# ADS-ADEA-APEG Consensus Statement: Management of Type 2 Diabetes in Young Adults (aged 18-30 years)

Jencia Wong[1], Glynis P Ross[1], Sophia Zoungas[2], Maria E Craig[3], Elizabeth A Davis[4], Kim C Donaghue[5], Louise Maple-Brown[6], Margaret J McGill[1], Jonathan E Shaw[7], Jane Speight[8], Natalie Wischer[9], Stephen Stranks[10]

[1]Department of Endocrinology, Diabetes Centre, Royal Prince Alfred Hospital and Central Clinical School, Charles Perkins Centre, Faculty of Medicine and Health, University of Sydney, Sydney, New South Wales, Australia
[2]Department of Epidemiology and Preventive Medicine and School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria
[3]Discipline of Paediatrics and Child Health, University of Sydney and Institute of Endocrinology and Diabetes and The Children's Hospital at Westmead, Sydney, NSW, Australia
[4]Perth Children's Hospital, Nedlands; Telethon Kids Institute; The University of Western Australia, Crawley, WA, 6009, Australia
[5]Discipline of Paediatrics and Child Health, University of Sydney, Institute of Endocrinology and Diabetes, The Children's Hospital at Westmead, Sydney, NSW, Australia.
[6]Menzies School of Health Research, Charles Darwin University; Department of Endocrinology, Royal Darwin Hospital, 0810 Darwin, Australia.
[7]Baker Heart and Diabetes Institute, Melbourne, VIC, Australia; School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia; School of Life Sciences, La Trobe University, Melbourne, VIC, Australia
[8]School of Psychology, Deakin University, Geelong, VIC 3216, Australia; The Australian Centre for Behavioural Research in Diabetes, Diabetes Victoria, Melbourne, VIC, Australia
[9]National Association Diabetes Centres, Sydney, NSW, Australia
[10]College of Medicine and Public Health, Flinders University, Flinders Drive, Bedford Park, SA, Australia; Southern Adelaide Diabetes and Endocrine Services, Flinders Medical Centre, Flinders Drive, Bedford Park, SA, Australia

V4 25.4.21

# Contents

## Abbreviations and Acronyms

ACEI angiotensin converting enzyme inhibitor
ACR albumin-to-creatinine ratio
ARB angiotensin receptor blocker
AUSDRISK Australian type 2 diabetes risk assessment tool
BMI body mass index
BP blood pressure
CCB calcium channel blocker
CKD chronic kidney disease
CVD cardiovascular disease
DASH Dietary Approaches to Stop Hypertension
DiRECT Diabetes Remission Clinical Trial
DKA diabetic ketoacidosis
DPP-4i dipeptidyl peptidase-4 inhibitor
GAD glutamic acid decarboxylase
GCK glucose kinase
HNF hepatic nuclear factor
GDM gestational diabetes mellitus
GI glycaemic index
GLP-1 RA glucagon-like peptide-1 receptor agonist
GP general practitioner
HbA1c glycated haemoglobin
HDL-C high-density lipoprotein-cholesterol
A-2 insulinoma antigen-2
IFG impaired fasting glucose
IGT impaired glucose tolerance
IR Insulin resistance
ESRD End stage renal disease
LDL-C low-density lipoprotein cholesterol
MODY maturity-onset diabetes of the young
NAFLD Non-alcoholic fatty liver disease
NICE National Institute for Health and Care Excellence
OGTT oral glucose tolerance test
OSA obstructive sleep apnoea
PAID Problem Areas in Diabetes
PBS Pharmaceutical Benefits Scheme
PCOS polycystic ovary syndrome
PHQ-2 Patient health questionnaire-2
RACGP Royal Australian College of General Practitioners
SGLT2i sodium glucose co-transporter 2 inhibitor
TZD thiazolidinedione
UACR urine albumin-to-creatinine ratio
VEGF vascular endothelial growth factor
VLED very low energy diet

## Introduction

Type 2 diabetes, traditionally considered a condition of older age, is becoming more prevalent in younger age-groups in Australia and worldwide (1, 2). It is increasingly clear that type 2 diabetes with onset in youth and young adulthood (nominally, 18-30 years of age) is a more aggressive condition than that seen in older age, with greater risks of major morbidity and early mortality (3, 4). It is estimated that onset in young adulthood comprises 16% of the adult type 2 diabetes population globally (1, 5). In the context of a still-limited evidence base, the objective of this Consensus Statement is to highlight the risks of this condition in young adults and to outline the specifics of management that may differ from later-onset type 2 diabetes. This Consensus Statement directly considers issues for the young adult population with type 2 diabetes (hereafter abbreviated as YT2D). Guidelines specifically for the management of type 2 diabetes in children and adolescents (<18 years of age) are available elsewhere (6). Special considerations with respect to Aboriginal and Torres Strait Islander Australians are highlighted separately.

## Risk screening and diagnosis

Risk factors for YT2D appear to be similar to those for older adults with a particular emphasis on obesity. A strong family history of type 2 diabetes is common, particularly a history of in-utero exposure to gestational hyperglycaemia or maternal obesity (7, 8). Additionally, YT2D is most prevalent in ethnicities with a high risk of type 2 diabetes overall and thus is relevant to multicultural Australia. Population screening is unlikely to be cost-effective (2), but risk-based screening criteria are recommended. Risk factors are chosen on the basis of their association with type 2 diabetes (see Table 1). This extends current general Australian guidance to testing young adults with obesity or overweight in the presence of additional risk factors, including a maternal history of type 2 diabetes or GDM during an individual's gestation. These recommendations do not preclude standard recommendations for diabetes testing in adults, although it is likely that the AUSDRISK score would lack accuracy for this age-group (9). In asymptomatic individuals, standard adult diagnostic criteria for diabetes apply (fasting glucose, 2hr post load glucose or HbA1c) and diagnosis requires two abnormal test results, either from the same sample or in two separate test samples. If fasting glucose is in the range 5.6-6.9 mmol/l or HbA1c are 5.7-6.4% (39-47 mmol/mol), it is recommended to proceed to an oral glucose tolerance test (OGTT), to identify post load hyperglycaemia defining IGT or diabetes. Thereafter, screening intervals are as for older adults; if IFG or IGT is found then screening for diabetes should be performed annually; if initial tests are within the normal range, screening should continue at a minimum of 3 yearly intervals or earlier if BMI is increasing. These recommendations are aligned with current guidance for paediatric and adolescent age-groups (2, 6). Specific guidance for Australian and Torres Strait Islander Australians are given below.

| **Table 1: Screening for type 2 diabetes and prediabetes is recommended in asymptomatic young adults with overweight or obesity (BMI ≥ 25 kg/m$^2$)* with one or more risk factor as listed**. |
|---|
| Maternal history of type 2 diabetes or GDM during an individual's gestation |
| Family history of type 2 diabetes in 1$^{st}$ degree relative |
| High risk ethnicity Aboriginal, Torres Strait Islander **, S Asian, SE Asian, N African and Latino, Middle-Eastern, Māori or Pacific Islander. Includes individuals of mixed ethnicity |
| Clinical evidence of insulin resistance (PCOS, acanthosis nigricans, dyslipidaemia, hypertension) or existing macrovascular disease, IFG, IGT or history of GDM |
| Use of anti-psychotic medications |

*Ethnic specific BMI cut-points recommended for S Asian and SE Asian [overweight BMI >23 kg/m$^2$ and obese as BMI >27.5 kg/m$^2$ thresholds for public health action (10)

**See section below for screening and testing recommendations for Aboriginal and Torres Strait Islander Australians

## Type 2 diabetes in young Aboriginal and Torres Strait Islander Australians

Aboriginal and Torres Strait Islander youth are disproportionately impacted by type 2 diabetes. Compared to non-Indigenous Australian youth, Aboriginal and Torres Strait Islander youth experience twenty-fold higher rates of type 2 diabetes and ten to twenty-fold higher hospitalisation rates (11, 12). They have an earlier age of type 2 diabetes onset than the general Australian population, with the condition reported in children as young as five years of age (13, 14).

Due to the high risk of type 2 diabetes among Aboriginal and Torres Strait Islander peoples, case-finding recommendations differ from those for the general population, such that annual screening is recommended from age 15 years as part of the MBS-funded well person's health check. Screening from age 10 years in those children with a risk factor is recommended in the Central Australian Rural Practitioner Guidelines for remote primary health care and this recommendation extends to the young adult onset population (15). Such risk factors include: overweight, family history of diabetes, mother with pre-existing or gestational diabetes during pregnancy, polycystic ovarian syndrome and acanthosis nigricans. An HbA1c is recommended for case-finding with a confirmation test of HbA1c, fasting glucose and/or 2 hour glucose on 75 gm OGTT with standard diagnostic criteria for diabetes applied. If the HbA1c is 5.7-6.4 % (39-47 mmol/mol), an OGTT is recommended in order to diagnose IGT (6), which is an important diagnosis to make, as dietary changes, physical activity changes, weight loss and/or metformin can then reduce the risk of progression to type 2 diabetes.

Key management principles when working with Aboriginal and Torres Strait Islander youth with type 2 diabetes include: culturally-relevant and culturally-safe care, involvement of an Aboriginal Health Practitioner as a key member of the multi-disciplinary team, assessment and management of social and emotional well-being and shared care between primary care and multi-disciplinary diabetes teams (16). Development of strong patient-provider relationships are particularly important in this context; thus minimising change in the provider team is a priority. Pregnancy planning and contraception are important considerations among young Aboriginal and Torres Strait Islander women with type 2 diabetes, as rates of type 2 diabetes in pregnancy are ten-fold higher than in non-Indigenous Australian women, and type 2 diabetes is a key contributor to higher rates of adverse perinatal outcomes among Aboriginal women (17).

Aboriginal and Torres Strait Islander youth with type 2 diabetes experience very high rates of diabetes complications from a young age (11, 14). Of great concern is the report that among Canadian First Nations peoples with youth-onset type 2 diabetes, renal survival was only 55% at twenty years after diagnosis: that is, nearly half of those with youth-onset type 2 diabetes require dialysis by age 40 years (18).

