Current insights and emerging trends in early-onset type 2 diabetes

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Type 2 diabetes diagnosed in childhood or early adulthood is termed early-onset type 2 diabetes. Cases of early-onset type 2 diabetes are increasing rapidly globally, alongside rising obesity. Compared with a diagnosis later in life, an earlier-onset diagnosis carries an unexplained excess risk of microvascular complications, adverse cardiovascular outcomes, and earlier death. Women with early-onset type 2 diabetes also have a higher risk of adverse pregnancy outcomes. The high burden of complications renders individuals with early-onset type 2 diabetes at future risk of multimorbidity and interventions to reverse these concerning trends should be a priority. Within the early-onset cohort, disease pathophysiology and interventions have been better studied in paediatric-onset (<19 years) type 2 diabetes compared to adults; however, young adults aged 19–39 years (a larger number proportionally) are not well characterised and are also invisible in the current evidence base supporting management, which is derived from trials in later-onset type 2 diabetes. Young adults with type 2 diabetes face challenges in self-management that older individuals are less likely to experience (being in education or of working age, higher diabetes distress, and possible obesity-related stigma and diabetes-related stigma). There is a major research gap as to the optimal strategies to deploy in managing type 2 diabetes in adolescents and young adults, given that current models of care appear to not work as well in this age group. In the face of manifold risk factors (obesity, female sex, social deprivation, non-White European ethnicity, and genetic risk factors) prevention strategies with tailored lifestyle interventions, where needed, are likely to have greater success, but more evidence is needed. In this Review, we draw on evidence from both adolescents and young adults to provide a contemporary update on the current insights and emerging trends in early-onset type 2 diabetes.

Introduction

Type 2 diabetes has typically been a disease with onset in middle age to older ages; however, incidence is now increasing in younger ages,[1] referred to as early-onset type 2 diabetes. Although the definition of the age ranges that constitute early onset is fluid, there is consensus that a diagnosis before age 40 years is distinct from a diagnosis later in life.[2]

Early-onset type 2 diabetes carries with it substantial risks compared with later-onset type 2 diabetes. These risks include a higher risk of cardiovascular disease,[3,4] earlier death,[5] and apparent faster progression to microvascular complications,[6] when compared to later-onset presentations, along with worse neonatal outcomes in pregnant women with pre-existing type 2 diabetes compared to those with type 1 diabetes.[7] Prevalence is greater in ethnicities already at high risk of type 2 diabetes, compared with white European populations, there appears to be a female preponderance up until the age of 25 years, and the presentation has been strongly associated with social deprivation and obesity.[8,9]

Early-onset type 2 diabetes has been better studied in adolescents (sometimes termed youth-onset diabetes) owing to two seminal prospective studies.[10,11] The higher risk of adverse outcomes is however also observed in adults diagnosed aged 19–39 years, although there is a comparative evidence gap in this group because they are under-represented in type 2 diabetes prospective and randomised controlled trials (RCTs), which are typically conducted in people with later-onset type 2 diabetes (table 1).[12,13]

As cases of early-onset type 2 diabetes increase, key considerations arise for scientists, health services, and communities. The first consideration is how best to treat individuals given the paucity of evidence: for example, are weight-lowering therapies preferable and what is the optimal cardiovascular risk reduction? There is also a need for more holistic care centred on lifestyle interventions, but the evidence and the optimal model of care for delivery is unclear. The second consideration is the need for tailored prevention strategies focused on reducing obesity, but also preventing the future development of several long-term conditions. Finally, a better understanding of the pathophysiology might reveal insights into optimal treatment strategies and heterogeneity in disease progression and outcomes.

In this Review we provide a contemporary update to the established epidemiology and pathophysiology of early-onset type 2 diabetes,[2] with new insights on the treatment and care of people affected by collating existing data derived from studies of type 2 diabetes in adolescents and young adults. We also prioritise evidence gaps that need to be addressed.

What defines early-onset type 2 diabetes?

The concept of early-onset type 2 diabetes first emerged with reports of non-insulin-requiring diabetes in children[14] and the emergence of this type of diabetes was closely followed up with population-level data showing the fastest rise of type 2 diabetes occurring in 30–39 year olds, strongly correlated with obesity.[15,16] Soon after, studies revealed poor cardiovascular outcomes in young adults relative to older adults with type 2 diabetes,[17] and

these findings were recapitulated in population-level epidemiological studies of adults[3,5,18] and prospective cohort studies in young people.[6,19]

However, the age at which this higher risk ends is unclear. More recent evidence suggests a continuum of risk in which each earlier year of diagnosis is associated with a higher risk of cardiovascular outcomes, when adjusted for current age or duration[20] However, other studies suggest a distinct relationship between risk of type 2 diabetes and weight gain in people younger than 40 years compared with older adults, in whom similar weight gain had a lower relative risk of type 2 diabetes compared with early adulthood.[21] Taken together, any age cutoff that defines early-onset diabetes is likely to oversimplify the drivers of excess risk because, similar to later-onset type 2 diabetes, there will almost certainly be disease heterogeneity. Pragmatically, a cutoff of younger than 40 years, which many researchers have applied, identifies a cohort that have distinct health-care needs, identifies ages of onset for which there might be uncertainty in diabetes classification, and captures women of child-bearing age, a particularly high-risk group.

