatric type 2 diabetes guidelines were reviewed.[6,7] The databases and search terms for the literature search are included in the Supporting Information, section 1.

The group met at endocrine meetings and via teleconference. The recommendations included National Health and Medical Research Council and Grading of Recommendations Assessment, Development and Evaluation (GRADE) levels of evidence (Box 1). After the recommendations were formulated by each subgroup based on available evidence and benefits and harms on implementation, the whole group cross-reviewed all the collated material and approved the final guidelines document. APEG, the New Zealand Society for the Study of Diabetes and the Australian Diabetes Educators Association reviewed and endorsed the guidelines.

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1 National Health and Medical Research Council (NHMRC) and Grading of Recommendations Assessment, Development and Evaluation (GRADE) levels of evidence

GRADE definition and NHMRC levels of evidence	A	B	C	D
	Excellent	Good	Satisfactory	Poor
Definition	Body of evidence can be trusted to guide practice	Body of evidence can be trusted to guide practice in most situations	Body of evidence provides some support for recommendations but care should be taken in its application	Body of evidence is weak and recommendation should be applied with caution
Evidence base	Several level I or II studies with low risk of bias	One or more level II studies with low risk of bias	Level III studies with low risk of bias, or level II studies with moderate risk of bias	Level IV studies or level I to III with high risk of bias
Consistency	All studies consistent	Most studies consistent and inconsistencies may be explained	Some inconsistency reflecting genuine uncertainty around clinical question	Evidence is inconsistent
Clinical impact	Very large	Substantial	Moderate	Slight or restricted
Generalisability	Populations studied in body of evidence are the same as the target population for the guideline	Populations studied in body of evidence are similar to the target population for the guideline	Populations studied in body of evidence differ to target population for guideline but it is clinically sensible to apply this evidence to target population	Populations studied in body of evidence differ from target population and it is hard to judge whether it is sensible to generalise to target population
Applicability	Directly applicable to Australian health care context	Applicable to Australian health care context with few caveats	Probably applicable to Australian health care context with some caveats	Not applicable to Australia health care context
GRADE quality of evidence and definition	High quality. Further research is unlikely to change our confidence in the estimate of effect	Moderate quality. Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate	Low quality. Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate	Very low quality. Any estimate of effect is very uncertain

Recommendations

Box 2 shows the summary of guidelines, including eight sections and grading of recommendations. It will be used for implementation of the guidelines and review adherence to the guidelines. It also highlights the need of high quality research into childhood type 2 diabetes.

Screening and diagnosis

Type 2 diabetes is a state of persistent hyperglycaemia characterised predominantly by increased insulin resistance with subsequent relative insulin deficiency.[6,8] Paediatric type 2 diabetes is typically diagnosed in the second decade of life, coinciding with pubertal increase in insulin resistance. Screening for type 2 diabetes should be considered according to the presence of risk factors (Box 3, Box 4 and Supporting Information, table 2).[6,7,9,10] Clinical presentations and diagnostic investigations are included in Box 5 and Box 6.[7,11,12] The features assisting in the exclusion of other common types of diabetes (type 1 diabetes and monogenic diabetes) are described in Box 7.[6,12–14]

Diabetes education

Initial education

At diagnosis, the child and family should receive individualised diabetes self-management education that is developmentally appropriate, culturally sensitive and promotes family-centred behavioural change (Supporting Information, table 3).[7] If English is not the patient's first language, an interpreter should be present at the consultation, and written and pictorial material in their first language should be provided if available. Unfortunately, educational materials for paediatric type 2 diabetes are limited (Supporting Information, section 2).

Assessment of preconceived beliefs, attitudes, learning styles and psychosocial factors will help to identify barriers to education and predictors of poor engagement. Success in maintaining lifestyle self-care changes and reaching therapeutic goals involves initial and regular diabetes self-management education, including collaborative goal setting for diet, activity, blood glucose monitoring, and medications.

Education should be facilitated by a specialised multidisciplinary team (eg, a credentialled diabetes educator, or a diabetes nurse specialist in New Zealand; a dietitian; a psychologist and/or social worker; and ideally a physiotherapist or exercise physiologist) considering the family sociocultural background. Social work input is indicated in families with financial stressors, food insecurity, housing instability, family dysfunction, low parental support, and possible abuse or neglect.

Monitoring diabetes management and follow-up

Specialised multidisciplinary paediatric follow-up should occur at least monthly or more often in the first 3 months to adjust medications to achieve target glucose levels and review lifestyle behaviour modifications and weight management (Box 8). A target glycated haemoglobin (HbA_{1c}) level of 48 mmol/mol or below (≤ 6.5%) is recommended due to the anticipated longer disease duration, the accelerated rate of developing complications and the higher mortality rate compared with type 1 diabetes and adult-onset type 2 diabetes.[5,15,16] This target should be achieved without hypoglycaemia and/or undue treatment burden. In the TODAY study, hypoglycaemia rates, even for patients taking insulin, were lower in children with type 2 diabetes.[17]

2 Australasian consensus guidelines for screening, assessment and management of children and adolescents with type 2 diabetes mellitus