## Determining diabetes type

Diabetes type in young adults can be difficult to determine as background population obesity rates mean that obesity is present in a significant proportion of individuals with classical type 1 diabetes (19). Furthermore, type 2 diabetes in youth can present with ketosis or ketoacidosis, so that clinical overlap features are common in youth. The main decision points in young adults are to distinguish type 1 diabetes from type 2 diabetes and to recognise rarer monogenic forms of diabetes. It should be noted that at this time there are no agreed diagnostic criteria for YT2D.

To assist in identifying type 1 diabetes, it is recommended that clinicians have a low threshold for checking islet autoantibodies (insulin, GAD, IA2 and ZnT8) if possible, regardless of BMI at diagnosis. Extrapolating from evidence in adolescents with typical clinical features of type 2 diabetes, antibody positivity is associated with an intermediate phenotype and a faster progression to insulin therapy; such cases are likely to represent slowly evolving type 1 diabetes (20, 21). In terms of other biomarkers, a low C-peptide is consistent with type 1 diabetes but does not exclude type 2 diabetes, especially in the context of prevailing glucotoxicity. In addition, C-peptide may be preserved early in the course of

type 1 diabetes, particularly in the presence of insulin resistance, however persistent C-peptide beyond 5 years from diagnosis of type 1 diabetes should prompt re-consideration of type 2 diabetes or monogenic forms (22, 23). Nevertheless, measurement of C-peptide or insulin is not recommended as part of routine evaluation in this population as there is likely to be considerable overlap in insulin or C-peptide measurements between T1D and T2D at onset of diabetes, as seen in children and adolescents (2).

A detailed family history of diabetes, particularly early onset diabetes should be taken. Monogenic diabetes can account for up to 6% of diabetes in children and adolescents (22). Clinical clues to monogenic diabetes include: a family history of diabetes in one parent and first-degree relatives of that affected parent in young adults who lack the characteristics of type 1 diabetes, lack of marked obesity and other metabolic syndrome features, isolated mild fasting hyperglycaemia (GCK MODY), an extreme sensitivity to hypoglycaemia on sulfonylurea medications (HNF1α-MODY / HNF4α-MODY), or the presence of renal cysts (HNF1β MODY). A MODY probability calculator is available online but this has not been validated in Australian multiethnic populations (24). If monogenic diabetes is suspected, genetic testing is available via clinical genetics services and should be considered, given therapy implications for a positive diagnosis of monogenic diabetes. Recommendations for determining diabetes type, based on guidelines for children and adolescents (2, 22) are shown in Table 2.

| **Table 2: Clinical clues to determining diabetes type** | |
|---|---|
| Test for islet cell autoantibodies to exclude autoimmune type 1 diabetes. GAD ab and IA2 ab are the most commonly available | |
| Consider monogenic forms of diabetes and take a detailed family history | |
| Clinical features suggestive of monogenic diabetes | A family history of diabetes may be present in one parent and first-degree relatives of that affected parent, in young adults who lack the characteristics of type 1 diabetes (no islet autoantibodies, low or no insulin requirements more than 5 years after diagnosis) |
| | Stable isolated fasting hyperglycaemia in the range of 5.5-8.5 mmol/l and a 2hr glucose rise of <3.5 mmol/l on 75gm OGTT (GCK MODY) |
| | Extreme sensitivity to sulfonylurea medications with large post load glucose rise > 5 mmol/l on 75 gm OGTT (HNF1αMODY / HNF4αMODY) |
| | Lack of marked obesity and other metabolic syndrome features (e.g. acanthosis nigricans) |
| | Specific features such as genitourinary tract abnormalities or renal cysts, pancreatic atrophy, hyperuricaemia or gout (HNF1β MODY) |
| | History of neonatal hyperglycaemia |
| | Maternal line inheritance and associated hearing loss (mitochondrial diabetes) |

## Dietary management and physical activity as first-line therapy

Intervention is recommended from diagnosis and needs to support three aims: i) to achieve adequate person-centred reduction in calorie consumption and portion control, as obesity is a common comorbidity in YT2D, ii) to increase physical activity and reduce sedentary time, and iii) to achieve recommended metabolic targets. Specific recommendations will need to be sensitive to individual resources, with consideration of the possibility of food insecurity, socioeconomic disadvantage and other social stressors, all often of specific relevance to this age-group.

### Dietary management and medical nutrition therapy

The choice of nutrient-dense, culturally-appropriate wholefoods in the context of an individual's preferences, together with calorie and portion control for weight management is recommended. A first-line intervention needs to be elimination of 'empty calories' e.g. sugar-sweetened beverages, including juices, and reduction of refined simple sugars and high fructose corn syrup, particularly in

pre-packaged, processed food. Beyond this, there is little evidence for one specific macronutrient approach in YT2D. Eating patterns with some proven benefit on glucose levels and metabolic risk factors in older adults include the Mediterranean diet, a plant-based diet, and the DASH diet. For adolescents with obesity, modified 'traffic light' interventions whereby foods are assigned colours depending on their nutritional quality in the context of an overall calorie-restricted lifestyle intervention, showed benefit in cardio-metabolic indices (25). Of interest, the VLED approach has shown benefit among children/adolescents with obesity and newly diagnosed type 2 diabetes but evidence for long term effects is lacking at present (26, 27). Similarly, in adults with type 2 diabetes, utilising a weight management program incorporating a low energy formula diet, the DiRECT trial achieved remission diabetes in almost half of the patients randomised to this intervention (28). Although young adults were not well represented in this trial and evidence for durability of effect is still limited, this approach merits further consideration given the potential pre-conceptual, occupational and other benefits of inducing remission in this age group. Further research is needed to identify the most effective nutritional approach for YT2D. Until then, it would seem reasonable to base dietary interventions on the evidence-based framework above. Given the complexities, all YT2D should be offered personalised advice from a registered dietician with specialist expertise in this area.

Although there is evidence for a lack of plasticity in modifying lifelong eating patterns in older adults, whether this is true for young adults is unclear. The inclusion of family members in diabetes management may still be important into early adulthood. It is particularly important to educate this vulnerable group given that lifelong eating behaviours are acquired during this period of life. For example, instructions on interpretation of nutrition labels and food preparation may be of particular benefit to young adults, and the use of mobile-phone-based apps may be of assistance in the understanding of calories, glycaemic index, and macronutrients (29). Clinicians should also be mindful that disordered eating may already exist in this age group and maintaining a healthy relationship with food is paramount (30).

## Physical activity and exercise

Recommendations for exercise reduce in time and intensity with age; paediatric guidelines suggest 60 mins of moderate-intensity aerobic activity a day, whilst adult recommendations range from 150-300 mins a week depending on intensity and fitness, with the addition of 1-2 sessions of resistance training (31). Therefore, the 300 mins/week of moderate intensity aerobic activity could be considered a minimum recommendation for young adults. Shorter durations are recommended if high-intensity exercise is undertaken. A reduction in sedentary time is also indicated for its metabolic benefit (32). Such a reduction may also be helped by limiting electronic activities (e.g. computer use, texting and video games). Screen-time has been shown to be positively associated with HbA1c (33) and restricting recreational screen-time to less than 2 hours is recommended for adolescents (6, 34) which might also mitigate sleep deprivation (35, 36). It would seem reasonable to recommend similar if not more stringent limits for YT2D whose work or study-related screen-time exposure may be even greater. This recommendation is supported by evidence that increasing screen-time above 2 hr/day from adolescence to young adulthood is associated with adverse cardiovascular risk factors in young adulthood (37). Similar associations of increased TV viewing time, screen-time and adverse metabolic risk factors have been reported in college age students and older Australian adults without diabetes (37-39).

## The efficacy of interventions in YT2D.

Extrapolation from studies in youth with obesity suggests that increased exercise and activity, coupled with nutritional intervention would promote weight loss, fitness, improved glucose control and improved cardiovascular risk factors. This has been challenging to prove in YT2D. One of the key learnings from the TODAY trial in young people with type 2 diabetes (up to age 17) (40) is that despite a comprehensive lifestyle approach in combination with pharmacotherapy and significant in-trial support, there were only moderate improvements in cardio-metabolic indices. Interventions did not result in greater durability of optimal glucose levels, had a modest effect on BMI, and there were

limited improvements in fitness measures (41-44). It is possible that the efficacy of lifestyle intervention in YT2D may be similarly blunted. Complex social and environmental factors are suggested to have contributed to these results. However, it is also possible that underlying physiological defects in response to an exercise stimulus exist for youth (34). It is notable that smaller studies examining exercise interventions in YT2D show a relative resistance to the effects of exercise, at least on fitness measures (45). Extrapolating the adolescent data to young adults, the practical application would be that clinicians should continue to promote dietary/physical activity management according to guidelines, but be aware that any suboptimal benefits for these interventions may not necessarily be a failure of personal action (or social environment) but may have a physiological background. Furthermore, the reliance on dietary/physical activity management for achieving optimal glucose levels should be realistic in this context. Therapeutic inertia towards initiating pharmacotherapy must be minimised and any psychological barriers experienced by the young adult need to be addressed. Further research is needed to identify the best methods for promoting and sustaining dietary/physical activity changes over time among YT2D.

| **Table 3: Summary recommendations for dietary/physical activity interventions in young adults with type 2 diabetes** | |
|---|---|
| Obesity is a common comorbidity. A sustained weight loss of 7-10% in those with excess weight is expected to provide benefits for blood glucose and CVD risk factors in young adults | |
| Culturally appropriate programs promoting healthy diet and increased physical activity need to be provided, and family involvement needs to be individualised as developmentally appropriate | |
| Current evidence suggests only a modest effect of dietary/physical activity intervention on weight loss and glycaemic control, which may in part have a physiological basis and lack of efficacy should not be considered a failure of personal action. Intensifying pharmacologic intervention for glucose control should not be delayed | |
| Specific recommendations will need to be sensitive to individual resources, with consideration of the possibility of food insecurity, socio-economic disadvantage and other social stressors, all often of specific relevance to this age-group | |
| Clinicians should need to be mindful that, in this age-group, disordered eating may already exist, and maintaining a healthy relationship with food is paramount | |
| Nutrition advice | No long-term data are available on the optimal eating pattern or in favour of a particular macronutrient approach. Emphasis is on nutrient-dense high-quality foods and portion control with restriction of low-nutrient calorie-dense foods and sugar-sweetened beverages |
| | Given the lifelong necessity for healthy eating, wherever possible and appropriate, young adults need to be offered education on healthy meal preparation and food labels to enable informed choice |
| | Individualised advice for weight management and glucose control with involvement of a Registered Dietician is recommended |
| Physical activity and exercise | Recommendations are as for a healthy young populations; a minimum of 300 min/week of moderate intensity exercise is recommended. An additional emphasis is on reducing sedentary time, limiting recreational screen time to <2hrs, and achieving adequate sleep in a sustainable way |

## Psychosocial factors

The great influence of psychosocial factors on type 2 diabetes management and outcomes in diabetes is well recognised (46). In addition, it is evident that YT2D experience psychological burden comparable to young adults with type 1 diabetes and greater than older adults with type 2 diabetes (47). In Australia, YT2D often come from ethnic minority groups or from socially disadvantaged groups with multiple stressors including employment and housing insecurity. As a group, they experience lower engagement and follow-up than older onset type 2 diabetes (48). Clinical care needs to be individualised to address these challenges and facilitate access, engagement, and improved outcomes.