Epidemiology

Variability in nationwide data hampers the ascertainment of true global trends, however it is clear the prevalence and incidence of early-onset type 2 diabetes are increasing.[1,9]

On a global scale, prevalence estimates of diabetes from the International Diabetes Atlas among people aged 20–39 years was 2·9% (63 million people) in 2013 rising to 3·8% (260 million) in 2021.[1] By region, the largest rise between 2013 and 2021 was observed in the Middle East North Africa region (MENA), increasing from 4·0% to 8·0%, whereas the increase in prevalence in Europe was the lowest (figure 1). Almost universally, populations of White ethnicity have a lower prevalence of early-onset type 2 diabetes compared with other ethnicities.[22] In some populations, type 2 diabetes now predominates as the leading cause of early-onset diabetes and in particular, Indigenous populations across the world have some of the highest prevalence estimates, including Australian and Canadian First Nation people, Native Americans in the US, and Maori people (appendix p 1).[23–25]

Prevalence of type 2 diabetes is generally higher in adolescent girls than in boys,[11] but not universally, which might reflect differences in distribution of obesity by gender; for example, if at the population level adolescent boys have higher rates of obesity than girls, the prevalence of type 2 diabetes would probably be higher in boys than girls.[26]

Incidence data of early-onset type 2 diabetes are sparser than prevalence data. Among people younger than 20 years, incidence varied across countries, ranging from 0·1 per 100 000 in Germany to 94·0 per 100 000 in the First Nations Canadian youth[25] (appendix p 2). In the UK, incidence was higher in people younger than 17 years from ethnic minorities than in those who were White (0·44 per 100 000 in children who were White *vs* 2·92 per 100 000 in children from Asian ethnic backgrounds and 1·67 per 100 000 in children from Black, African, Caribbean, and Black British ethnic backgrounds in 2015–16).[27] Similar patterns can be seen in the US SEARCH study;[22] in 2017–18, incidence among young people aged 0–19 years was 16·6 per 100 000 among those from Asian and Pacific Islander ethnicities, 25·8 per 100 000 among those from Hispanic ethnicities, 50·1 per 100 000 among those from non-Hispanic Black ethnicities respectively, and only 5·2 per 100 000 among those from non-Hispanic White ethnicities. In 2023, updated incidence of type 2 diabetes showed the annual incidence of youth-onset type 2 diabetes (17·9 per 100 000) now approaches the incidence of type 1 diabetes (22·2 per 100 000) int the USA.[22] In India, a country where later-onset type 2 diabetes is common, incidence in people younger than 19 years was relatively low at 0·5 per 100 000 per year.[28]

The Global Burden of Disease study, reporting age-standardised incidence of type 2 diabetes in people aged 15–39 years across 204 countries, showed an increase from 117·22 per 100 000 (95% CI 117·07–117·36) in 1990 to 183·36 per 100 000 (183·21–183·51) in 2019.[9]

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See **Online** for appendix

	Early-onset type 2 diabetes		Later-onset type 2 diabetes
	Young people	Early adulthood	Later life
Age group	≤18 years	19–39 years	≥40 years
Alternative nomenclature	Young-onset type 2 diabetes, childhood-onset type 2 diabetes, and youth-onset type 2 diabetes	Young-onset type 2 diabetes	NA
Diagnosis	Age at presentation overlaps with other types of diabetes, such as type 1 diabetes and monogenic diabetes	Age at presentation overlaps with other types of diabetes, such as type 1 diabetes and monogenic diabetes	Most likely type 2 diabetes
Evidence in age group			
Epidemiology associating diagnosis to outcomes	Yes	Yes	Yes
Prospective cohort studies	Yes	No	Yes
Cardiovascular outcome studies of GLT	No	No	Yes
Interventional studies of GLT, diet, and surgery	Yes	Not specifically targeting this age group	Yes
Care delivery in each age group			
Specialist care	Usually under specialists	Mostly under primary care	Mostly under primary care
Age-specific guidelines	Yes	Same as later-onset type 2 diabetes, no guidelines tailored to younger adults	Standard guidelines for all adults with type 2 diabetes

GLT=glucose-lowering therapy. NA=not applicable.

Table 1: **Differences in evidence and care delivery to young people versus those in early adulthood with type 2 diabetes**

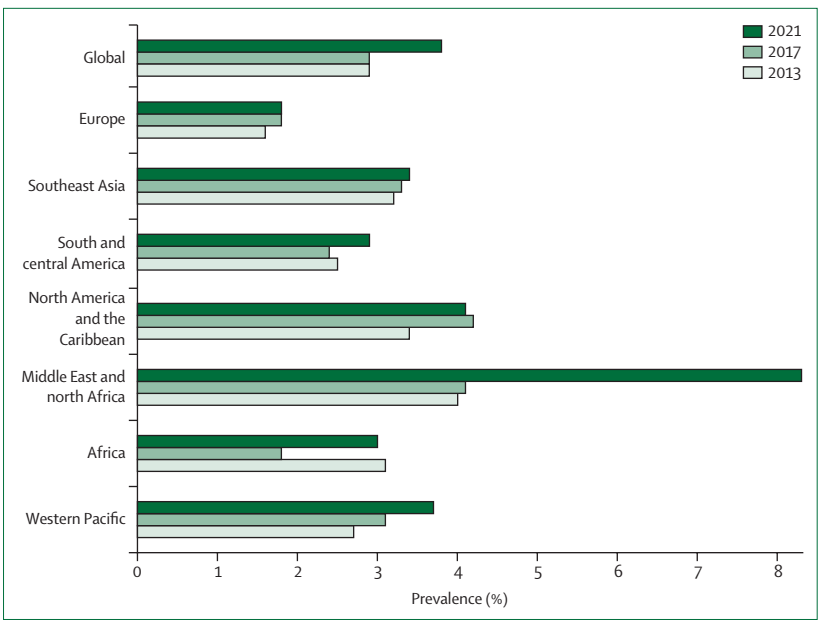

Figure 1: **Prevalence of type 2 diabetes in people aged 20–39 years globally and by world region**
Data are from the Diabetes Atlas for 2013 and 2017, and from the International Diabetes Federation for 2021.