Guidelines sections and subsections	Recommendations	GRADE category
Screening diagnosis	Targeted screening for non-Indigenous populations should occur in children and adolescents (aged > 10 years or at onset of puberty, whichever occurs earlier) who are overweight (BMI ≥ 85th percentile) or obese (BMI ≥ 95th percentile) and have one or more additional risk factors: • maternal history of diabetes, including gestational diabetes during the child's gestation; • first degree relative with type 2 diabetes; • race or ethnicity (South Asian, South East Asian, Middle Eastern, North African and Latino) — for Indigenous populations: Aboriginal, Torres Strait Islander, Māori and Pacific Islander (see section below on considerations for children and adolescents of Indigenous backgrounds in Australasia); • signs of insulin resistance (acanthosis nigricans); • other conditions associated with obesity and metabolic syndrome (ie, hypertension, dyslipidaemia, fatty liver disease, polycystic ovary syndrome, small for gestational age); and • use of psychotropic medications	B
	Diagnosis of type 2 diabetes can be made using fasting glucose, 2-hour glucose level from oral glucose tolerance or HbA_{1c} tests	B
	Diabetes autoantibodies testing (glutamic acid decarboxylase and islet tyrosine phosphatase 2) should be considered in all children and adolescents with clinical phenotype of type 2 diabetes due to higher prevalence of type 1 diabetes mellitus in this age group	B
	Genetic testing for monogenic diabetes should be considered if diabetes is present in two or more consecutive generations and diabetes autoantibodies are negative	B
Diabetes education	All children and adolescents with type 2 diabetes need comprehensive and specific diabetes self-management education that is family-centred, individualised, and developmentally and culturally appropriate	B
	Education should be delivered by a specialised multidisciplinary team with expertise in managing paediatric type 2 diabetes	C
Monitoring glycaemia	Self-monitoring of blood glucose needs to be individualised according to treatment type and need to improve glycaemia	D
	Aim for blood glucose levels 4–6 mmol/L (fasting) and 4–8 mmol/L (2 hours postprandial)	D
	Target HbA_{1c} levels should be ≤ 48 mmol/mol (≤ 6.5%) given the significant morbidity and mortality, but without causing hypoglycaemia and/or undue treatment burden	C
	HbA_{1c} should be assessed every 3 months	D
Healthy lifestyle	Weight management and multicomponent approach to lifestyle modification is required at diagnosis and ongoing	C
Weight management	Optimise weight management	B
Diet	Aim for healthy eating: eliminate sugar-sweetened beverages, reduce calorie-dense and nutrient-poor foods, provide education regarding carbohydrates (role, sources, portion control and, if appropriate, counting of carbohydrates) and ensure adequate intake of nutrient-dense and low glycaemic index foods	B
	Reduce total energy intake to achieve ≥ 7% decrease in excess weight	B
Physical activity	Aim for at least 60 min/day of moderate to vigorous physical activity to improve body composition, glucose management and insulin sensitivity	B
	Exercise programs should include resistance activities to increase muscle mass, contributing to improved blood glucose management	B
Sedentary behaviour	Recreational screen time should be limited to ≤ 2 hours a day	C
Sleep	Encourage quality sleep of 8–11 hours duration according to age, with consistent bed and wake-up times and reduction of electronic media use in the evening	C
Considerations for children and adolescents of Indigenous backgrounds in Australasia (Aboriginal, Torres Strait Islander, Māori and Pacific Islander)	Consider point-of-care HbA_{1c} screening in all Aboriginal and Torres Strait Islander children from 10 years of age (or at onset of puberty, whichever occurs earlier) who have one or more risk factors: • overweight or obesity (BMI ≥ 85th or ≥ 95th percentile respectively, and/or waist circumference to height ratio > 0.5); • maternal history of diabetes or gestational diabetes during the child's gestation; • first degree relative with type 2 diabetes; • signs of insulin resistance (acanthosis nigricans); • other conditions associated with obesity and metabolic syndrome (ie, hypertension, dyslipidaemia, fatty liver disease, polycystic ovary syndrome, small for gestational age); and • use of psychotropic medications	C
	Consider provision of health services using non-traditional locations or structures, with opportunities for young people and families to meet each other and improving engagement with health care professionals*	C
	Identify the priorities of the adolescent, avoid blame and stigmatising language, and individualise health messages, empowering adolescents to manage their risk*	C

Continues

2 Continued

Guidelines sections and subsections	Recommendations	GRADE category
Pharmacotherapy	Metformin up to 2 g per day should be used as the first line medication in patients presenting with mild symptoms or in those who are diagnosed after screening	A
	Insulin should be the first line treatment for patients who present with diabetes ketoacidosis, hyperglycaemic hyperosmolar state or ketosis, and should be added to metformin where glycaemic targets have not been achieved or maintained with metformin monotherapy	B
	If glycaemic targets are not achieved with metformin (with or without insulin), other glucose-lowering medications approved for adults should be considered. Such medications should only be prescribed under the guidance of a paediatric endocrinologist, given limited evidence for safety and efficacy in children and adolescents	D
Complications and comorbidities	Screen for all complications and comorbidities soon after diagnosis of type 2 diabetes to establish prompt management and ongoing assessment and management†	A
Retinopathy	Assess retina using dilated pupil exam or retinal photography by an optometrist or ophthalmologist at diagnosis and yearly unless abnormal†	A
Nephropathy	Assess early morning urine albumin to creatinine ratio at diagnosis and yearly unless abnormal†	A
Neuropathy	Foot examination at diagnosis and yearly unless abnormal†	C
Overweight/obesity	Optimise weight management as well as glycaemia to reduce risk of comorbidities and complications†	B
	Consider bariatric surgery for selected post-pubertal adolescents with type 2 diabetes with severe obesity, taking into account special considerations in relation to consent, procedure, family support and availability of adequate services†	C
Psychosocial	Quick screening tools for psychosocial comorbidities and diabetes distress should be used regularly after diagnosis†	B
	Consider screening for disordered eating behaviour†	D
Reproductive health	For adolescent girls, a review of menstrual cycle regularity, symptoms and signs of hyperandrogenism, and need of contraception should be done at every visit, especially if the HbA_{1c} level is above target or the patient is using teratogenic medications†	B
Liver disease	Assess liver function test (aspartate aminotransferase and alanine aminotransferase) at diagnosis and yearly unless abnormal†	B
Obstructive sleep apnoea	Evaluate symptoms of obstructive sleep apnoea in children and adolescents with obesity†	C
Hypertension	Assess blood pressure using appropriate cuff at every visit†	A
Lipids	Assess lipid profile when glycaemic targets have been achieved after diagnosis and yearly unless abnormal†	B
Transition	Transition to adult endocrinologist within a multidisciplinary team due to the severity of disease progression and higher risk of diabetes complications	C