Current data in young adults are limited, but studies including adolescents suggest high rates of diabetes-distress, depression, psychiatric symptoms, and disordered eating, at least equivalent to or more prevalent than those seen in older type 2 diabetes or type 1 diabetes (47, 49-51). Diabetes distress is the emotional burden of living with diabetes. It is more common than and sometimes mistaken for depression (52). Clinicians need to be aware of, and ask about, depressive symptoms and diabetes distress to enable appropriate intervention where needed-practical guidance is available (52, 53). If standardised tools are used to assess and identify depressive symptoms, and diabetes specific distress, they need to be age appropriate. For monitoring purposes, the self-administered PHQ 9 can be applied routinely to assess depressive symptoms, and the PAID scale can be used to assess diabetes distress (54, 55). Additionally, there is considerable social stigma associated with T2D generally (48) and emerging evidence that shame can be a pervasive negative emotion in YT2D (56). Clinicians should also be vigilant for alcohol and substance abuse (57). Psychosocial assessments are recommended at the initial review and at any time when emotional health or self-care appears impaired. Common signs for psychosocial distress include: loss of interest or pleasure in usual activities; difficulties with concentration, sleep or relationships; ineffective coping strategies; multiple life stressors; appearing passive during consultations or not attending clinic appointments (52). If required, early referral to social work and mental health professionals with expertise in dealing with young adults is recommended.

| **Table 4: Summary recommendations regarding psychosocial care in YT2D** |
|---|
| Emotional health problems, e.g. diabetes distress, depression, disordered eating, and psychiatric symptoms, are relatively common among young adults with diabetes. In addition, clinicians need to be mindful that young adults may be susceptible to, and internalise, the social stigma surrounding type 2 diabetes |
| Clinicians need to be aware of, and ask about, depressive symptoms and diabetes distress to enable appropriate intervention where needed |
| Screening tools such as the PHQ-9 and PAID can be used to identify those who may need additional support and intervention |
| Individualised strategies to assist engagement and follow-up are necessary for this group. This may include flexible appointment times, strong continuity of care with a single point of contact for the person living with diabetes |
| Clinicians need to be vigilant for alcohol and substance abuse issues |
| Early referral to social work and mental health professionals with expertise in dealing with young adults is recommended |

## Glucose management and pharmacotherapy

Control of symptoms and prevention of acute and chronic complications are the treatment goals for YT2D (1). Glucose targets have not been specifically established for this age-group and extrapolations are made from data derived from those with older onset diabetes (1). The aggressive natural history of YT2D and the high prevalence of co-existing medical, psychiatric, and social issues need to be considered when individualising glucose targets (58). HbA1c should generally be measured every three months with a goal of ≤ 48 mmol/mol (≤ 6.5 %) for most people, if this can be achieved without undue hypoglycaemia risk or treatment burden.

As mentioned, dietary and exercise interventions alone are generally insufficient to maintain adequate glucose levels, with less than 20% achieving or maintaining adequate glucose management with lifestyle intervention alone (1). Less than half of young adults aged 18-39 (47%) with type 2 diabetes have optimal (>90%) medication-taking (59). To facilitate optimal treatment, it is critical that management is individualised, goal-setting is collaborative, culturally appropriate, and that necessary patient education and psychological support is provided.

Metformin is approved by the Australian Therapeutic Goods Administration for the management of

type 2 diabetes in those >10 years of age (60). In the absence of contraindications, including reduced renal function (CrCl <30 ml/min), metformin should be used as first line pharmacotherapy and should be initiated in most YT2D at diagnosis (61). Young adults with newly diagnosed type 2 diabetes may have an increased response to metformin compared with those with later onset diabetes (62).

YT2D is thought to be caused by similar mechanisms to later onset T2DM, including pancreatic β-cell failure, insulin resistance, lipolysis, alterations in incretin and pancreatic a-cell function, and kidney glucose filtration (61). However, YT2D is generally a more aggressive phenotype than later onset diabetes with a faster decline in β-cell function, up to 20-35% per year (61). Rapid decline in β-cell function with relatively stable insulin resistance may result in an early failure of metformin monotherapy and more rapid requirement of second line therapy (61, 63).

Insulin may be beneficial at the time of diagnosis to achieve rapid metabolic improvements. Although the specific effects in young adults is not known, one third of adolescents are able to subsequently cease basal insulin (64) and those who commence insulin at initial diagnosis have improved glucose and lipid profiles (65). However, the early use of metformin plus insulin has not been found to attenuate ongoing decline in β-cell function in adolescent type 2 diabetes (66).

Second-line and third-line treatment options of sulfonylureas, thiazolidinediones, SGLT2i, DPP-4i, and GLP-1RA, are licensed for use in individuals from 18 years of age, although have not all have been specifically studied in the YT2D age group. Nevertheless, efficacy in young adults is supported by recent studies in children and adolescents; specifically liraglutide has been shown to be as efficacious in children and adolescents with type 2 diabetes (aged 10-17) as in adults and has been recommended as second-line therapy add onto metformin in paediatric guidelines (67, 68). Similarly, a single-dose study of sitagliptin in YT2D aged 10-17 has shown similar pharmacodynamics, pharmacokinetic and safety trends as for adults and it is expected that other agents in paediatric populations will report soon (69, 70). There have been too few young participants in the cardio-renal outcome trials to draw conclusions regarding non-glycaemia-mediated cardiac and reno-protective effects of specific therapies (SGLT2i and GLP-1 RA) in this age-group (71). Nevertheless, given the high cardio-renal risk in YT2D and the need to avoid iatrogenic weight gain and hypoglycaemia, GLP-1 RA, SGLT2i and DDP4i are the likely best second-line agents. The need for effective contraception is a requirement in females given unknown teratogenic effects of these newer agents.

Bariatric surgery is an effective treatment for obesity in adolescents and for T2DM in the late-onset population. While there is limited evidence for its use in YT2D, in the young-onset cohort it is likely to result in improved glucose levels and weight (72).

| **Table 5: Summary recommendations regarding glucose management and pharmacotherapy in young adults with type 2 diabetes** |
|---|
| Given high risk of complications, the HbA1c target should be ≤6.5 % (≤ 48mmol/mol) if it can be achieved without undue hypoglycaemia risk and management burden |
| Insulin may be beneficial at the time of diagnosis to achieve rapid metabolic improvements in the context of symptomatic hyperglycaemia, with a proportion likely to be able to subsequently cease insulin |
| Metformin remains first-line therapy but durability of achieving glucose targets may be less than for older adults |
| There is limited but emerging evidence for the use of newer agents GLP-1 RA, SGLT2i and DPP4i in YT2D. Given low hypoglycaemic risk and neutral or beneficial effects on weight, these should be considered early in the treatment algorithm. Consideration of effective contraception in women given the pregnancy category C and D status of newer agents |
| Cardio-renal outcomes are not yet proven for YT2D, however SGLT2i and GLP-1 RA could be considered preferentially in the context of persistent albuminuria/CKD or known CVD (see Table 6) |

| |
|---|
| Caution recommended when using SGLT2i in ketosis-prone YT2D |
| Regular 3 monthly HbA1c monitoring is warranted given risk of therapy failure and progressive β-cell decline |

## Diabetes complications and comorbidities

Clinicians should be aware that some diabetes complications are more prevalent in YT2D in comparison to type 1 diabetes, with evidence for more rapid progression and a higher mortality (73-77). Furthermore, complications are occurring at a much earlier age, with a higher impact on mortality in comparison to later-onset type 2 diabetes (78-80). In general, guidance for complications management are as for older adults, however caveats for usual care of YT2D are discussed below.

### Nephropathy and hypertension

Despite the young age, the prevalence of albuminuria is reported to be as high as 27% at diagnosis, and hyperfiltration (eGFR 120-150 ml/min/1.72m$^2$) is also common (74). Obesity before the onset of diabetes is a potential contributor (81). These early changes indicate an increased risk of progression to diabetic kidney disease and an increased vascular risk. Current evidence suggests a more rapid progression to ESRD than that seen in type 1 diabetes with onset in this age-group (82). Thus, as for older adults, eGFR and urine ACR should be obtained at diagnosis and annually thereafter with albuminuria confirmed on repeat specimens. An elevated ACR (>30 mg/g or 3 mg/mmol) should be confirmed by repeat measure and represents an increased risk of progression of diabetic kidney disease (83).

The thresholds for treatment and targets for blood pressure (BP) continue to be debated for older adults and evidence for optimal thresholds are even less clear for YT2D. In adolescents younger than 18 years, pharmacological treatment of hypertension is recommended for persistent elevation of BP >130/80 following lifestyle intervention; BP targets are recommended to be <120/80 (6). Therefore, for YT2D over 18 years old, the recommended adult BP targets of <130/80 mmHg should be considered to be a minimum target. Recent recommendations for BP targets of 140 /90 for adults are likely to be too high in this age-group and particularly so for women. Furthermore, current guidance for adults to utilise evidence-based CVD risk calculators to assess thresholds for blood pressure intervention, may not accurately quantify risk for this population and should not be used to influence therapeutic decisions.

ACEi or ARB remain as the first-line therapeutic option for hypertension, especially in the context of an elevated ACR; CCB are an alternative or may be added in combination. Use of ACEi in combination with ARB is not recommended. The effects of this approach are extrapolated from evidence of type 2 diabetes in older adults and remain unproven in YT2D. Nevertheless, the safety of ACEi over 4 years has been demonstrated by recent studies of CVD risk-factor management in children and adolescents with type 1 diabetes and safety is likely similar for YT2D (84).