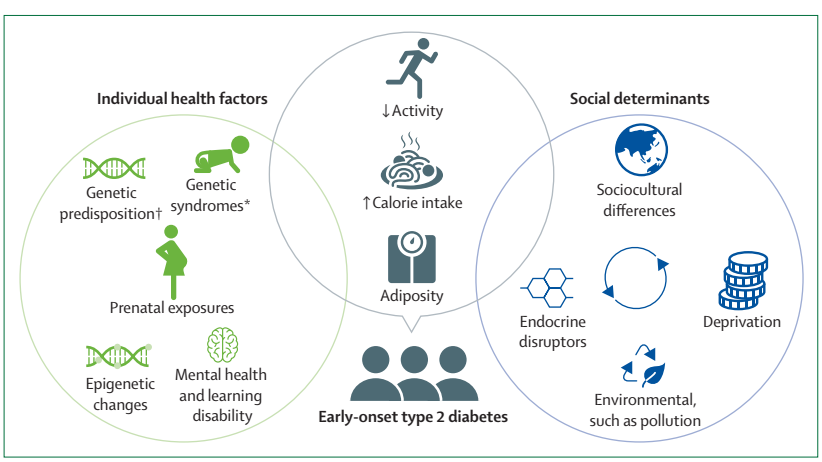

Figure 2: **Risk factors for early-onset type 2 diabetes**
*Down's syndrome, Turner syndrome, Klinefelter syndrome, Bardet Biedl syndrome, Alström syndrome, and Prader-Willi syndrome. †Genes implicated include *PHF2, TCF7L2, MC4R, CDC123, KCNQ1, IGFBP2, SLC16A11*.

Why incidence varies by country even among populations of the same ancestry is unclear. This characteristic might be a feature of case ascertainment methods; estimates can be based on studies that have undertaken screening for early-onset type 2 diabetes or that used clinical diagnoses expressed against an age-adjusted population denominator (appendix p 1–2). However, these differences might reflect genuine variations in disease susceptibility or environmental factors. For example, studies of the ancestrally similar O'odham (Native American people in Arizona) and Pima Bajo (in Mexico) tribes show vastly different age-adjusted prevalence of early-onset type 2 diabetes (diagnosed 20–35 years), with 18·5% in O'odham women and 15·3% in O'odham men, versus 0% in Pima Bajo women and 1·8% in Pima Bajo men.[29] These differences are likely to reflect divergence in lifestyles, diet, and other modifiable risk factors.[29]

Disease mechanisms

Risk factors

The risk factors for developing type 2 diabetes early in life are similar to those of later-onset type 2 diabetes. However, studies suggest these risk factors are amplified in younger presentations (figure 2).[9,30] Obesity remains a major risk factor, with about 90% of children with early-onset type 2 diabetes living with obesity.[31] Earlier and greater cumulative exposure to obesity appears to be an important factor[32] driving type 2 diabetes. When examining proportions in each weight category by age, there is a graded reduction in obesity as age increases from adolescence to 40 years.[8] Earlier exposure to obesity might increase the risk of early-onset type 2 diabetes, but this risk might be reduced if weight normalises before puberty.[33]

More than 80% of UK adolescents with type 2 diabetes reported a family history of type 2 diabetes, 56–71% as first-degree relatives.[31] The association of family history is mediated through shared genetic risk and similarities in the home environments and lifestyles, which can propagate obesity. In cohort studies of early-onset type 2 diabetes, female sex predominates in adolescents and up to the age of 25 years[8,10,11] before sex distribution equalises and male sex predominates after age 40 years. These sex differences might reflect differences in weight gain and weigh distribution before and after puberty.

The disproportionately high prevalence in Asian, MENA, Hispanic, and Black ethnic populations[34] points to genetic or shared environmental drivers. Countries with a low-middle and middle sociodemographic index (a representation of the economic development of a country) had the highest age-standardised incidence rate relative to those with a low index (less developed).[9] In high-income regions, earlier onset of type 2 diabetes is associated with socioeconomic deprivation.[8]

Prenatal exposures, such as maternal undernutrition or obesity and diabetes during pregnancy, can increase the risk of obesity and diabetes in offspring.[35,36] For people with early-onset type 2 diabetes, the SEARCH study specifically showed that maternal gestational diabetes (odds ratio [OR] 5·7, 95% CI 2·4–13·4) and maternal obesity (OR 2·8, 1·5–5·2) were associated with risk of early-onset type 2 diabetes compared with controls, adjusted for age, ethnicity, and socioeconomic factors.[37] In an analysis of the TODAY study over 12 years of follow-up, maternal history of diabetes was associated with faster glycaemic progression in off-spring with early-onset type 2 diabetes and worsening β-cell function.[38]

Additionally, environmental pollutants[9] along with endocrine disruptors,[39] such as perfluoroalkyl and polyfluoroalkyl substances, have been implicated in increasing risk.

Irrespective of the drivers, it is clear that at diagnosis of early-onset type 2 diabetes, there is a large deviation in traditional risk factors from healthy with differential weight, blood pressure, and triglyceride concentrations between affected and age-matched controls, far exceeding the differences observed at later ages; for example, in one study there was an 18·7 kg mean weight excess in people aged 20–39 years with type 2 diabetes versus those without type 2 diabetes, but only a 5 kg excess in people older than 80 years.[30]

Rapid progression

It is well established that adolescents with type 2 diabetes appear to have an accelerated rate of β-cell function loss;[40–42] 25–30% of β-cell function was lost per year in young people versus 7% in those with later-onset type 2 diabetes in one study.[42] However, the drivers for this higher rate of β-cell function loss are unclear[43] and extend beyond youth as more rapid progression to glycaemic failure is observed up to the age of 40 years.[44,45]

One theory is the timing of disease onset. During puberty, growth hormone secretion increases, insulin sensitivity decreases, and insulin secretion doubles.[46] Although 65% of youth with obesity and impaired glucose tolerance revert to normoglycaemia within 3 years, 8% progress to early-onset type 2 diabetes because of obesity-related insulin resistance and glucolipotoxicity.[46] The prevalence of obesity (above the 95th centile) in childhood type 2 diabetes varies from 64·5% in Asian populations to 89·9% in European populations[47] reflecting variable metabolic thresholds at which adiposity might drive type 2 diabetes in different ethnicities in children.