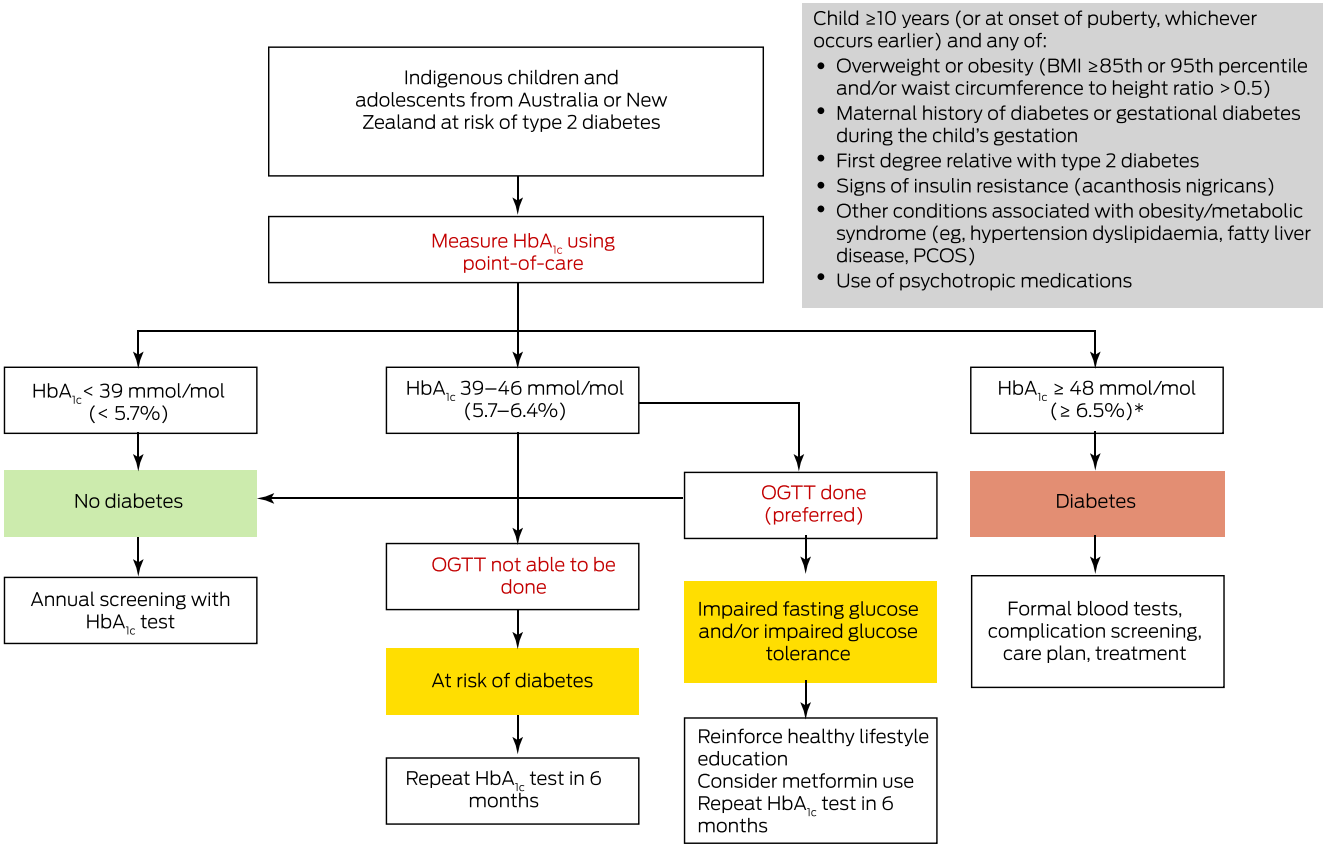
BMI = body mass index; GRADE = Grading of Recommendations Assessment, Development and Evaluation; HbA_{1c} = glycated haemoglobin. * This will also apply to non-Indigenous adolescents. † Refer to Box 13. ◆

3 Recommendations for type 2 diabetes screening in non-Indigenous children and adolescents

	Recommendations
Population (non-Indigenous children and adolescents)	Consider targeted screening in children and adolescents aged > 10 years (or at onset of puberty, whichever occurs earlier) in those who are overweight (BMI ≥ 85 and < 95%) or obese (BMI ≥ 95%) and who have one or more additional risk factors: • maternal history of diabetes or gestational diabetes mellitus during the child's gestation; • family history of type 2 diabetes in first degree relative; • race and ethnicity (South Asian, South East Asian, Middle Eastern, North African and Latino); • signs of insulin resistance (acanthosis nigricans); • conditions associated with obesity and metabolic syndrome (hypertension, dyslipidaemia, fatty liver disease, polycystic ovary syndrome, or small for gestational age); and • use of psychotropic medications
Screening method	HbA_{1c} or OGTT
Screening frequency	Every 2–3 years or earlier if excessive weight gain

BMI = body mass index; HbA_{1c} = glycated haemoglobin; OGTT = oral glucose tolerance test. ◆

4 Recommendations for type 2 diabetes screening in Indigenous children and adolescents from Australia or New Zealand



BMI = body mass index; HbA_{1c} = glycated haemoglobin; OGTT = oral glucose tolerance test; PCOS = polycystic ovary syndrome. * If the initial HbA_{1c} ≥ 48 mmol/mol (≥ 6.5%) measurement was done via point-of-care, need to confirm with formal laboratory measure. Source: adapted from the Northern Territory Diabetes Network. ◆

5 Clinical presentations of paediatric type 2 diabetes[11]

Clinical presentation	Percentage of patients	Symptoms, signs and investigations
Asymptomatic	33%	• Boils, thrush • Positive screening or random testing
Symptomatic	67%	• Polyuria • Polydipsia • Weight loss • Fatigue • Absent to mild ketosis
Diabetic ketoacidosis	11%	• Kussmaul breathing, vomiting, abdominal pain, drowsiness • Plasma glucose > 11 mmol/L • Venous pH < 7.3 • Serum bicarbonate > 15 mmol/L • Ketosis
Hyperglycaemic hyperosmolar state	2%	• Altered consciousness, seizures • Plasma glucose > 33.3 mmol/L • Venous pH > 7.25 • Serum bicarbonate > 15 mmol/L • Absent to mild ketosis • Effective serum osmolality > 320 mOsm/kg

The frequency of monitoring needs to be individualised (Box 8). Continuous glucose monitoring sensors have not been evaluated in paediatric type 2 diabetes but showed benefits in adults. They should be offered, if available, for children receiving insulin therapy.

Low attendance for follow-up reviews occurs in children and adolescents with type 2 diabetes.[18] Providing ongoing follow-up by telehealth services may be a feasible option for families in regional and remote settings to facilitate the establishment and maintenance of ongoing therapeutic relationships with health professionals.[19] Schools should also be involved in the management of diabetes to facilitate ongoing support.

Healthy lifestyle: diet, physical activity and sleep

A multicomponent approach to healthy lifestyle modification for weight management is a priority after a type 2 diabetes diagnosis. This approach includes dietary change to improve nutrition; daily physical activity that is enjoyable, accessible and of an intensity that enhances cardiometabolic health; reduction of sedentary time; improvement of sleep patterns; positive role-modelling and promotion of family-based problem-solving skills.[20] Long term behaviour change requires both family and community-centred approaches to address physical inactivity, cardiovascular risks and excessive weight gain.[21]

6 Criteria for diagnosis of type 2 diabetes

	Criteria
Diagnosis (glucose measurements)	• Classic symptoms of diabetes or hyperglycaemic crisis and random plasma glucose ≥ 11.1 mmol/L,* or • Fasting† plasma glucose ≥ 7.0 mmol/L, or • 2-hour plasma glucose ≥ 11.1 mmol during an OGTT,‡ or • HbA_{1c} ≥ 48 mmol/mol (≥ 6.5%)§
Other investigations at diagnosis	• Consider diabetes autoantibody testing in all paediatric patients with the clinical phenotype of type 2 diabetes due to higher prevalence of type 1 diabetes — GAD and IA2 are the most commonly available. Insulin antibodies and zinc transporter 8 antibodies can also be measured if negative GAD and IA2, and type 1 diabetes is suspected • Insulin and C-peptide measurements are not recommended as glucotoxicity and lipotoxicity can acutely affect insulin secretion