Given the poor renal outcomes for YT2D and the evidence in older populations of the reno-protective effects of SGLT2i and GLP-1RA (85), namely that i) both SGLT2i and GLP-1 RA reduce albuminuria and prevent macroalbuminuria and ii) SGLT2i reduce the risk of eGFR decline and end-stage kidney disease, these agents could be considered for YT2D. Although cardio-renal outcomes are not yet proven for YT2D, in the context of persistent albuminuria or CKD, the use of SGLT2i for glucose lowering should be considered with GLP-1RA as an alternative if not tolerated or contraindicated.

The potential teratogenic effects of SGLT2i, ACEi/ARB therapy should be noted and effective contraception offered where appropriate. In view of the often-aggressive progression seen, an early referral to nephrology specialists is recommended where there is concern regarding aetiology or there is worsening of UACR or there is eGFR decline. Further, one should consider non-diabetes aetiology in the presence of ACR > 30 mg/mmol or 300 mg/g.

## Retinopathy

As for the other complications, YT2D are at high risk and a retinopathy prevalence of 42% of YT2D aged in their early 20s has been reported (86); the age-adjusted prevalence has been shown to be higher in YT2D than for comparable youth with type 1 diabetes (87). There is some evidence, albeit conflicting, to support a younger age of diabetes onset as an independent risk factor for retinopathy in type 2 diabetes (87-89). In this context, the current recommendations for screening in older adults apply with an added caveat that once retinopathy is detected there is the propensity for rapid progression. Thus, more frequent eye examinations, even if baseline examinations are clear (i.e. annually as opposed to two yearly which is currently recommended), may be considered for YT2D; this would be particularly important in the setting of sub-optimal glycaemic control or diabetes of long duration. Clinicians need to be mindful that YT2D experience many barriers to retinal screening including unrealistic optimism, concerns about the impact on time or family and misconceptions about the procedure. For prevention, and to reduce the risk of progression, optimising glycaemia is recommended as for older adults. In Australia, there is regulatory approval for the use of fenofibrate for the management of diabetic retinopathy. Again, the evidence base for this did not include YT2D and if used, potential teratogenicity should be considered. Similarly, in the setting of proliferative retinopathy, the use of anti-VEGF agents should consider pregnancy plans and effective contraception ensured for young women.

## Neuropathy

Despite their young age, YT2D should be screened at diagnosis and annually thereafter for the presence of neuropathy and foot problems by foot inspection, evaluation of small fibre function (pin prick, or temperature sensation) and large fibre function (10 g monofilament and vibration perception and soft touch sensation), ankle and knee reflexes and pulses. Studies in adolescents have determined that the prevalence of peripheral neuropathy and autonomic neuropathy are higher than in their type 1 diabetes counterparts (87-91). Long term, this is likely to result in a higher prevalence of foot problems and a heightened amputation risk at a young age. Extrapolating from studies in youth with type 1 diabetes, attaining glucose goals is the primary management, and foot-care education should be emphasised early (92).

## CVD and dyslipidaemia

The prevalence of CVD risk factors (hypertension, albuminuria, dyslipidaemia and abdominal obesity) is high in YT2D (93) . It is evident that the atherosclerotic process can begin in adolescence with subclinical vascular disease such as elevated aortic pulse wave velocity and increased carotid intima media thickness being reported in YT2D (94, 95). Several lines of evidence suggest an increased prevalence of early CVD and death compared to type 1 diabetes, with deaths occurring in excess by the third decade of life (73, 96). Thus, if intervention is to be optimally effective, its early application is indicated.

BP and glucose management are discussed above. In the absence of direct longitudinal evidence for prevention and treatment in YT2D in addition to lifestyle intervention, the issue of when to commence cholesterol-lowering therapy is relevant. A large evidence base supports the use of statins in older adults with type 2 diabetes, however intervention studies have not traditionally included this younger group. Furthermore, as mentioned before, absolute CVD risk calculators, which are predicated on age and 10-year risks as an arbiter for intervention, are not likely to be accurate given a sparse evidence base. Lifetime risk might be a better criterion for therapy decisions.

It is recommended that the risk/benefits of statin therapy should be discussed for YT2D with particularly high CVD risk, as in the following groups:

1. Aboriginal and Torres Strait Islander people with high CVD risk. Assessment of CVD risk is recommended from age 20 years. See (15) for further guidance

2. YT2D with established elevated ACR
3. YT2D with diabetes duration >10 years. This would be in accordance with guidance for type 1 diabetes and predicated on the increased risk for YT2D in comparison (97, 98)
4. YT2D with established CVD.

Additional guidance based on absolute lipid levels are as follows:
1. A statin should be considered in the context of YT2D and a total cholesterol level >7.5 mmol/l. At this level, a diagnosis of Familial Hypercholesterolemia (FH) should be considered.
2. Paediatric/Adolescent guidelines recommend lipid lowering for LDL levels >3.4 mmol/l persisting after dietary and glucose management, with a target of 2.6 mmol/l, and this could be continued into later years or newly considered in YT2D noting that this specific approach is currently supported by the PBS for total cholesterol levels > 5.5 mmol/L.

Although long-term risks of statin use in YT2D have not been quantified, experience in familial hypercholesterolemia has not identified any excess risk for youth (99). Recently, the four-year safety and lipid-lowering efficacy of statin therapy has been demonstrated in young type 1 diabetes which is reassuring for YT2D (84). If used, pregnancy and teratogenicity risks should be considered. In the context of diabetes-related dyslipidaemic profiles characterised by high triglyceride and low HDL, combination statin-fibrate treatment although promising, has not been definitely proven for primary prevention in older adults, and this approach cannot yet be recommended for YT2D (100). Fibrate therapy for severe hypertriglyceridemia to reduce pancreatitis risk is indicated as in older adults. Smoking habits should be ascertained at diagnosis and regularly thereafter. Aspirin is not recommended for YT2D for primary prevention of CVD and is generally contraindicated in those <21 years due to the risk of Reyes Syndrome.

## Polycystic Ovary Syndrome, sleep disturbance and Non Alcoholic Fatty Liver Disease

PCOS and type 2 diabetes share the common risk factor of insulin resistance. Thus, in young women with type 2 diabetes, a menstrual history and assessment for hyperandrogenism should be undertaken. Lifestyle modification and metformin may improve the menstrual disorder and, if oral-contraceptive treatment is considered, lipid and insulin effects should be considered in agent selection.

Sleep disturbance and OSA are recognised to be associated with obesity and IR in adolescents and adults (101). In a large study of mainly older adults with diabetes, although treatment of OSA did not result in improvements in glycaemic control, improvements in diastolic blood pressure, sleepiness, and parameters of well-being were found (102). Further study on the benefits of intervention in youth are needed. Enquiry as to sleep disturbance, sleep duration and symptoms of OSA would seem reasonable in obese YT2D despite their young age.

In YT2D, the frequency of NAFLD has not been established. Nevertheless, compared to older type 2 diabetes there is an association with a greater histologic severity of liver disease that may signal an increased risk of progression of fibrosis and cirrhosis, leading to hepatic failure (103). In this context, clinicians are recommended to evaluate all young adults with type 2 diabetes for the potential for NAFLD, with AST and ALT at diagnosis and then annually. The preferred non-invasive diagnostic imaging thereafter has not been standardised. Weight loss is currently the most beneficial treatment. Specialist gastroenterology consultation should be considered for persistent biochemical disturbances not responding to weight loss.

| Table 6: Summary recommendations for the prevention and management of complications and comorbid conditions in young adults with type 2 diabetes | |
|---|---|
| **Complication Comorbidity** | **Summary Recommendation** |
| **Nephropathy and BP** | eGFR and urine ACR should be obtained at diagnosis and annually thereafter with albuminuria confirmed on repeat specimens |
| | Recommended BP targets of <130/80 mmHg regardless of the presence of albuminuria should be considered to be a minimum target. Recent recommendations for BP targets of 140 /90 are too high in this age-group and particularly so for women |
| | ACEi or ARB are first line therapeutic options for hypertension, especially in the context of an elevated ACR; CCB are an alternative or may be added in combination |
| | In the context of persistent albuminuria/CKD, ACEi or ARB and glucose-lowering with SGLT2i therapy should be considered. A GLP-1 RA is an alternative if SGLT2i are not tolerated or are contraindicated |
| | Early referral to a nephrology specialist is recommended where there is concern regarding aetiology or there is worsening of ACR or there is eGFR decline |
| | Consider non-diabetes aetiology particularly in the presence of ACR > 30 mg/mmol or 300 mg/g |
| | Potential teratogenic effects of ACEi/ARB, SGLT2i, and GLP-1 RA therapy should be noted and effective contraception offered where appropriate |
| **Retinopathy** | Screening should begin at diagnosis |
| | Given propensity for rapid progression, even if baseline examinations are normal, screening should be annually as opposed to two-yearly |
| | Optimisation of glycaemia for prevention and to slow progression |
| | If fenofibrate or anti VEGF therapy is considered in the management of diabetic retinopathy, effective contraception should be offered given potential teratogenicity and adverse pregnancy outcomes |
| **Peripheral Neuropathy** | Screening for the presence of neuropathy and foot problems at diagnosis |
| | Focus on attaining glucose goals is primary management |
| | Foot care should be emphasised early |
| **CVD and Dyslipidaemia** | The following groups are considered as having particularly high lifetime risk and statin treatment should be considered with the aim to lower global CVD risk: 1. Aboriginal and Torres Strait Islander Australians 2. YT2D with established elevated ACR 3. Duration of YT2D >10 years 4. YT2D with established CVD |
| | Lipids should be checked once initial glucose levels have been as optimised as possible and annually thereafter. |
| | Statin should be considered in the context of a person aged <30 years and a total cholesterol level > 7.5 mmol/l and familial hypercholesterolemia considered |
| | Paediatric guidelines recommend lipid lowering for LDL levels >3.4 mmol/l with a target of 2.6 mmol/l and this could be continued or newly considered in YT2DM, noting that this specific approach is currently supported by the PBS for total cholesterol levels > 5.5 mmol/L. |
| | Fibrate therapy reserved for severe hypertriglyceridemia (Tg >4 mmol/l) to reduce pancreatitis risk |
| | Smoking habits should be ascertained regularly |
| | Aspirin is not recommended for primary prevention in YT2D |
| | Screening for CVD in asymptomatic youth is not warranted |
| **PCOS** | Assessment for hyperandrogenism should be undertaken for all YT2D females |

| | |
|---|---|
| | Weight loss and metformin may improve the menstrual disorder. If hormonal contraception is commenced, lipid and insulin effects should be considered in agent-selection |
| **NAFLD** | People with YT2D should be assessed for the potential for NAFLD, with AST and ALT at diagnosis and then annually. Gastroenterology review recommended if persistent abnormality not responding to weight loss |
| **OSA** | Assessment for sleep disturbance and symptoms of OSA at diagnosis |
| **Psychological co-morbidity** | Please see Table 4. |

## Pregnancy and pre-conceptual care

Pregnancies associated with pre-gestational diabetes have higher rates of adverse outcomes than pregnancies without diabetes, especially congenital anomalies, pre-eclampsia, pre-term birth, large-for-gestational-age babies, and pregnancy loss. In the TODAY study, around 30% of pregnancies in female adolescents with type 2 diabetes were complicated by pre-term birth or fetal malformation (104).