It is likely that β-cell dysfunction might have a bigger role in progression; in the TODAY study evaluating therapeutic options for type 2 diabetes in young people (<20 years),[48] the initial β-cell reserve and HbA_{1c} at randomisation were independent predictors of glycaemic durability; participants experiencing treatment failure had significantly lower β-cell function than those who did not, without significant differences in insulin sensitivity between groups. A similar finding was observed in the RISE study[42] and was not ameliorated by early-insulin treatment, suggesting that faster progression is not related to inadequate glycaemic control. These patterns have been reproduced in large population-based studies in European and Chinese populations.[44,45,49]

In addition to β-cell dysfunction, studies have also noted lower insulin sensitivity in young people versus adults with type 2 diabetes[50] and in BMI-matched, race-matched, and sex-matched young people and adults with impaired glucose tolerance.[51] Therefore there appears to be a synergistic effect in worsening β-cell function and insulin resistance in young people (compared with older adults) driving progression.

Ethnic differences in pathophysiology

The observed variation in prevalence between ethnicities might be due to differences in a genetically programmed threshold for developing type 2 diabetes along with differential lifestyle exposures, driving weight gain.

In a prospective study,[48] after diagnosis of early onset type 2 diabetes, glycaemic failure rates were higher in people of non-Hispanic Black ethnicities (52·8%) and Hispanic (45·0%) adolescents than those of non-Hispanic White (36·6%) ethnicities.[48] In young people with obesity and impaired glucose tolerance, those of non-Hispanic Black ethnicities had odds five times lower of reverting to normoglycaemia than those of non-Hispanic White ethnicities.[46]

South Asian and Chinese populations might be predisposed to accelerated β-cell function loss.[52] Cluster analyses classifying incident diabetes into five subgroups[53] were deployed in Indian and European cohorts younger than 45 years; Indians had more than double the prevalence of early-onset type 2 diabetes with normal BMI and a higher proportion of subgroups with severe insulin deficiency (non-autoimmune) than people from White ethnic backgrounds (53–67% *vs* 24–26%).[54] These differences were explained by a greater burden of genetic risk variants for compromised β-cell function in Indians.[55] Similar findings were replicated in Chinese populations.[56,57]

The role of genetics in the pathophysiology

The heritability of type 2 diabetes is estimated to be in the range of 30% to 70% on the basis of family and twin studies[58] and depending on the characteristics of the populations from which the estimates were calculated. Since the first genome-wide association study (GWAS) for type 2 diabetes in adults was published,[59] more than 700 genetic variants have been identified in adults, explaining close to 50% of type 2 diabetes heritability, with most individual variants having only a small-to-modest effect size on risk.[60] The first GWAS for type 2 diabetes in young people was done in 2021, in 3006 young people of multiethnic backgrounds and 6061 adult controls.[61] Seven genome-wide significant loci were identified, including a novel locus (rs10992863) in *PHF2*. The remaining six loci were previously reported adult loci, comprising *TCF7L2, MC4R, CDC123, KCNQ1, IGFBP2,* and *SLC16A11*. *TCF7L2* has one of the strongest effects on the risk of type 2 diabetes among common variants (OR of about 1·4). Both common and rare variant associations contributed more to early-onset type 2 diabetes liability variance than they did to adult-onset type 2 diabetes, with a five-times higher increase for rare variant associations and a 3·4-times higher increase with common variant associations. The findings demonstrate that the genetic architecture of type 2 diabetes in young people overlaps with adults, but that genetics probably contribute more to disease risk in young people than in adults.

Complications in early-onset type 2 diabetes

Proposed hypotheses for the high risk of complications observed include an intrinsically more aggressive pathophysiology with difficult-to-manage glycaemia, a longer exposure to glycaemic burden or concurrent cardiometabolic risk factors, and an unrecognised period of untreated hyperglycaemia before diagnosis. Other factors include structural barriers (eg, racial discrimination), socioeconomic factors, therapeutic inertia, concurrent mental health, self-management capacity, and reduced engagement of affected individuals with health services. A combination of all these factors is most probable.

Microvascular and macrovascular complications and mortality

Although epidemiological studies have reported large declines in incidence rates of most complications in type 2 diabetes (including cardiovascular disease, end-stage kidney disease, lower-extremity amputation, and all-cause mortality), these improvements have not extended to the youngest age groups.[62–65] Population surveillance in the USA showed a resurgence of complications most apparent in people aged 18–44 years from 1995 to 2015.[66] The complication burden is immense; in the 15 years of follow-up of the TODAY study, 80% of adolescents had developed at least one microvascular complication by a mean age 26 years.[6]

Several studies have shown that at the same age, risks of cardiovascular and kidney diseases and mortality were higher in people with early-onset versus later-onset type 2 diabetes.[67–69] However, it is challenging to draw definite conclusions on whether younger age at onset independently influences complication risks beyond duration, because cardiometabolic morbidity and mortality increase with age. To address this competing risk, analyses have been adjusted for diabetes duration,[70] or have shown differences at any given duration between individuals with different ages of diabetes onset.[5,18] A meta-analysis of 26 observational cohorts comprising 1·3 million individuals demonstrated that for every 1 year increase in age at diabetes diagnosis, there was an associated 3–5% reduction in cardiorenal disease risk and all-cause mortality adjusted for current age.[20]

Countering the narrative that a long duration explains excess risk of complications is the observation of higher odds for developing complications in adolescents with type 2 diabetes versus type 1 diabetes;[19,71] two-times to three-times higher odds of microvascular complications were observed in type 2 diabetes than with type 1 diabetes, adjusted for demographics, duration, and glycaemia.[19] Although individual complications might differ in their likelihood of development between type 2 diabetes and type 1 diabetes, these analyses show an excess risk of all complications, adjusted for traditional risk factors.

Excess risk of mortality associated with type 2 diabetes is greatest in the youngest age group and attenuates with age.[3–5,62,63,67] In a population-based study in Sweden, type 2 diabetes was found to confer a two-times to-three-times higher risk of all-cause mortality in people younger than 55 years, compared with older individuals.[5] Notably, when stratified by glycaemia and albuminuria, excess mortality persisted in the youngest group with HbA_{1c} below 7% (53 mmol/mol) and normoalbuminuria, suggesting that optimisation of blood glucose and measures to prevent kidney complications are not enough to lower mortality.