GAD = glutamic acid decarboxylase; HbA_{1c} = glycated haemoglobin; IA2 = islet tyrosine phosphatase 2; OGTT = oral glucose tolerance test. * Asymptomatic individuals without ketosis should have repeat testing the following day. Hyperglycaemia can occur transiently during physiological stress (acute infection, trauma, surgery, respiratory distress, circulatory compromise) and should not be considered diagnostic of diabetes in these circumstances. † No caloric intake for at least 8 hours. ‡ An OGTT may be required if diabetes cannot be diagnosed on fasting, random or postprandial criteria. OGTT has poor reproducibility in adolescents and should be repeated if the child does not have hyperglycaemic symptoms. OGTT should include a glucose load containing equivalent 1.75 g/kg anhydrous glucose dissolved in water to maximum 75 g and a high carbohydrate intake 3 days before the OGTT. § Point-of-care measurement of HbA_{1c} may vary between ethnic populations and should be interpreted with caution, particularly in the setting of haemoglobinopathies and anaemia. HbA_{1c} should be performed in a laboratory using a method that is certified by the National Glycohaemoglobin Standardization Program and standardised to Diabetes Control and Complications Trial (DCCT) assay. ◆

Diet

The general principles for dietary and weight management include:

- maintaining a nutritionally adequate diet for growth and development;
- preventing further weight gain for adolescents who are overweight, or encouraging weight loss for adolescents with obesity, with a sustained weight loss greater than 7% of excess body weight, while maintaining normal linear growth;[7,21]
- providing dietetic support to help achieve optimal glycaemic control and manage comorbidities; and
- establishing regular follow-ups to monitor growth, achievement of dietary goals, and weight and glycaemic management.

Strategies to promote positive dietary change are included in Box 9.[6,7,20–23] More evidence is needed regarding the long term outcomes of certain diets, and their use must be closely supervised by a qualified dietitian (Box 10).[20,24,25]

Physical activity and sedentary behaviour

Australian and New Zealand guidelines specify at least 60 minutes per day of moderate to vigorous physical activity including muscle-strengthening exercises 3 days per week, depending on other pre-existing conditions.[26,27] Education about the positive impact of physical activity on diabetes management and supporting sustained engagement in a physical activity program are required.

Strength training such as skipping or climbing improves muscle mass, body composition, insulin sensitivity and glycaemic management. Body weight resisted exercise and light resistance bands or light free weights are safe for children who have not achieved skeletal maturity. Skeletally mature adolescents may use external resistance, such as gymnasium equipment, which may also increase motivation.

There are few high intensity interval training studies in adolescents, but studies in adolescents without type 2 diabetes and in adults with type 2 diabetes show a feasible and time-efficient approach for improving fitness, body composition, glucose management and cardiovascular health.[28]

Reduction of sedentary behaviour (maximal recreational screen time < 2 h/day) must also be addressed.[27]

Sleep behaviour

Inadequate sleep duration and poor sleep quality is common among adolescents, who have to sleep 9 hours on average to meet physiological needs. Sleep deprivation (ie, < 8 h sleep per night) and obstructive sleep apnoea in adolescence is associated with obesity and metabolic syndrome. Strategies

7 Differential diagnosis of paediatric type 2 diabetes*

	Type 1 diabetes	Monogenic diabetes
Key points	Most common cause of diabetes in white children from Australia or New Zealand Features include: • population frequency of obesity; • absence of acanthosis nigricans with or without other characteristics of metabolic syndrome; • ketosis or DKA at diagnosis in ≥ 25% of cases; • positive type 1 diabetes autoantibodies (> 90%);† • family history of type 1 diabetes in up to 4%‡,[12]	Up to 8% of children with type 2 diabetes phenotype have monogenic diabetes[13] Features include: • population frequency of obesity; • absence of acanthosis nigricans with or without other characteristics of metabolic syndrome; • ketosis in neonatal diabetes, rare in other forms; • negative diabetes autoantibodies; • family history of diabetes in 90% of individuals • mild fasting hyperglycaemia occurs in some forms (eg, MODY2)
Investigations	Autoantibodies: • GAD and IA2 are the most commonly available • Insulin antibodies and zinc transporter 8 antibodies can also be measured	• Genetic testing: all children with diabetes diagnosed under 6 months of age or diagnosed at 6–12 months of age with negative autoantibodies • Paired C-peptide and glucose 2–5 years after diagnosis may be useful to distinguish MODY from type 1 diabetes and type 2 diabetes

DKA = diabetes ketoacidosis; GAD = glutamic acid decarboxylase; IA2 = islet tyrosine phosphatase 2; MODY = maturity onset diabetes of the young. * Other uncommon differential causes of type 2 diabetes include diseases of the exocrine pancreas (cystic fibrosis, haemochromatosis, pancreatitis), endocrinopathies and drug-induced diabetes among others. † 10–20% of children with phenotypic type 2 diabetes may have one positive autoantibody.[8,14] ‡ More than 15% of children diagnosed with type 1 diabetes have positive family history for type 2 diabetes.[8] ◆

8 Monitoring diabetes management and targets in children and adolescents with type 2 diabetes

	Targets*	Frequency
HbA_{1c}	≤ 48 mmol/mol (≤ 6.5%)	Every 3 months
Self-monitoring blood glucose	• Fasting blood glucose levels: 4–6 mmol/L • 2-Hour postprandial blood glucose levels: 4–8 mmol/L	According to treatment regimen and/or intercurrent illness: • if receiving lifestyle management and/or metformin: fasting, before and 2 hours after a main meal three times a week, unless HbA_{1c} is unreliable or target HbA_{1c} is not achieved; • if taking basal insulin or oral agent with hypoglycaemia risks: fasting and bedtime; • if receiving multiple daily injections, initiating or changing treatment, or treatment goals not met: at least three times a day (fasting, before and 2 hours after a main meal) • if unwell: four times a day (fasting, before and 2 hours after one main meal and overnight) • if showing symptoms of hyper- or hypoglycaemia
Ketones testing	Negative in urine or capillary blood (β-hydroxybutyrate)	If unwell, if showing symptoms or signs of ketosis or DKA, or if there is a history of DKA at diagnosis

DKA = diabetes ketoacidosis; HbA_{1c} = glycated haemoglobin. * Target blood glucose levels are determined on the basis of achieving a target HbA_{1c} level ≤ 48 mmol/mol (6.5%). ◆