Adolescents and young women with type 2 diabetes have a similar or higher presence of hypertension and albuminuria compared to young women with type 1 diabetes. Nephropathy, when present, increases the likelihood of pre-eclampsia, pre-term delivery, low-birth-weight babies and caesarean-section (105, 106). Further, the emotional, psychological and social burden of a pregnancy on adolescent girls and emerging adults may be greater than on older women.

There is evidence that diabetes begets early diabetes in offspring, not only via the inheritance of diabetes-susceptibility genes but also potentially via a mechanism of in-utero hyperglycaemia, subsequent fetal hyperinsulinaemia and adiposity, supporting the development of later obesity and insulin resistance in youth (107). Additionally, comorbid maternal obesity itself has a negative impact (108). Thus, diabetes in pregnancy is a likely contributor to intergenerational cycles of early-onset type 2 diabetes. Optimal peri-conceptual and antenatal glucose levels and avoidance of excessive gestational weight gain, may attenuate at least some of the risks mentioned above.

On this background, clinicians should emphasise the need for pre-pregnancy counselling for young women of childbearing potential with diabetes, which should be incorporated into routine clinic visits from puberty onwards. Effective contraception should be offered as necessary, and it should be recognised that young women may face unseen barriers to accessing contraception based on age, marital or financial status, and including the occasional professional with a lack of willingness to acknowledge sexual-health needs in youth. Long-acting reversible contraceptives (LARCs), which include hormonal and non-hormonal intra-uterine contraceptive devices (IUCDs) and subcutaneous progestogen implants, have been recommended as first-line contraceptive options for adolescents and young women (109, 110). A proactive approach to contraception is recommended.

Practically, recommendations for pregnancy planning and management are as for older women (111); high dose periconceptual folate (2.5-5 mg inclusive of folate in other pregnancy supplements) should be commenced ideally three months prior to pregnancy. Ideally, the periconceptual HbA1c should be ≤ 6.5% (48 mmol/mol) while minimising risk of hypoglycaemia. During pregnancy, insulin and metformin are the pharmacological management options of choice for achieving glucose targets. All glucose lowering treatments other than insulin and metformin should be stopped prior to conception and glycaemia stabilised prior to conception. However, when pregnancy occurs outside an optimal pre- conceptual setting, sudden withdrawal of metformin and/or sulfonylureas may lead to rapid deterioration in glucose levels. It is then recommended that metformin and sulfonylureas be continued initially until specialist review. However, GLP-1 RA, SGLT2i and other oral agents should be discontinued immediately as there is limited safety evidence for their use in pregnancy. Breastfeeding

should be encouraged as it may offer some protection against the development of YT2D in the next generation (112).

| **Table 7: Summary recommendations regarding pregnancy in young adults with type 2 diabetes (111)** |
|---|
| Pre-pregnancy counselling and contraception advice for young women with diabetes of childbearing potential should be incorporated into routine clinic visits form puberty onwards |
| High-dose periconceptual folate (2.5-5 mg inclusive of folate in other pregnancy supplements) should be commenced three months before pregnancy |
| Ideally the HbA1c should be ≤ 6.5% (48 mmol/mol ) while minimising the risk of hypoglycaemia |
| All glucose lowering pharmacotherapy other than insulin and metformin should be stopped prior to conception, and glycaemia should be stabilised prior to conception |
| When pregnancy occurs outside an optimal pre-conceptual setting, sudden withdrawal of metformin and/or sulfonylureas in early pregnancy may lead to rapid deterioration in glucose levels. It is recommended that metformin and/or sulfonylureas be continued initially until specialist review. |
| GLP-1 RA, SGLT2i, and other oral agents (other than metformin or sulphonylurea) should be discontinued immediately, as there is limited safety evidence for their use in pregnancy |

## Education

Diabetes self-management through education is a cornerstone of diabetes therapy (113). Whilst it is well known that structured education in older people with type 2 diabetes is effective, there is a dearth of literature about appropriate approaches to educating those diagnosed with type 2 diabetes under the age of 30 years. Few educational resources are available directly targeted at this young adult group. It is likely that structured education programs designed for older adults will not meet the needs of younger people, and it is not appropriate to mix the age-groups. Moreover, the TODAY study suggests that the benefits of traditional lifestyle interventions in YT2D may be limited and this requires more detailed exploration. Key barriers to this may include being time-poor, a lack of motivation to undertake the rigours of diabetes self-management, and not understanding the serious nature of their condition resulting in a loss to follow-up (40). Bespoke structured education programs for young people that are person, not disease-focussed, could be effective and need to be developed and evaluated. Similar to type 1 diabetes in this age-group, there are some key factors around education that apply. These are outlined in Table 8 and expanded below.

Health professionals delivering this education require specialised training in the principles of effective approaches to education and behaviour change. A healthcare team (comprised ideally of physician, nurse, dietitian, psychologist, and exercise physiologist) that provides a consistent message and is empathic, is critical to improving clinical outcomes (114). As loss to follow-up is a major concern, expert consultation, communication skills, and use of technology including telehealth to ensure ongoing engagement in the healthcare system, are essential.

Family history of diabetes is very common among YT2D and many live with an older adult with diabetes and obesity and diabetes-related complications. The experience of the young person to this influence could be further explored. This shared family experience may lead to acceptance of complications as an inevitable course of diabetes (115). Thus, when designing programs, there is a need to be cognisant of and sensitive to family, social, and cultural beliefs. Some involvement of the family may be critical.

Use of interactive education tools such as the Conversation Map (116) can enhance effective interaction, peer support, and problem-solving skills. For some, drawing how they feel about their diabetes can be helpful. Written resources need to be targeted to an 11-year-old reading age, which is the age to which the tabloid newspapers are pitched. Apps that motivate through competition with self or others, in a process known as gamification, can add motivation and engagement with recording,

monitoring, and achieving health goals (117, 118).

The format of delivering the education may need to differ from older adults' programs and may embrace technologies such as mobile-based apps or internet sites and programmes to enhance connections. Peer support groups, either face-to- face or via social media, appear to assist in improving healthy living and weight loss. Online groups and apps that combine social interaction, entertainment, and education could offer significant benefits toward their engagement and mastery of self-care practices. Reminder systems for appointments are often valuable, and text messaging is more popular than email in this age-group (119).

Quality-assured, structured education programs developed collaboratively between young people and skilled professionals should be made available in Australia to all under the age of 30 years with type 2 diabetes, irrespective of their ethnicity, geographic location, socio-economic status, and health literacy. Realistic and achievable goals need to be agreed upon and set.

Structured education and an assessment of the individual's learning needs and follow up education should be integrated into every clinical consultation. The availability of ongoing learning and support, vital in this high-risk group who often struggle to understand the complexities of the health and hospital system, is required. Structured discussion and education comprising several topic areas, designed to assist young people to become proactive in their diabetes management that could be addressed, are outlined in Table 9.

| **Table 8: Key principles for the delivery of diabetes education to young adults with type 2 diabetes** |
|---|
| Health professionals delivering this education require specialised training in the principles of effective approaches to education and behaviour change |
| A healthcare team that provides a consistent message and are empathic is critical to improving clinical outcomes |
| As loss to follow-up is a major concern, strategies involving expert consultation, communication skills, technology including telehealth, and text communication to ensure ongoing engagement in the healthcare system, are recommended |

| |
|---|
| A shared family experience of diabetes should be explored as it may have a negative impact on disease perception and identify areas for specific education |
| Delivery of education should be in forums specific for young people alone, rather than in group settings with older adults |
| Structured education, an assessment of the individual's learning needs, and follow up education should be integrated into every clinical consultation |
| Education formats with interactive tools, including conversation maps, mobile apps, competition and gamification may be of specific benefit to assist in engagement of YT2D |
| Peer-peer interactions should be encouraged. Peer support groups and apps that combine social interaction, entertainment and education could offer significant benefits toward engagement and mastery of self-care practices for YT2D |
| The impact of co-existent depression, feelings of anxiety and shame should be considered |

| **Table 9: Topic guidance for structured discussion within the consultation with young adults with type 2 diabetes** |
|---|
| Dealing with the diagnosis of diabetes and its seriousness and impact on their health and wellbeing |
| Importance of nutrition and weight loss, adopting healthy choices, and an exploration of attitudes to food and eating behaviours |
| Recommendations for exercise, physical activity and limits on recreational screen time and how they may be achieved |
| Understanding that traditional lifestyle interventions while important, may be less effective for youth so as not promote feelings of failure or shame |
| Importance of early and intensive management with combination therapies to achieve tight glycaemic targets, which may be stricter than for older patients |
| Strategies to improve medication-adherence such as using a Webster pack or smartphone type reminders |
| Practical skills such as how Medicare functions, how to fill a prescription, and the need for a referral if seeing a specialist |
| Discuss early the potential use of insulin therapy and identify cultural, recreational, and employment concerns or other barriers to insulin therapy |
| Discuss the higher complication-risk and importance of screening for micro and macrovascular complications from diagnosis and aggressive treatment of cardiovascular risk factors, despite a young age |
| Contraceptive advice and pregnancy planning |
| The changing needs of the person (e.g. leaving home, contraception, planning a pregnancy, recreational drugs, alcohol, transitioning from school to university/work, etc.) |
| Assessment and management of anxiety and depression |
| How to use technology-supports such as apps to record and monitor food, exercise, medication and blood glucose levels |

## Transition from paediatric services and Models of Care

The relatively recent recognition of the occurrence of type 2 diabetes in children and adolescents together with the rapid increase in rates mean that models of care for this age group and young adults are not yet well established. Although the majority of type 2 diabetes in adults is managed in primary care, this model may be less effective in YT2D for a number of reasons. Current recommendations for children and adolescents with type 2 diabetes are to have care provided by a specialist team (6). Given all the challenges outlined, it is recommended that adolescents and emerging adults with type 2 diabetes also be referred to age-appropriate specialist care. Wherever possible, specialist endocrine teams that include an endocrinologist and a diabetes nurse educator, who can coordinate multidisciplinary and interdisciplinary care to include dietetic, podiatric, psychological, and other specialist services as needed, are appropriate.