Multiple long-term conditions (multimorbidity)

It is now clear that early-onset type 2 diabetes is associated both at diagnosis and beyond with other long-term conditions.[72] This association has important implications because complications arise at an age when there is potential to disrupt education, employment, and family life along with a greater burden on health-care costs. In one analysis, women younger than 30 years with type 2 diabetes had a greater disease burden than any other age group with type 2 diabetes.[9] People with early-onset type 2 diabetes develop typical cardiometabolic long-term conditions, such as hypertension and dyslipidaemia. In one study, at diagnosis 19·2% of people with type 2 diabetes also had hypertension, rising to 46·8% after 10 years of follow-up, and hypertension was independently associated with the highest odds for development of several microvascular complications (OR 3·18, 95% CI 2·35–4·30), which was three times higher than the effect of a 1% increase in HbA_{1c}.[6]

At the time of diagnosis, 11% of Black American and non-Hispanic White individuals (aged 18–39 years) already had two or more long-term conditions, such as stroke, myocardial infarction, chronic kidney disease, hypertension, and depression.[72]

Depression and anxiety often co-exist with type 2 diabetes in young people; in a small cohort study, 20% of adolescents with type 2 diabetes had mental health conditions.[71] In another registry-based study, 40% of hospitalisations occurring in young individuals with type 2 diabetes were related to mental health conditions.[73] In a Swedish population study, people with type 2 diabetes diagnosed when younger than 45 years had 3·4-times to 4·2-times increased odds of having depression, bipolar disorder, anxiety, or stress-related disorders.[74] Another study demonstrated a high prevalence of depressive symptoms, diabetes distress, and lower self-compassion in individuals who were younger than those who were older.[75] The co-occurrence of early-onset type 2 diabetes with mental health conditions might reflect challenges in managing a chronic disease and associated stigma, genetic liability,[74] or people with pre-existing mental health conditions might have shared cardiometabolic risk factors. Research on mental health conditions in young people with type 2 diabetes is scarce and existing

studies have limitations; it is not known whether the association reflects better screening for mental health conditions in young people with type 2 diabetes or whether having a mental health condition somehow predisposes to developing type 2 diabetes at an early age.

Increased frequency of diabetes-related cancers have also been associated with earlier onset of type 2 diabetes[76] than later-onset type 2 diabetes. The Nurses' Health study, which reported outcomes from 228 073 participants who were followed up for 38 years, showed that early-onset type 2 diabetes was associated with a 1.47-times increased

	Study year	Sample size	Mean (range) age, years	Mean BMI (kg/m²) or BMI z-score	Follow-up	Treatments tested	Main findings
TODAY study group, Zeitler et al, 2012[10]	2004–09	699	14 (10–17)	BMI z-score 2·23	3·86 years	Metformin alone; metformin plus rosiglitazone; or metformin plus lifestyle interventions	Monotherapy with metformin was associated with durable glycaemic control in only half of the participants; combination of metformin and rosiglitazone significantly improved durability of glycaemic control compared with metformin alone (treatment failure 38·6% *vs* 51·7%; p=0·006); no significant difference in maintaining glycaemic control between metformin plus lifestyle interventions (treatment failure 46·6%) compared with metformin alone or metformin plus rosiglitazone
Gottschalk et al, 2007[88]	2002–04	285	13·8 (8·0–17·0)	31·6	26 week single-blind period	Glimepiride (1–8 mg) once per day or metformin (500–1000 mg) twice per day	Significant reduction in HbA1c in both glimepiride (–0·54%; p=0·001) and metformin (–0·71%; p=0·0002) groups; significantly higher weight gain in the glimepiride group (mean BMI change 0·26 kg/m² *vs* –0·33 kg/m²; p=0·003)·
RISE Consortium, 2018[89]	2013–16	91	Glargine group, 14·9 (10·0–19·0) and metformin alone group, 13·9 (10·0–19·0)	Glargine group, 36·5 and metformin alone group, 36·9	15 months	3 months of insulin glargine followed by 9 months of metformin or 12 months of metformin alone	In both intervention groups, clamp-measured β-cell function was significantly lower at 12 months (on treatment) and 15 months (off treatment) versus baseline; no significant differences were observed between groups at 12 months or 15 months in β-cell function, BMI percentile, HbA1c, fasting glucose, or oral glucose tolerance test results at 2 h
Ellipse study group, Tamborlane et al, 2019[90]	2012–18	135	14·6 (10·0–17·0)	33·9	26 week double-blind period, followed by a 26 week open-label extension	Subcutaneous liraglutide added to metformin, with or without basal insulin, or placebo added to metformin, with or without insulin	Liraglutide (up to 1·8 mg per day), when added to metformin, with or without basal insulin, was superior at improving glycaemic control (estimated HbA1c difference of 1·06%, 95% CI, 0·46–1·65 at 26 weeks and 1·30%, 0·70–1·89 at 52 weeks) compared with placebo; liraglutide use was associated with higher numbers of adverse events and gastrointestinal adverse events than placebo
Taheri et al, 2020[82]	2017–18	158	42·1 (18·0–50·0)	34·9	12 months	Intensive lifestyle intervention or usual medical care control	Significant difference in mean weight loss in the intervention group compared with the control group (11·96 kg *vs* 3·98 kg, adjusted mean difference –6·08 kg, 95% CI –8·37 to –3·79 kg) at 12 months; diabetes remission occurred in 61% of participants in the intervention group compared with 12% in the control group
AWARD–PEDS study group, Arslanian et al, 2022[91]	2016–20	154	14·5 (10·0–18·0)	34·1	26 week double-blind period, followed by a 26 week open-label extension period	Dulaglutide 0·75 mg once per week added to lifestyle modifications alone or with metformin, with or without basal insulin; dulaglutide 1·5 mg once per week added to lifestyle modifications alone or with metformin, with or without basal insulin; or placebo added to lifestyle modifications alone or with metformin, with or without basal insulin	Treatment with dulaglutide at a dose of 0·75 mg or 1·5 mg once per week was superior to placebo at improving glycaemic control (estimated HbA1c difference 1·4%, 0·8–1·9) at 26 weeks; the incidence of gastrointestinal adverse events was higher with dulaglutide therapy than with placebo