9 Strategies to promote positive dietary change

- Decrease total energy intake and lower carbohydrate intake. Ensure there is adequate knowledge of the role of carbohydrates and their sources — this includes skills regarding label reading, portion control and, if appropriate, counting of carbohydrates
- Eliminate consumption of sugar-sweetened beverages (eg, soft drinks, juices, fruit drinks)
- Reduce intake of energy-dense, nutrient-poor foods and snacks (address frequency of intake and portion sizes)
- Ensure adequate fruit (two serves per day) and vegetable (five serves per day) intake
- Reduce saturated fat to less than 7% and total dietary fat to 25–35% of total energy intake
- Ensure appropriate intake of low glycaemic index, high fibre foods
- Promote healthy food choices and regular mealtimes for all family members
- Encourage strategies to improve food skills in order to reduce reliance on processed, pre-prepared and takeaway foods

to improve sleep hygiene, such as earlier and consistent bed and wake-up times and reduced evening exposure to electronic media, may assist children and adolescents to achieve adequate quality sleep duration (ie, 9–11 h/night for children aged 5–13 years, and 8–10 h/night for adolescents aged 14–17 years).[29]

Considerations for Indigenous children and adolescents in Australasia

Screening

In Australasia, a high proportion of children with type 2 diabetes are of Aboriginal, Torres Strait Islander, Māori or Pacific Islander descent.[1,2] Due to high diabetes rates at a younger age and the high incidence of obesity and cardiovascular disease among these children and adolescents screening is required.[10,30,31] In this region, screening should be performed in any Indigenous child older than 10 years (or at onset of puberty) with one risk factor using point-of-care HbA_{1c} testing (Box 4).

Non-pharmacological management

Box 11 describes strategies to improve engagement with families usually disengaged from traditional services (not necessarily from Indigenous background groups). These families will require collaboration with services beyond the health sector.[10,19,32–34]

Pharmacotherapy

Initial therapy will depend on clinical presentation at diagnosis (Box 12).[35]

Metformin

Metformin should be commenced in all children and adolescents with non-acute type 2 diabetes presentations after urea, creatinine and electrolytes are reviewed (Box 12).[36] Metformin should be avoided in children who have intolerable side effects, a known allergy to biguanides, or renal insufficiency (estimated glomerular filtration rate, < 30 mL/min/1.73m^2). Either immediate release (IR) (can be crushed if required) or extended release (XR) metformin 500 mg (250 mg if the child is aged < 10 years) should be started after the evening meal. Metformin liquid (available as 100 mg/mL and 1000 mg/5mL) should be limited to younger children due to its high cost as it is sourced from overseas. Increase metformin up to 2000 mg/day (once daily for XR, 1000 mg twice daily for IR) over 3–4 weeks, as tolerated.[37]

Discontinue metformin 48 hours before elective surgery, radiological studies involving iodinated contrast media, and during gastrointestinal illness. Gastrointestinal side effects are common with initial metformin use, with 40% of patients experiencing abdominal pain, nausea or diarrhoea. Slow dose escalation, good adherence, and administration with food reduce or prevent these symptoms. A minority of children (8%) are unable to tolerate the side effects of metformin IR but may tolerate the XR formulation.[17,36] Metformin is not associated with hypoglycaemia and may aid weight loss and reduce cardiovascular risk.[38] Vitamin B12 deficiency and lactic acidosis are other rare potential side effects.[17]

Insulin

Insulin is the first line medication in children and adolescents presenting with symptoms, or during times of metabolic decompensation in a child with known type 2 diabetes (Box 12).[6,7] Insulin therapy achieves rapid improvement in glycaemic levels,

10 Specific dietary interventions according to evidence

Evidence	Dietary interventions	Features	GRADE category
Interventions supported by some evidence	Healthy eating advice with appropriate portions and calories	• Based on the Australian Guide to Healthy Eating and the New Zealand Food and Nutrition Guidelines for Healthy Children and Young People[22,23] (aged 2–18 years) with age-specific dietary recommendations • Foods are categorised as low, moderate and high calorie to guide intake frequency • Demonstrated effective modest weight loss in adolescents in the short to medium term	B
	Lower GI	• Higher GI foods are replaced with nutritious and lower GI foods (GI < 55) to reduce glycaemic load alongside appropriate total energy intake • It has demonstrated significant reductions in waist circumference, BMI z-score, and insulin resistance if combined with appropriate total energy intake • A lower-GI diet alone significantly reduces insulin resistance	C
Interventions requiring further evidence regarding long term outcomes	Very low carbohydrate diet	• Typically 20–50 g/day or 5–15% of total calories • Improves hyperinsulinaemia in adolescents with obesity	C
	Very low energy diet	• Typically < 800 kcal and < 50 g carbohydrate per day, aiming to induce ketosis • Recommended only for short periods (8–12 weeks) • Can achieve short term rapid weight loss while preserving lean body mass, decreasing BMI and improving HbA_{1c} levels in adolescents with obesity • A modified approach, closely supervised by a qualified dietitian, is required to ensure adequate provision of micronutrients • Prior screening for disordered eating using an age-appropriate validated tool should be considered	D
	Intermittent modified fasting	• Carbohydrate is moderately restricted overall to account for 26–44% of total calories • Effective in the adult population in terms of weight loss, reduced body fat, improved insulin sensitivity and other risk factors • Limited evidence is available regarding the use of this strategy in adolescents	D

GI = glycaemic index; BMI = body mass index; GRADE = Grading of Recommendations Assessment, Development and Evaluation; HbA_{1c} = glycated haemoglobin. ◆

with low rates of symptomatic hypoglycaemia.[17] Depending on glycaemic management, insulin can be reduced by 30–50% weekly until ceased, leaving metformin as a monotherapy. An HbA_{1c} level of 69 mmol/mol or greater (≥ 8.5%) at diagnosis or longer duration of diabetes are more likely to lead to ongoing insulin requirements.[39] More than 50% of adolescents with type 2 diabetes require insulin within 5 years of diagnosis.[3] The RISE study has shown that short term insulin therapy in newly diagnosed adolescents with type 2 diabetes was not successful in halting the progressive deterioration of β-cell function.[40]

Long-acting insulin (commenced at 0.25–0.5 U/kg/day and increased up to 1.5 U/kg/day) may be used if glycaemic targets are not met with metformin. Prandial insulin should be introduced as a next step (Box 12). Insulin pump therapy may be a viable option in the future.

Long term follow-up should occur at least quarterly to allow titration or change of medications and review of lifestyle measures and agreed glycaemic targets (Box 8 and Box 12). Clinicians should not blame children and adolescents or their families for being unable to achieve agreed glycaemic targets, but should explore any barriers together in a supportive manner. Treating to a target HbA_{1c} level rather than waiting for the HbA_{1c} level to rise provides better long term glycaemic management.[6]

When discharging from hospital a newly diagnosed child or adolescent with type 2 diabetes or when changing or adding a medication, the clinician should ensure that appropriate storage of medications is possible at home. Children and adolescents taking several medications benefit from the use of a dosage administration aid and the support of an adult family member. The family should be provided with written information and/or pictorial information regarding the medication, especially if literacy is low. Their general practitioner should be notified regarding medication changes.