Transition provides a period of risk for vulnerable patients to engage poorly with the health system and a high risk of being 'lost to follow up' for prolonged periods of time. For these patients, young adulthood is a time when long term complications become evident and regular screening and timely treatment is critical. If transitioning from paediatric services, there is a need for planning well before the actual transition care is to occur with progressive familiarisation with adult service introduced over months. Although the empirical evidence does not exist for benefit, favourable outcomes using this approach can largely be extrapolated from young type 1 diabetes populations.

## Conclusion

In response to the growing problem of YT2D, this first Australian Consensus Statement on the management of type 2 diabetes in young adults provides advice for health care professionals in areas where current guidance, largely directed at older adults may not be appropriate or relevant to young adults. Where possible, recommendations are harmonised with current national guidance for those less than 18 years of age (6). Despite a growing understanding of the excess risks associated with YT2D and a likely different physiology to older-onset type 2 diabetes, at present there is still a great need to develop a rigorous evidence-base and systems to collect data on outcomes, to further inform approaches to therapy and models of care for this high-risk group.

# References


1. Lascar N, Brown J, Pattison H, Barnett AH, Bailey CJ, Bellary S. Type 2 diabetes in adolescents and young adults. The lancet Diabetes & endocrinology. 2018;6(1):69-80.
2. Zeitler P, Arslanian S, Fu J, Pinhas-Hamiel O, Reinehr T, Tandon N, et al. ISPAD Clinical Practice Consensus Guidelines 2018: Type 2 diabetes mellitus in youth. Pediatric diabetes. 2018;19 Suppl 27:28-46.
3. Sattar N, Rawshani A, Franzen S, Rawshani A, Svensson AM, Rosengren A, et al. Age at Diagnosis of Type 2 Diabetes Mellitus and Associations With Cardiovascular and Mortality Risks. Circulation. 2019;139(19):2228-37.
4. Morton JI, Liew D, McDonald SP, Shaw JE, Magliano DJ. The Association Between Age of Onset of Type 2 Diabetes and the Long-term Risk of End-Stage Kidney Disease: A National Registry Study. Diabetes Care. 2020;43(8):1788.
5. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes Research and Clinical Practice. 2014;103(2):137-49.
6. Peña AS, Curran JA, Fuery M, George C, Jefferies CA, Lobley K, et al. Screening, assessment and management of type 2 diabetes mellitus in children and adolescents: Australasian Paediatric Endocrine Group guidelines. Medical Journal of Australia. 2020;213(1):30-43.
7. Kawasaki M, Arata N, Ogawa Y. Obesity and abnormal glucose tolerance in the offspring of mothers with diabetes. Current opinion in obstetrics & gynecology. 2018;30(6):361-8.
8. Pettitt DJ, Lawrence JM, Beyer J, Hillier TA, Liese AD, Mayer-Davis B, et al. Association between maternal diabetes in utero and age at offspring's diagnosis of type 2 diabetes. Diabetes Care. 2008;31(11):2126-30.
9. Practitioners. TRACoG. The Royal Australian College of General Practitioners. Management of type 2 diabetes: A handbook for general practice. . Vic: : RACGP; 2020.
10. Consultation WE. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet (London, England). 2004;363(9403):157-63.
11. Haynes A, Kalic R, Cooper M, Hewitt JK, Davis EA. Increasing incidence of type 2 diabetes in Indigenous and non-Indigenous children in Western Australia, 1990-2012. The Medical journal of Australia. 2016;204(8):303.
12. Craig ME, Femia G, Broyda V, Lloyd M, Howard NJ. Type 2 diabetes in Indigenous and non-Indigenous children and adolescents in New South Wales. The Medical journal of Australia. 2007;186(10):497-9.
13. Kevat D, Wilson D, Sinha A. A 5-year-old girl with type 2 diabetes. Lancet (London, England). 2014;383(9924):1268.
14. Titmuss A, Davis EA, Brown A, Maple-Brown LJ. Emerging diabetes and metabolic conditions among Aboriginal and Torres Strait Islander young people. The Medical journal of Australia. 2019;210(3):111-3.e1.
15. Health CfR. Central Australian Rural Practitioners Association.CARPA Standard Treatment Manual 7th Edition. Alice Springs; 2017.
16. Nguyen HD, Chitturi S, Maple-Brown LJ. Management of diabetes in Indigenous communities: lessons from the Australian Aboriginal population. Internal Medicine Journal. 2016;46(11):1252-9.
17. Maple-Brown L, Lee IL, Longmore D, Barzi F, Connors C, Boyle JA, et al. Pregnancy And Neonatal Diabetes Outcomes in Remote Australia: the PANDORA study-an observational birth cohort. International journal of epidemiology. 2019;48(1):307-18.
18. Dart AB, Sellers EA, Martens PJ, Rigatto C, Brownell MD, Dean HJ. High burden of kidney disease in youth-onset type 2 diabetes. Diabetes Care. 2012;35(6):1265-71.
19. Islam ST, Abraham A, Donaghue KC, Chan AK, Lloyd M, Srinivasan S, et al. Plateau of adiposity in Australian children diagnosed with Type 1 diabetes: a 20-year study. Diabetic medicine : a journal of the British Diabetic Association. 2014;31(6):686-90.
20. Klingensmith GJ, Pyle L, Arslanian S, Copeland KC, Cuttler L, Kaufman F, et al. The presence of GAD and IA-2 antibodies in youth with a type 2 diabetes phenotype: results from the TODAY study.

Diabetes Care. 2010;33(9):1970-5.
21. Tfayli H, Bacha F, Gungor N, Arslanian S. Islet cell antibody-positive versus -negative phenotypic type 2 diabetes in youth: does the oral glucose tolerance test distinguish between the two? Diabetes Care. 2010;33(3):632-8.
22. Hattersley AT, Greeley SAW, Polak M, Rubio-Cabezas O, Njølstad PR, Mlynarski W, et al. ISPAD Clinical Practice Consensus Guidelines 2018: The diagnosis and management of monogenic diabetes in children and adolescents. Pediatric diabetes. 2018;19 Suppl 27:47-63.
23. Shields BM, McDonald TJ, Oram R, Hill A, Hudson M, Leete P, et al. C-Peptide Decline in Type 1 Diabetes Has Two Phases: An Initial Exponential Fall and a Subsequent Stable Phase. Diabetes Care. 2018;41(7):1486-92.
24. Calculator MD. [Available from: https://www.diabetesgenes.org/exeter-diabetes-app/.
25. ADA. Obesity Management for the Treatment of Type 2 Diabetes: Standards of Medical Care in Diabetes-2021. Diabetes Care. 2021;44(Suppl 1):S100-s10.
26. Andela S, Burrows TL, Baur LA, Coyle DH, Collins CE, Gow ML. Efficacy of very low-energy diet programs for weight loss: A systematic review with meta-analysis of intervention studies in children and adolescents with obesity. Obes Rev. 2019;20(6):871-82.
27. Gow ML, Pham-Short A, Jebeile H, Varley BJ, Craig ME. Current Perspectives on the Role of Very-Low-Energy Diets in the Treatment of Obesity and Type 2 Diabetes in Youth. Diabetes, metabolic syndrome and obesity : targets and therapy. 2021;14:215-25.
28. Lean MEJ, Leslie WS, Barnes AC, Brosnahan N, Thom G, McCombie L, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. The Lancet. 2018;391(10120):541-51.
29. Hood M, Wilson R, Corsica J, Bradley L, Chirinos D, Vivo A. What do we know about mobile applications for diabetes self-management? A review of reviews. Journal of behavioral medicine. 2016;39(6):981-94.
30. Wilfley D, Berkowitz R, Goebel-Fabbri A, Hirst K, Ievers-Landis C, Lipman TH, et al. Binge eating, mood, and quality of life in youth with type 2 diabetes: baseline data from the today study. Diabetes Care. 2011;34(4):858-60.
31. Health Do. Australia's Physical Activity and Sedentary Behaviour Guidelines and the Australian 24-Hour Movement Guidelines [Available from: https://www1.health.gov.au/internet/main/publishing.nsf/Content/health-pubhlth-strateg-phys-act-guidelines.
32. Hadgraft NT, Winkler E, Climie RE, Grace MS, Romero L, Owen N, et al. Effects of sedentary behaviour interventions on biomarkers of cardiometabolic risk in adults: systematic review with meta-analyses. British Journal of Sports Medicine. 2021;55(3):144.
33. Li C, Beech B, Crume T, D'Agostino RB, Jr., Dabelea D, Kaar JL, et al. Longitudinal association between television watching and computer use and risk markers in diabetes in the SEARCH for Diabetes in Youth Study. Pediatric diabetes. 2015;16(5):382-91.
34. McGavock J, Dart A, Wicklow B. Lifestyle therapy for the treatment of youth with type 2 diabetes. Current diabetes reports. 2015;15(1):568.
35. Okoli A, Hanlon EC, Brady MJ. The Relationship between Sleep, Obesity, and Metabolic Health in Adolescents - a Review. Current opinion in endocrine and metabolic research. 2021;17:15-9.
36. Christensen MA, Bettencourt L, Kaye L, Moturu ST, Nguyen KT, Olgin JE, et al. Direct Measurements of Smartphone Screen-Time: Relationships with Demographics and Sleep. PLoS One. 2016;11(11):e0165331-e.
37. Grøntved A, Ried-Larsen M, Møller NC, Kristensen PL, Wedderkopp N, Froberg K, et al. Youth screen-time behaviour is associated with cardiovascular risk in young adulthood: the European Youth Heart Study. European journal of preventive cardiology. 2014;21(1):49-56.
38. Thorp AA, Healy GN, Owen N, Salmon J, Ball K, Shaw JE, et al. Deleterious Associations of Sitting Time and Television Viewing Time With Cardiometabolic Risk Biomarkers. Australian Diabetes, Obesity and Lifestyle (AusDiab) study 2004–2005. 2010;33(2):327-34.
39. Vella CA, Taylor K, Nelson MC. Associations of leisure screen time with cardiometabolic biomarkers in college-aged adults. Journal of behavioral medicine. 2020;43(6):1014-25.