(Table 2 continues on next page)

	Study year	Sample size	Mean (range) age, years	Mean BMI (kg/m²) or BMI z-score	Follow-up	Treatments tested	Main findings
(Continued from previous page)							
Tamborlane et al, 2022[92]	2016–20	83	15 (10·0–18·0)	36·4	24 week double-blind period, followed by a 28 week open-label extension period	Exenatide 2 mg once per week added to lifestyle intervention, with or without metformin and with or without insulin; or placebo added to lifestyle intervention, with or without metformin and with or without insulin	Add-on therapy with exenatide once per week was superior in glycaemic control (least squares mean change in HbA1c −0·36% in exenatide *vs* 0·49% in placebo; between group difference 0·85%, 95% CI 0·19–1·51) at 24 weeks; lowering of HbA1c was evident in participants in the placebo group who crossed over to treatment with exenatide during the 28 week extension period of the study; exenatide once per week was well tolerated, with a safety profile similar to the placebo group
Tamborlane et al, 2022[93]	2016–19	72	16·1 (10·0–24·0)	32·4	24 week, double-blind period, followed by a 28 week open-label extension period	Dapagliflozin 10 mg once per week added to standard of care (ie, metformin alone, insulin alone, or metformin and insulin); or placebo added to standard of care (ie, metformin alone, insulin alone, or metformin and insulin)	In the intention-to-treat analysis, there was no significant difference in change in HbA1c concentration at 24 weeks between the two groups (−0·25% for dapagliflozin *vs* 0·50% for placebo); in a prespecified analysis of protocol-compliant participants (n=60), there was a significant difference in change in HbA1c at 24 weeks with dapagliflozin versus placebo (−1·13%, 95% CI −1·99% to −0·26%); no diabetic ketoacidosis events were recorded and no new safety signals were identified
DINAMO study group, Laffel et al, 2023[94]	2018–22	158	14·4 (10·0–17·0)	35·5–36·5	26 week double-blind period for glycaemic efficacy, followed by a 26 week double-blind safety extension period	Linagliptin 5 mg once per day or empagiflozin 10 mg or 25 mg once per day	Empagiflozin provided clinically meaningful and statistically significant reduction in HbA1c versus placebo (−0·84%, 95% CI −1·50 to −0·19; p=0·012), whereas linagliptin did not (−0·34%, −0·99 to 0·30; p=0·29)
PIONEER TEENS, 2023 (unpublished; NCT04596631)	2020–25	132	NA	NA	52 weeks	Semaglutide tablets once per day in addition to background treatment with metformin or basal insulin or both, in addition to diet and exercise; or placebo in addition to background treatment with metformin or basal insulin or both, in addition to diet and exercise	Not yet reported
VERIFY study subgroup analysis, Chan et al, 2021[87]	2012–19	186	35·8 (18·0–40·0)	30·5	5 years	Metformin up to 1 g twice per day or metformin up to 1 g twice per day plus vildagliptin 50 mg twice per day	Compared with metformin monotherapy, combination therapy reduced the risk of initial treatment failure (HbA1c >7% on two consecutive visits) by 48% (50·5% *vs* 73·3%; p=0·0006)

Table 2: **Clinical trials of lifestyle/ pharmacotherapy interventions in early-onset type 2 diabetes**

risk of early-onset cancers, a 1·75-times increased risk of obesity-related cancers, and a 2·11-times increased risk of diabetes-related cancers, but these trends were observed in people who had a BMI higher than 21 kg/m². These findings in early-onset type 2 diabetes were in excess of those observed for type 2 diabetes across all ages.[77,78]

Pregnancy outcomes

There is increasing awareness of the poor pregnancy outcomes in women with pre-existing type 2 diabetes. The TODAY study[79] reported pregnancy outcomes in 141 participants with a total of 260 pregnancies. Notably, a third of pregnant women already had hypertension and a third had HbA_{1c} concentrations higher than 8% (64 mmol/mol). In addition, congenital abnormalities were observed in 10% of pregnancies and 3·7% of pregnancies resulted in stillbirths (triple the reported national rates for the USA at the time). Similar trends have been observed in the UK National Pregnancy data, when compared with women with type 1 diabetes, pregnant women with type 2 diabetes had higher rates of perinatal deaths in all HbA_{1c} categories and were less likely to receive preconception folic acid or contraception advice.[7] In a cross-sectional study of 22 general practices in England, 64% of women with type 2 diabetes were on potentially harmful drugs compared with 36% of women with type 1 diabetes aged 14–49 years, with fewer than 50% on contraception.[80] These findings suggest that

women with early-onset type 2 diabetes might not receive or access adequate preparation for pregnancy.

Management

Lifestyle interventions and potential for remission

Similar to later-onset type 2 diabetes, interventions that promote healthy lifestyle behaviours are considered the cornerstone of management. DiRECT,[81] an RCT (n=306 [98%] White individuals, mean age 54-years), tested the efficacy of very-low calorie diets for 12 weeks versus standard care, demonstrating a mean adjusted weight loss of –8·8kg (95% CI –10·3 to –7·3) with remission in 36% of individuals by 2 years.

Very-low calorie diets have been tested in two further RCTs. In adolescents, the TODAY study tested a lifestyle intervention (200–300 min of moderate exercise per week and a 1200–1500 kcal diet per day) in the metformin group, which did not result in differential weight loss or change in HbA_{1c} compared with metformin alone or metformin plus rosiglitazone.[48] The Diabetes Intervention Accentuating Diet and Enhancing Metabolism (DIADEM-1) RCT enrolled 158 MENA participants (18–50 years, 73% men and 27% women) with type 2 diabetes (duration <3 years) and BMI 27·0 kg/m² or higher.[82] The intervention comprised very-low calorie diets of 800–820 kcal/day for 3 months, followed by food reintroduction plus physical activity, and structured lifestyle support in the maintenance period. At 12 months, the intervention group had 11·98 kg of weight loss versus 3·98 kg in controls (adjusted mean difference –6·08 kg, 95% CI –8·37 to –3·79). Remission occurred in 61% of the intervention group versus 12% in the control group (OR 12·03, 95% CI 5·17–28·03). As of yet, DIADEM-1 is the only RCT to have studied remission in young adults and in non-White ethnicities.