Other available oral and injectable hypoglycaemic agents

Metformin and insulin are the only medications currently approved in Australasia for use in children and adolescents with type 2 diabetes aged less than 18 years. A wide range of medications are approved for use in adults with type 2 diabetes, including sulfonylureas, thiazolidinediones, glucagon-like peptide 1 (GLP-1) receptor agonists, dipeptidyl peptidase-4 (DPP4) inhibitors, and sodium–glucose cotransporter type 2 (SGLT2) inhibitors. Of these agents, a few have been evaluated for safety and efficacy in randomised controlled trials in children (Supporting Information, table 4). Sulfonylureas improve HbA_{1c} levels, similar to metformin, but cause weight gain and hypoglycaemia (Supporting Information, table 4). GLP-1

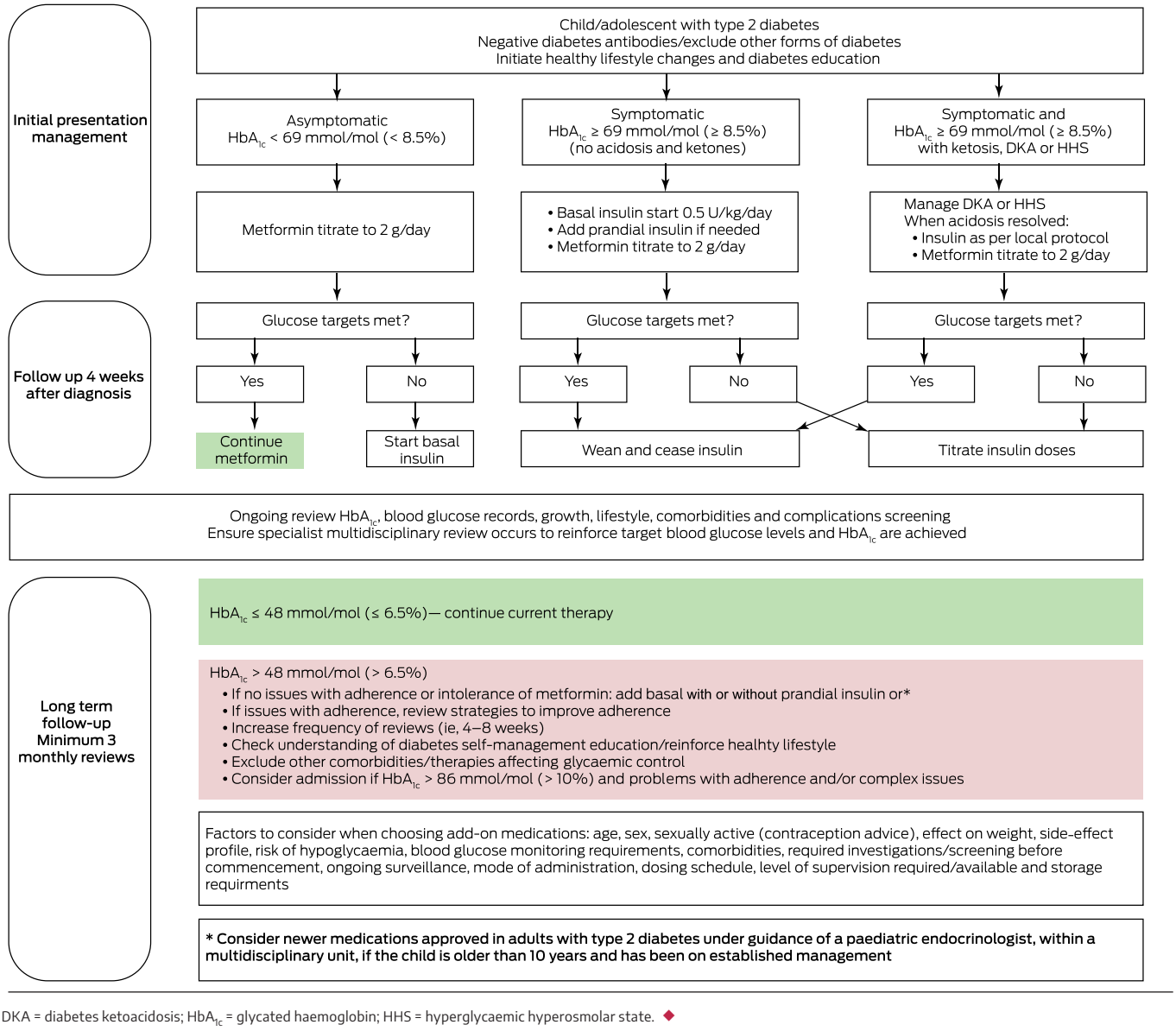
11 Strategies and issues to consider in the management of Indigenous children and adolescents with type 2 diabetes from Australasia (some can also be applied for non-Indigenous groups)

Strategy	Specific issues to consider	Reasons
Engagement of adolescents, families and communities	Utilise Indigenous/cultural (diabetes) health workers and/or practitioners who are well educated on local cultural knowledge, and ideally also include Indigenous/cultural community members to deliver DSME	Mistrust of non-Indigenous health workers relates to lack of understanding of the culture and the assignment of blame
	Use a yarning approach involving a holistic family-centred discussion about diabetes using pictures, manikins and collaborative goal setting	Overcome literacy issues and encourage family support
	Deliver DSME to all family members within the home, community centre and/or non-clinical settings	Encourage family and community support
	Explain causes of diabetes and how to access safe spaces for physical activity and food security	Decrease guilt and stigma
	Connect adolescents with peers	Alleviate the stigma, embarrassment and isolation associated with type 2 diabetes
	Identify barriers and empowering factors to self-management at each visit	Improve engagement
	Understand reasons for non-attendance to clinics and keep working on engagement with increased social and family support	Non-attendance may not represent lack of concern
Language considerations	Avoid a language of blame and shame when discussing type 2 diabetes	Adolescents from high risk populations, where multiple family members have type 2 diabetes and associated complications, may be ambivalent or apathetic, feeling that having diabetes is inevitable and that little can be done
	Keep messages positive, simple, easily understood and targeted to the adolescents and their family, acknowledging their priorities, fears, misconceptions, preferences and beliefs	Low literacy, low health literacy and need of different types of communication. Explanations are needed to overcome myths and misconceptions (eg, insulin use causes kidney failure and need for dialysis)
	Use of an interpreter if required but need to maintain confidentiality and ensure all the concerns are raised and addressed appropriately	Overcome language barriers if English is not first language
Whole family approach	Engaging the whole family	Increase the likelihood of the adolescent being able to modify behaviour, and reduce unhelpful reactions of isolation, blame or guilt. It may also benefit the health of the whole family
	Social support, particularly from other family members with type 2 diabetes who may influence health advocacy, beliefs and behaviour	Other family members with type 2 diabetes may hinder or help the adolescent
Psychosocial health	Screen for psychosocial health; HEEADDSS framework approach exploring the many domains of young people's lives	Adolescents with type 2 diabetes are at higher risk of mental health issues; these are important in their own right but also associated with increased risk of renal complications
	Access to Indigenous/cultural health workers or health professionals from relevant ethnic and community groups	There may be fear of disclosure due to mental health stigma
Food security	Social programs and locally developed cooking and nutrition programs can be useful, illustrating foods that can be prepared from the local store, and at a lower cost than highly processed, energy-dense and low nutritional value foods	There is limited access to affordable, fresh and healthy food choices in rural or remote settings. Less than 10% of housing in remote Indigenous Australian communities have functioning food preparation space, storage facilities and cooking equipment, limiting capacity for healthy lifestyle management of type 2 diabetes
Social welfare	Offer free transport to appointments and subsidise medications using schemes such as Closing the Gap	This may assist with attendance to appointments and achieve treatment outcomes