40. Zeitler P, Hirst K, Pyle L, Linder B, Copeland K, Arslanian S, et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. The New England journal of medicine. 2012;366(24):2247-56.
41. Berkowitz RI, Marcus MD, Anderson BJ, Delahanty L, Grover N, Kriska A, et al. Adherence to a lifestyle program for youth with type 2 diabetes and its association with treatment outcome in the TODAY clinical trial. Pediatric diabetes. 2018;19(2):191-8.
42. Marcus MD, Wilfley DE, El Ghormli L, Zeitler P, Linder B, Hirst K, et al. Weight change in the management of youth-onset type 2 diabetes: the TODAY clinical trial experience. Pediatric obesity. 2017;12(4):337-45.
43. Group TS. Rapid rise in hypertension and nephropathy in youth with type 2 diabetes: the TODAY clinical trial. Diabetes Care. 2013;36(6):1735-41.
44. Group TS. Lipid and inflammatory cardiovascular risk worsens over 3 years in youth with type 2 diabetes: the TODAY clinical trial. Diabetes Care. 2013;36(6):1758-64.
45. Burns N, Finucane FM, Hatunic M, Gilman M, Murphy M, Gasparro D, et al. Early-onset type 2 diabetes in obese white subjects is characterised by a marked defect in beta cell insulin secretion, severe insulin resistance and a lack of response to aerobic exercise training. Diabetologia. 2007;50(7):1500-8.
46. Skinner TC SJ. Psychological factors and behaviouarl aspects of type 2 diabetes management. . Oxford Textbook of Endocrinology and Diabetes. 4th (in press) ed.
47. Browne JL, Nefs G, Pouwer F, Speight J. Depression, anxiety and self-care behaviours of young adults with Type 2 diabetes: results from the International Diabetes Management and Impact for Long-term Empowerment and Success (MILES) Study. Diabetic medicine : a journal of the British Diabetic Association. 2015;32(1):133-40.
48. Browne JL, Scibilia R, Speight J. The needs, concerns, and characteristics of younger Australian adults with Type 2 diabetes. Diabetic medicine : a journal of the British Diabetic Association. 2013;30(5):620-6.
49. Van Buren DJ, Wilfley DE, Marcus MD, Anderson B, Abramson NW, Berkowitz R, et al. Depressive symptoms and glycemic control in youth with type 2 diabetes participating in the TODAY clinical trial. Diabetes Res Clin Pract. 2018;135:85-7.
50. Anderson BJ, Edelstein S, Abramson NW, Katz LE, Yasuda PM, Lavietes SJ, et al. Depressive symptoms and quality of life in adolescents with type 2 diabetes: baseline data from the TODAY study. Diabetes Care. 2011;34(10):2205-7.
51. Lawrence JM, Standiford DA, Loots B, Klingensmith GJ, Williams DE, Ruggiero A, et al. Prevalence and correlates of depressed mood among youth with diabetes: the SEARCH for Diabetes in Youth study. Pediatrics. 2006;117(4):1348-58.
52. Halliday JA, Speight J, Bennet A, Beeney LJ, Hendrieckx C. The Diabetes and Emotional Health Handbook and Toolkit for Health Professionals Supporting Adults With Type 1 and Type 2 Diabetes: Formative Evaluation. JMIR Form Res. 2020;4(2):e15007-e.
53. Hendrieckx C HJ, , Beeney L, Speight J. . Diabetes and Emotional Health:a Handbook for Health Professionals Supporting Adults With Type 1 and Type 2 Diabetes. . Canberra National Diabetes Services Scheme; 2016.
54. Polonsky WH, Anderson BJ, Lohrer PA, Welch G, Jacobson AM, Aponte JE, et al. Assessment of diabetes-related distress. Diabetes Care. 1995;18(6):754-60.
55. Hagger V, Hendrieckx C, Cameron F, Pouwer F, Skinner TC, Speight J. Cut Points for Identifying Clinically Significant Diabetes Distress in Adolescents With Type 1 Diabetes Using the PAID-T: Results From Diabetes MILES Youth-Australia. Diabetes Care. 2017;40(11):1462-8.
56. Renae. K. Improving outcomes for Indigenous Australian Youth with Diabetes: where are we now? . Australasian Diabetes Congress
13 November 20202021.
57. Pastor A, Conn J, MacIsaac RJ, Bonomo Y. Alcohol and illicit drug use in people with diabetes. The lancet Diabetes & endocrinology. 2020;8(3):239-48.
58. DiMeglio LA, Acerini CL, Codner E, Craig ME, Hofer SE, Pillay K, et al. ISPAD Clinical Practice Consensus Guidelines 2018: Glycemic control targets and glucose monitoring for children, adolescents, and young adults with diabetes. Pediatric diabetes. 2018;19 Suppl 27:105-14.

59. Kunasegaran S, Beig J, Khanolkar M, Cundy T. Adherence to medication, glycaemic control and hospital attendance in young adults with type 2 diabetes. Intern Med J. 2018;48(6):728-31.
60. Information TGAMhP. Metformin hydrochloride Product Information - Australia 2013
61. Viner R, White B, Christie D. Type 2 diabetes in adolescents: a severe phenotype posing major clinical challenges and public health burden. Lancet (London, England). 2017;389(10085):2252-60.
62. Li FF, Liu BL, Yin GP, Zhang DF, Zhai XF, Chen MY, et al. Young onset type 2 diabetic patients might be more sensitive to metformin compared to late onset type 2 diabetic patients. Scientific reports. 2017;7(1):16382.
63. Group TS. Effects of metformin, metformin plus rosiglitazone, and metformin plus lifestyle on insulin sensitivity and β-cell function in TODAY. Diabetes Care. 2013;36(6):1749-57.
64. Zuhri-Yafi MI, Brosnan PG, Hardin DS. Treatment of type 2 diabetes mellitus in children and adolescents. Journal of pediatric endocrinology & metabolism : JPEM. 2002;15 Suppl 1:541-6.
65. Le PT, Huisingh CE, Ashraf AP. Glycemic control and diabetic dyslipidemia in adolescents with type 2 diabetes. Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists. 2013;19(6):972-9.
66. Consortium R. Impact of Insulin and Metformin Versus Metformin Alone on β-Cell Function in Youth With Impaired Glucose Tolerance or Recently Diagnosed Type 2 Diabetes. Diabetes Care. 2018;41(8):1717-25.
67. Association. AD. Children and Adolescents: Standards of Medical Care in Diabetes-2020. Diabetes Care. 2020;43(Suppl 1):S163-s82.
68. Tamborlane WV, Barrientos-Pérez M, Fainberg U, Frimer-Larsen H, Hafez M, Hale PM, et al. Liraglutide in Children and Adolescents with Type 2 Diabetes. New England Journal of Medicine. 2019;381(7):637-46.
69. Colesevelam for Children With Type 2 Diabetes (WELKid DM) [Available from: https://clinicaltrials.gov/ct2/show/NCT01258075.
70. Fraser IP, Neufeld ND, Fox LA, Kipnes MS, Miller TL, Zeitler PS, et al. A randomized clinical trial to evaluate the single-dose pharmacokinetics, pharmacodynamics, and safety of sitagliptin in pediatric patients with type 2 diabetes. Pediatric diabetes. 2019;20(1):48-56.
71. Ke C, Shah BR, Luk AO, Di Ruggiero E, Chan JCN. Cardiovascular outcomes trials in type 2 diabetes: Time to include young adults. Diabetes, obesity & metabolism. 2020;22(1):3-5.
72. Shah AS, Nadeau KJ, Helmrath MA, Inge TH, Xanthakos SA, Kelsey MM. Metabolic outcomes of surgery in youth with type 2 diabetes. Seminars in pediatric surgery. 2020;29(1):150893.
73. Constantino MI, Molyneaux L, Limacher-Gisler F, Al-Saeed A, Luo C, Wu T, et al. Long-term complications and mortality in young-onset diabetes: type 2 diabetes is more hazardous and lethal than type 1 diabetes. Diabetes Care. 2013;36(12):3863-9.
74. Dart AB, Martens PJ, Rigatto C, Brownell MD, Dean HJ, Sellers EA. Earlier onset of complications in youth with type 2 diabetes. Diabetes Care. 2014;37(2):436-43.
75. Eppens MC, Craig ME, Cusumano J, Hing S, Chan AK, Howard NJ, et al. Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes. Diabetes Care. 2006;29(6):1300-6.
76. Reynolds K, Saydah SH, Isom S, Divers J, Lawrence JM, Dabelea D, et al. Mortality in youth-onset type 1 and type 2 diabetes: The SEARCH for Diabetes in Youth study. Journal of diabetes and its complications. 2018;32(6):545-9.
77. Waernbaum I, Blohmé G, Ostman J, Sundkvist G, Eriksson JW, Arnqvist HJ, et al. Excess mortality in incident cases of diabetes mellitus aged 15 to 34 years at diagnosis: a population-based study (DISS) in Sweden. Diabetologia. 2006;49(4):653-9.
78. Al-Saeed AH, Constantino MI, Molyneaux L, D'Souza M, Limacher-Gisler F, Luo C, et al. An Inverse Relationship Between Age of Type 2 Diabetes Onset and Complication Risk and Mortality: The Impact of Youth-Onset Type 2 Diabetes. Diabetes Care. 2016;39(5):823-9.
79. Huo L, Magliano DJ, Rancière F, Harding JL, Nanayakkara N, Shaw JE, et al. Impact of age at diagnosis and duration of type 2 diabetes on mortality in Australia 1997-2011. Diabetologia. 2018;61(5):1055-63.
80. Song SH, Hardisty CA. Early onset type 2 diabetes mellitus: a harbinger for complications in later