The findings from DIADEM-1 are reassuring in that similar weight loss to DiRECT study was observed in a younger population with an even greater remission rate, perhaps reflecting shorter duration of diabetes.[83] However, these studies have not been replicated in other young adult populations and findings in children are limited to the TODAY study and small observational studies with conflicting results.[48,84]

Whether very-low calorie diets can lead to durable remission in early-onset type 2 diabetes, across different ethnicities and in the context of socioeconomic deprivation, remains unclear. Protocol modifications might be needed, for example intermittent very-low calorie diets, to overcome the substantial lifestyle drivers of early-onset type 2 diabetes.

Irrespective of the potential for remission, targeted dietary advice to facilitate weight loss should be the cornerstone of management.

Pharmacological management

Pharmacological options for type 2 diabetes are different for people younger than 18 years than for those in early adulthood. Individuals in early adulthood are treated in the same way as individuals with later-onset type 2 diabetes. However, as previously noted in this Review, younger adults with type 2 diabetes are under-represented in major pharmaceutical studies.[12,13] A limited number of pharmacotherapy options have been approved for treatment of type 2 diabetes in adolescents, and these include metformin, insulin, and GLP-1 receptor agonists.[85,86]

One study, the VERIFY study,[87] has compared durability of glycaemic control in metformin versus metformin and vildagliptin specifically in early adulthood (mean age, 35 years) showing that early combination therapy achieved target glycaemic control for longer compared with metformin alone. Other than that study, the evidence for efficacy of pharmacotherapy in early-onset type 2 diabetes is predominantly derived from paediatric studies (table 2).

In the TODAY study,[48] metformin alone did not achieve durable glycaemic control in approximately half of adolescents with type 2 diabetes, and the addition of rosiglitazone, but not lifestyle intervention, was associated with improved durability of glycaemic control. Other studies have proven that early initiation of insulin has no effect on halting progression of β-cell failure.[42]

GLP-1 receptor agonists have been evaluated for type 2 diabetes in adolescents (table 2). The Evaluation of Liraglutide in Paediatrics with Diabetes study[90] was a phase 3 RCT that demonstrated superior glycaemic control (estimated HbA_{1c} difference of 1·06% at 26 weeks) with liraglutide (up to 1·8 mg) compared with placebo, when added to metformin with or without basal insulin, among 135 adolescents with overweight or obesity with type 2 diabetes. However, no difference in BMI z-scores were observed between groups.

Another phase 3 RCT[92] concluded the superior glycaemic efficacy of exenatide therapy given once per week compared with placebo, when added to existing treatments in adolescents with type 2 diabetes not optimally controlled. Similar results were reported for dulaglutide given once per week in the phase 3 AWARD-PEDS trial;[91] however, no changes in BMI were observed at 26 weeks or 52 weeks between placebo and dulaglutide. Although glycaemic outcomes and safety profiles of GLP-1 receptor agonists are encouraging, the absence of weight reduction is concerning. The primary outcome in all three studies was HbA_{1c}, not change in weight, so it is possible these results could reflect inadequate sample sizes. Equally, that the pathophysiology of early-onset type 2 diabetes might render these medications less effective could be postulated; for example, in adult studies of GLP-1 receptor agonists in type 2 diabetes,[95] higher baseline hyperglycaemia was associated with attenuation of weight loss. In young people, there could possibly be catabolic changes associated with worsening glycaemia that might attenuate differences in weight between control and intervention. Further longer-term follow-up studies are needed to disentangle these effects.

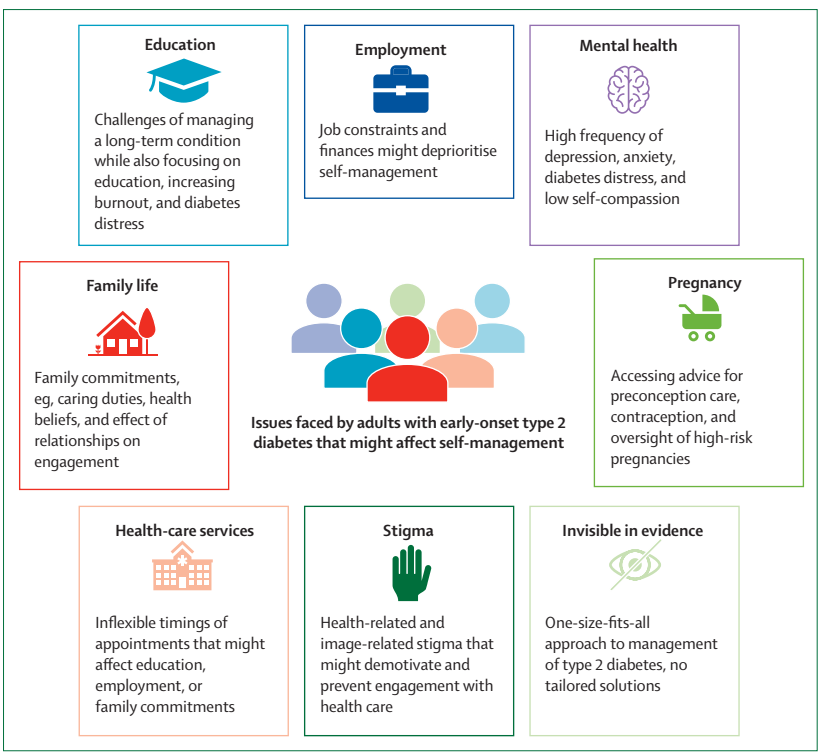

Figure 3: **Issues faced by adults who have early-onset type 2 diabetes that might affect self-management, motivation, and access to health-care services**