DSME = diabetes self-management education; HEEADDSS = H (Home environment), E (Education and employment), E (Exercise and healthy eating), A (Activity and peers), D (Drugs, smoking and alcohol), D (Depression and suicide ideation), S (sexuality and sexual health), S (Sleep). ◆

receptor agonists, DPP4 inhibitors and SGLT2 inhibitors have shown benefits in adults with type 2 diabetes, and studies suggest a similar pharmacokinetic profile in children. In adults, GLP-1 receptor agonists and SGLT2 have beneficial effects on HbA_{1c} levels, weight, and cardiovascular disease, with low hypoglycaemic risk. Evidence for safety and efficacy in children older than 9 years include two randomised controlled trials of GLP-1 receptor agonists which showed beneficial effects on glycaemia, with one study on the use of liraglutide showing a significant treatment difference in HbA_{1c} level of –1.06% after 26 weeks.[41] Multiple trials are currently being conducted to examine these agents in paediatric type 2 diabetes (Supporting Information, table 4). The use of these medications should be under the guidance of a paediatric endocrinologist if glycaemic

12 Treatment in children and adolescents with type 2 diabetes



DKA = diabetes ketoacidosis; HbA_{1c} = glycated haemoglobin; HHS = hyperglycaemic hyperosmolar state. ◆

targets are not achieved with metformin (with or without insulin) (Box 12). Effective contraception is required when using these medications in adolescent girls.

Complications and comorbidities

All adult and paediatric type 2 diabetes guidelines have emphasised the importance of evaluating complications and comorbidities at diagnosis.[6,7,9,37] Large cohorts demonstrate high prevalence of comorbidities at type 2 diabetes diagnosis.[8,42] Nevertheless, screening and management of comorbidities is suboptimal in children and adolescents with type 2 diabetes.[43]

Diabetes-related complications include retinopathy, nephropathy, neuropathy and cardiovascular disease. The evaluation and management of cardiovascular complications rely on careful assessment and aggressive treatment of cardiovascular risk factors (eg, increased weight, dyslipidaemia, hypertension, diet, activity and glycaemia) as there is not a single early cardiovascular disease marker that is an accurate predictor of cardiovascular events in adulthood (Box 13).

The most important comorbidity and contributor to type 2 diabetes is obesity. Most children with type 2 diabetes have obesity and a small number are overweight, except in Asian children and adolescents, for whom cut-offs for obesity and overweight are lower.[44] Increased weight is associated with higher glycaemia and other comorbidities (Box 13).[8,45] For postpubertal adolescents with type 2 diabetes with severe obesity, bariatric surgery may be an option for weight management and improvement of diabetes control achieving target HbA_{1c}.[46] Special considerations for bariatric surgery include consent issues, family support, lack of multidisciplinary teams with expertise in paediatric bariatric surgery attached to transition services, and availability in the public sector in Australasia. In addition, there is a lack of adequate long term data (> 10 years) in relation to re-operations, complications and nutritional deficiencies.

Psychosocial comorbidities, including depressive symptoms, disordered eating and high risk-taking behaviour, are common.[42] Early identification of these problems and prompt referral to psychology, social work and/or counselling are important,

13 Evaluation and management of complications and comorbidities in children and adolescents with type 2 diabetes

Complication/ comorbidity	Evaluation at diagnosis and yearly unless abnormal or specified*	Treatment	Treatment goals	Other considerations
Retinopathy	• Dilated pupil exam or retinal photograph with a non-mydriatic camera by an optometrist or ophthalmologist • Early stages are asymptomatic	• According to retinal findings by ophthalmologist	• Reduce/stop progression of proliferative retinopathy • Preservation of vision	• Optimise diabetes and weight management and treatment of dyslipidaemia/ hypertension, if present
Nephropathy microalbuminuria	• Proper collection of three early morning urine samples for albumin to creatinine ratio (random samples if unable to do it in the morning) • Review if any interference with urine sample (contamination, menstruation, prior exercise, orthostatic proteinuria, or infections) • Renal function assessed by eGFR • Early stages are asymptomatic	• ACE inhibitors after confirming two urine samples > 30 mg/g (microalbuminuria) • Refer to renal specialist if significant albuminuria (> 300 mg/g; macroalbuminuria) or hypertension to evaluate different aetiologies	• Maintain normal renal function, urine albumin to creatinine ratio, and blood pressure	• Optimise diabetes and weight management and treatment of dyslipidaemia/ hypertension, if present • Consider other causes of nephropathy
Peripheral neuropathy	• Foot examination, ankle reflexes, vibration sensation testing using 128 Hz tuning fork, pin prick sensation, and 10 g monofilament pressure (distal plantar aspect of great toes and metatarsal joints)	• Foot care education • Refer to neurologist for further evaluation if abnormal neurological signs	• Individualised according to symptoms and signs	• Optimise diabetes and weight management and treatment of dyslipidaemia/ hypertension, if present
Overweight and obesity	• Family history of obesity and other modifiable risk factors including environment • Plot BMI according to age and gender (overweight, BMI 85th–95th percentile; obesity, BMI > 95th percentile)* • Identify other comorbidities related to obesity*	• Healthy lifestyle and family involvement • Reinforce adherence to metformin • If taking insulin, optimise management to avoid further weight gain • Treat other obesity comorbidities	• Small changes in BMI can improve comorbidities and are easier to achieve • BMI closer to healthy range is ideal, as weight has impact on other comorbidities	• Possible use of newer treatments for type 2 diabetes that improve weight • Bariatric surgery in selected cases with special considerations
Psychosocial: depression, high risk behaviour, eating disorders	• Quick screening tools for depression and/or referral for formal evaluation, if suspected, using PHQ-2 or HEEADDSS assessment for adolescents • Evaluation in every visit according to general impression on review*	• Early referral to mental health professionals • School counselling • Discuss involvement with peer support groups	• Should be individualised but aiming to improve general emotional wellbeing and social functioning (school/ family)	• Presence of psychosocial disorders affects medication taking and increases overall morbidity
Reproductive health Menstrual cycle irregularities (PCOS)	• Menstrual cycle regularity* • Presence of hyperandrogenism (hirsutism using the Ferriman–Gallwey scale and/or moderate to severe acne, and/or androgenic alopecia) • Testosterone levels, Free Androgen Index, and sex hormone binding globulin if menstrual irregularities are present	• Treat according to symptoms and recent international evidence-based guidelines for PCOS • Combined oral contraceptive if irregular menstrual cycles and/or hirsutism • Cosmetic therapies for treating hirsutism	• Individualised according to main complaining symptoms	• Discuss/educate about contraception, especially if sexually active and HbA_{1c} level is above target due to the high risks of hyperglycaemia in unplanned pregnancies • Contraception is also required if taking teratogenic medications (ACE inhibitors, statins, newer oral/injectable agents • Weight management
Liver disease	• Assess liver enzymes (aspartate aminotransferase and alanine aminotransferase)	• Refer to gastroenterologist if liver enzymes persist over three times the upper limit of the reference interval after 6 months despite weight loss and improved glycaemic control with treatment, or if there is further deterioration in liver enzymes	• Individualised according to liver enzymes results	• Optimise diabetes and weight management