years--clinical observation from a secondary care cohort. QJM : monthly journal of the Association of Physicians. 2009;102(11):799-806.
81. Burgert TS, Dziura J, Yeckel C, Taksali SE, Weiss R, Tamborlane W, et al. Microalbuminuria in pediatric obesity: prevalence and relation to other cardiovascular risk factors. International journal of obesity (2005). 2006;30(2):273-80.
82. Luk AO, Lau ES, So WY, Ma RC, Kong AP, Ozaki R, et al. Prospective study on the incidences of cardiovascular-renal complications in Chinese patients with young-onset type 1 and type 2 diabetes. Diabetes Care. 2014;37(1):149-57.
83. Levin A, Stevens PE. Summary of KDIGO 2012 CKD Guideline: behind the scenes, need for guidance, and a framework for moving forward. Kidney international. 2014;85(1):49-61.
84. Marcovecchio ML, Chiesa ST, Bond S, Daneman D, Dawson S, Donaghue KC, et al. ACE Inhibitors and Statins in Adolescents with Type 1 Diabetes. New England Journal of Medicine. 2017;377(18):1733-45.
85. Li J, Albajrami O, Zhuo M, Hawley CE, Paik JM. Decision Algorithm for Prescribing SGLT2 Inhibitors and GLP-1 Receptor Agonists for Diabetic Kidney Disease. Clinical Journal of the American Society of Nephrology. 2020;15(11):1678.
86. Mayer-Davis EJ, Davis C, Saadine J, D'Agostino RB, Jr., Dabelea D, Dolan L, et al. Diabetic retinopathy in the SEARCH for Diabetes in Youth Cohort: a pilot study. Diabetic medicine : a journal of the British Diabetic Association. 2012;29(9):1148-52.
87. Dabelea D, Stafford JM, Mayer-Davis EJ, D'Agostino R, Jr., Dolan L, Imperatore G, et al. Association of Type 1 Diabetes vs Type 2 Diabetes Diagnosed During Childhood and Adolescence With Complications During Teenage Years and Young Adulthood. Jama. 2017;317(8):825-35.
88. Liu Y, Yang J, Tao L, Lv H, Jiang X, Zhang M, et al. Risk factors of diabetic retinopathy and sight-threatening diabetic retinopathy: a cross-sectional study of 13 473 patients with type 2 diabetes mellitus in mainland China. BMJ open. 2017;7(9):e016280.
89. Middleton TL, Constantino MI, Molyneaux L, D'Souza M, Twigg SM, Wu T, et al. Young-onset type 2 diabetes and younger current age: increased susceptibility to retinopathy in contrast to other complications. Diabetic medicine : a journal of the British Diabetic Association. 2020;37(6):991-9.
90. Jaiswal M, Divers J, Dabelea D, Isom S, Bell RA, Martin CL, et al. Prevalence of and Risk Factors for Diabetic Peripheral Neuropathy in Youth With Type 1 and Type 2 Diabetes: SEARCH for Diabetes in Youth Study. Diabetes Care. 2017;40(9):1226-32.
91. Jaiswal M, Divers J, Urbina EM, Dabelea D, Bell RA, Pettitt DJ, et al. Cardiovascular autonomic neuropathy in adolescents and young adults with type 1 and type 2 diabetes: The SEARCH for Diabetes in Youth Cohort Study. Pediatric diabetes. 2018;19(4):680-9.
92. Martin CL, Albers JW, Pop-Busui R. Neuropathy and related findings in the diabetes control and complications trial/epidemiology of diabetes interventions and complications study. Diabetes Care. 2014;37(1):31-8.
93. Hillier TA, Pedula KL. Complications in young adults with early-onset type 2 diabetes: losing the relative protection of youth. Diabetes Care. 2003;26(11):2999-3005.
94. Gungor N, Thompson T, Sutton-Tyrrell K, Janosky J, Arslanian S. Early signs of cardiovascular disease in youth with obesity and type 2 diabetes. Diabetes Care. 2005;28(5):1219-21.
95. Shah AS, Dolan LM, Kimball TR, Gao Z, Khoury PR, Daniels SR, et al. Influence of duration of diabetes, glycemic control, and traditional cardiovascular risk factors on early atherosclerotic vascular changes in adolescents and young adults with type 2 diabetes mellitus. The Journal of clinical endocrinology and metabolism. 2009;94(10):3740-5.
96. Harding JL, Shaw JE, Peeters A, Davidson S, Magliano DJ. Age-Specific Trends From 2000–2011 in All-Cause and Cause-Specific Mortality in Type 1 and Type 2 Diabetes: A Cohort Study of More Than One Million People. Diabetes Care. 2016;39(6):1018-26.
97. Pease A, Earnest A, Ranasinha S, Nanayakkara N, Liew D, Wischer N, et al. Burden of cardiovascular risk factors and disease among patients with type 1 diabetes: results of the Australian National Diabetes Audit (ANDA). Cardiovascular diabetology. 2018;17(1):77.
98. https://www.nice.org.uk/guidance/cg181/chapter/1-recommendations#lipid-modification-therapy-for-the-primary-and-secondary-prevention-of-cvd- Ng. [Available from:

https://www.nice.org.uk/guidance/cg181/chapter/1-recommendations#lipid-modification-therapy-for-the-primary-and-secondary-prevention-of-cvd-2.
99. Vuorio A, Kuoppala J, Kovanen PT, Humphries SE, Tonstad S, Wiegman A, et al. Statins for children with familial hypercholesterolemia. The Cochrane database of systematic reviews. 2017;7:Cd006401.
100. Ginsberg HN, Elam MB, Lovato LC, Crouse JR, 3rd, Leiter LA, Linz P, et al. Effects of combination lipid therapy in type 2 diabetes mellitus. The New England journal of medicine. 2010;362(17):1563-74.
101. Koren D, Taveras EM. Association of sleep disturbances with obesity, insulin resistance and the metabolic syndrome. Metabolism: clinical and experimental. 2018;84:67-75.
102. Shaw JE, Punjabi NM, Naughton MT, Willes L, Bergenstal RM, Cistulli PA, et al. The Effect of Treatment of Obstructive Sleep Apnea on Glycemic Control in Type 2 Diabetes. American Journal of Respiratory and Critical Care Medicine. 2016;194(4):486-92.
103. Newton KP, Hou J, Crimmins NA, Lavine JE, Barlow SE, Xanthakos SA, et al. Prevalence of Prediabetes and Type 2 Diabetes in Children With Nonalcoholic Fatty Liver Disease. JAMA pediatrics. 2016;170(10):e161971.
104. Klingensmith GJ, Pyle L, Nadeau KJ, Barbour LA, Goland RS, Willi SM, et al. Pregnancy Outcomes in Youth With Type 2 Diabetes: The TODAY Study Experience. Diabetes Care. 2016;39(1):122-9.
105. Damm JA, Asbjörnsdóttir B, Callesen NF, Mathiesen JM, Ringholm L, Pedersen BW, et al. Diabetic nephropathy and microalbuminuria in pregnant women with type 1 and type 2 diabetes: prevalence, antihypertensive strategy, and pregnancy outcome. Diabetes care. 2013;36(11):3489-94.
106. Kapur A, McIntyre HD, Hod M. Type 2 Diabetes in Pregnancy. Endocrinology and metabolism clinics of North America. 2019;48(3):511-31.
107. Wicklow BA, Sellers EAC, Sharma AK, Kroeker K, Nickel NC, Philips-Beck W, et al. Association of Gestational Diabetes and Type 2 Diabetes Exposure In Utero With the Development of Type 2 Diabetes in First Nations and Non-First Nations Offspring. JAMA pediatrics. 2018;172(8):724-31.
108. Yang Z, Phung H, Freebairn L, Sexton R, Raulli A, Kelly P. Contribution of maternal overweight and obesity to the occurrence of adverse pregnancy outcomes. The Australian & New Zealand journal of obstetrics & gynaecology. 2019;59(3):367-74.
109. Temple-Smith M, Sanci L. LARCs as first-line contraception – What can general practitioners advise young women? Australian Family Physician. 2017;46:710-5.
110. Salinas A, Merino PM, Giraudo F, Codner E. Long-acting contraception in adolescents and young women with type 1 and type 2 diabetes. Pediatric diabetes. 2020.
111. Rudland VL, Price SAL, Callaway L. ADIPS position paper on pre-existing diabetes and pregnancy. The Australian & New Zealand journal of obstetrics & gynaecology. 2020;60(6):831-9.
112. Mayer-Davis EJ, Dabelea D, Lamichhane AP, D'Agostino RB, Liese AD, Thomas J, et al. Breast-feeding and type 2 diabetes in the youth of three ethnic groups: the SEARCh for diabetes in youth case-control study. Diabetes care. 2008;31(3):470-5.
113. Davies MJ, Heller S, Skinner TC, Campbell MJ, Carey ME, Cradock S, et al. Effectiveness of the diabetes education and self management for ongoing and newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cluster randomised controlled trial. BMJ (Clinical research ed). 2008;336(7642):491-5.
114. Smart CE, Annan F, Bruno LP, Higgins LA, Acerini CL. ISPAD Clinical Practice Consensus Guidelines 2014. Nutritional management in children and adolescents with diabetes. Pediatric diabetes. 2014;15 Suppl 20:135-53.
115. Jones KL. Non-insulin dependent diabetes in children and adolescents: the therapeutic challenge. Clinical pediatrics. 1998;37(2):103-10.
116. Yang Q, Fang P. Impact of the conversation map tools in patients with type 2 diabetes mellitus: A PRISMA-compliant meta-analysis of randomized controlled trials. Medicine (Baltimore). 2016;95(40):e4664-e.
117. Miller AS, Cafazzo JA, Seto E. A game plan: Gamification design principles in mHealth applications for chronic disease management. Health informatics journal. 2016;22(2):184-93.
118. Von Bargen T, Zientz C, Haux R. Gamification for mHealth - A Review of Playful Mobile Healthcare. Studies in health technology and informatics. 2014;202:225-8.

119. Kamel Boulos MN, Gammon S, Dixon MC, MacRury SM, Fergusson MJ, Miranda Rodrigues F, et al. Digital games for type 1 and type 2 diabetes: underpinning theory with three illustrative examples. JMIR serious games. 2015;3(1):e3.