13 Continued

Complication/ comorbidity	Evaluation at diagnosis and yearly unless abnormal or specified*	Treatment	Treatment goals	Other considerations
Obstructive sleep apnoea	• Evaluate symptoms of obstructive sleep apnoea (snoring, morning sleepiness and stop breathing episodes)*	• Refer to a pulmonary physician for oximetry and/ or sleep study	• Individualised according to sleep study results	• Weight management • Sleep apnoea is associated with dyslipidaemia, hypertension and insulin resistance
Hypertension	• BP using appropriate cuff* • Plot BP in percentiles charts for age, gender and height* ▸ pre-hypertension: BP, > 90th to < 95th or 120/80–129/80 mmHg ▸ hypertension: BP ≥ 95th or 130/80 mmHg • Ambulatory 24-hour BP monitors can be useful if available	• Healthy lifestyle and family involvement if BP > 90 to < 95th or 120/80–129/80 mmHg • ACE inhibitors if BP ≥ 95th or 130/80 mmHg after 6 months of improved lifestyle, and start at lower dose ARB as alternative if not tolerating ACE	• BP < 90th percentile for age and gender	• Weight management • Renal referral if other pathology is suspected and/or treatment goals are hard to achieve • Review other risk factors for cardiovascular disease and manage accordingly
Dyslipidaemia: high LDL cholesterol, low HDL cholesterol, high triglycerides	• Family history of dyslipidaemia • Lipid profile (LDL, > 3.36 mmol/L; HDL, < 0.9 mmol/L; and triglycerides, > 1.7 mmol/L) ideally fasting and when lower HbA_{1c} level is achieved	• Healthy lifestyle and family involvement • Reduce total dietary fat < 35% and saturated fat < 7% of total energy intake • No trans fat intake • Statins if high LDL cholesterol in spite of improved lifestyle for 6 months • Fish oil/fibrates if high triglycerides	• LDL cholesterol < 2.6 mmol/L • HDL cholesterol > 0.9 mmol/L • Triglycerides < 1.7 mmol/L	• Weight management • Review other risk factors for cardiovascular disease and manage accordingly

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; BMI = body mass index; BP = blood pressure; eGFR = estimated glomerular filtration rate; HDL = high-density lipoprotein; HEEADDSS = H (Home environment), E (Education and employment), E (Exercise and healthy eating), A (Activity and peers), D (Drugs, smoking and alcohol), D (Depression and suicide ideation), S (sexuality and sexual health), S (Sleep); LDL = low-density lipoprotein; PHQ-2 = two-item version of the Patient Health Questionnaire; PCOS = polycystic ovary syndrome.
* Evaluation at every visit after diagnosis. ◆

as it affects the adolescent's willingness and ability to take medications as recommended and increases hospital admissions.[47] Depression can be evaluated initially by a simple questionnaire — the two-item version of the Patient Health Questionnaire (PHQ-2) — with only two questions ("little interest or pleasure in doing things" and "feeling down, depressed or hopeless"), which are scored from zero (symptom not present) to three (symptom present nearly every day) (Box 13).[48] Appropriate counselling is required on prevention of risk-taking behaviour (eg, smoking and drugs and alcohol use) and safe sex education (including contraception, sexually transmitted infections, and teenage pregnancy risks).[9,49] Diabetes-specific distress, although less studied in adolescents with type 2 diabetes, is more prevalent in young adults with diabetes and in adolescents with type 1 diabetes than in older adults with diabetes. It is associated with depression and suboptimal glycaemia. Patients with diabetes distress require a supportive diabetes care team who appreciate the extra burden that diabetes presents in addition to other comorbidities.

Transition to adult services

During transition, there may be low attendance at health appointments and/or inadequate health care use, which is associated with suboptimal medication taking, worsening of glycaemic management, and increased risk of acute and chronic complications.[5,50] The reason for this is multifactorial, including geographical changes (for education or employment), changes in timetables, financial barriers, long-standing bonds to paediatric providers, disengagement with adult providers, prioritising the competing demands of adolescence, and inherent feelings of invincibility to long term consequences. Higher rates of lower educational level may influence medication taking and delay the development of independence and self-care responsibility.[8] There is also often significant stigma arising from myths and misconceptions of the condition. These all lead to poor engagement with any health service, making adolescents very vulnerable to the transition process.

Given paediatric type 2 diabetes is an aggressive disease, it is recommended that all adolescents, in particular those with comorbidities or taking insulin, transition to adult endocrinologists working within a multidisciplinary team.[50] This will allow transition from insulin therapy to newer oral or injectable medications. However, the lack of accessibility to clinicians in some areas may be a potential barrier to this approach.

Conclusion

These first Australasian guidelines for children and adolescents with type 2 diabetes provide guidance to health care providers in relation to screening, diagnosis, diabetes education, monitoring including targets, healthy lifestyle, pharmacotherapy, assessment and management of complications and comorbidities, and transition. The guidelines emphasise the challenges and specifics of caring for these children in Australasia. This includes recommendations regarding screening and management

of children and adolescents from Indigenous backgrounds in Australia and New Zealand, tighter diabetes targets, consideration of using newer medications approved for adults with type 2 diabetes under the guidance of a paediatric endocrinologist if glycaemic targets are not met, and the need to transition adolescents with type 2 diabetes to a multidisciplinary diabetes care team that includes an adult endocrinologist for their ongoing care. The grading of the recommendations provided according to current available evidence highlights the need of high quality research into childhood type 2 diabetes.

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Supporting Information

Additional Supporting Information is included with the online version of this article.