Dapagliflozin, a SGLT2i, was studied in a phase 3 RCT[93] involving 72 participants with type 2 diabetes aged 10–24 years (table 2). In the primary intention-to-treat analysis, there was no significant difference in change in HbA_{1c} at 24 weeks between groups. However, in a pre-specified analysis of protocol-compliant participants, the between-group difference was statistically significant (–1·13%, 95% CI –1·99 to –0·26). There were no diabetic ketoacidosis events or safety concerns. More recently, the DINAMO study[94] randomly assigned 158 young people aged 10–17 years previously treated with metformin or insulin to linagliptin, empagliflozin, or placebo, with a primary outcome of change in HbA_{1c} at 26 weeks. The HbA_{1c} reduction was 0·84% (9·2 mmol/mol; 95% CI –1·50 to –0·19) in the empagliflozin group versus placebo and 0·34% (3·8 mmol/mol, 95% CI –0·99 to 0·30) in the linagliptin group versus placebo. These studies highlight the potential utility of SGLT-2i inhibitors in early-onset type 2 diabetes and future larger studies to inform regulatory approval for these agents are needed.

There are few studies that make use of sulphonylureas in adolescents with type 2 diabetes. A 26-week single-blind study[88] among 285 children and adolescents aged 8–17 years reported that both glimepiride (–0·54%, p=0·001) and metformin (–0·71%, p=0·0002) reduced HbA_{1c}, however, treatment with glimepiride was associated with greater weight gain (mean BMI change 0·26 kg/m² *vs* –0·33 kg/m²; p=0·003).

Notable progress has been made in evaluating safety and glycaemic efficacy of unlicenced glucose-lowering therapies in adolescents with type 2 diabetes. Further studies are needed to better understand how medications should be escalated, whether early double or triple therapy has greater benefit, and the effect of prioritising treatments with greater efficacy in weight reduction. These studies are needed both in young adults and adolescents, however recruiting younger participants for pharmaceutical studies in sufficient numbers can be challenging.

Bariatric surgery

In adults, high-quality RCT evidence supports bariatric surgery as a means for sustained weight loss, type 2 diabetes remission,[96] and reduction in mortality.[97] International paediatric guidelines recommend bariatric surgery for adolescents with type 2 diabetes and severe obesity (BMI ≥35 kg/m² or a BMI ≥120% of the 95th percentile for age and sex). In a US study of bariatric surgery in adolescents (Teen-longitudinal assessment of bariatric surgery),[98] participants (mean age, 17 years) had an average 27% weight reduction 3 years after bariatric surgery. In 29 adolescents with obesity and type 2 diabetes who underwent surgery, remission occurred in 95% of individuals.[98] A comparison of remission rates with adults who underwent bariatric surgery showed that adolescents with type 2 diabetes who underwent gastric-bypass surgery were more likely to experience remission at 5 years than adults (86% *vs* 53%).[99] Overall, remission rates in adolescents with type 2 diabetes are higher than in adults, suggesting that bariatric surgery performed earlier in life induces remission. However, the effects on growth and longer-term risks are unknown.

Models of care and treatment targets

Unique issues faced by young people with type 2 diabetes

The need for conventional approaches to diabetes care and education to be tailored to the unique pathophysiological, behavioural, and psychosocial characteristics of young people with type 2 diabetes is increasingly recognised.[73,100–102] Several facets of managing type 2 diabetes earlier in life warrant deviation from the standard care of older individuals with type 2 diabetes[102] (figure 3), although even within the early-onset age group, there will be substantial variation in life experiences, education, and employment. This variation includes individual factors (being in full-time education or of working age, having high diabetes distress, and concurrent poor mental health) that might affect engagement with health-care providers or personal motivation. However, medical aspects might also benefit from different approaches, such as the need for contraception and preconception counselling in pregnant women with type 2 diabetes. Recognising that early-onset type 2 diabetes overlaps with the age at presentation of monogenic diabetes and type 1 diabetes might warrant

diagnostic tests.[102] Young people might be equally or more likely to have diabetes types other than type 2 diabetes. Paediatric guidelines usually recommend pancreatic autoantibody testing in all children with hyperglycaemia and testing for monogenic diabetes in those with negative antibodies.[103] However, in adults, pancreatic autoantibody testing is recommended in people with suspected type 1 diabetes, not all types of diabetes.[104] Although the evidence to suggest routine antibody testing should be recommended in all young adults with newly diagnosed diabetes is limited, it is important for practitioners to consider whether features in the history could point to an alternative diagnosis, such as type 1 diabetes or monogenic diabetes in adults with early-onset diabetes.

Who should be involved in care?

Models of care for early-onset type 2 diabetes vary widely. Adults with type 2 diabetes are typically managed in primary care in Europe and North America whereas children receive care from specialist services. However, current care models might not be meeting the needs of young adults with type 2 diabetes. For instance, in the UK, an audit revealed that adults aged 19–39 years received the lowest number of nationally agreed diabetes care processes, but this is most likely due to non-attendance.[8] In Taiwan, pay for performance incentivisation of health-care providers to deliver higher standards of care (for example more frequent appointments) improved cardiovascular outcomes and mortality over a 15-year follow-up period in people with type 2 diabetes aged 20–40 years versus those without pay for performance.[105]

A structured evaluation and data-driven prediction of future risk of complications could guide the setting frequency and type of ongoing care for people with early-onset type 2 diabetes. Patients at low risk of diabetes complications can be managed in primary care with less intensive support, whereas patients at high risk require more specialised follow-up.[106] In Hong Kong, a standardised protocol-based approach to risk assessment and individualised management resulted in 32–55% reductions in complications mortality compared with usual care across all ages.[107] Technological innovations (mobile applications, telemedicine, and continuous glucose monitors) are increasingly available to support management and improve outcomes,[108,109] including quality of life,[110] but their effectiveness in younger populations with type 2 diabetes requires further study.

Approximately 24–44% of people diagnosed with type 2 diabetes in childhood are not appropriately transitioned from paediatric to adult care providers.[111,112] This gap appears to be greater than that observed in type 1 diabetes and is exacerbated by inadequate support in adult practice settings, insufficient preparation, life transitions (eg, moving for higher education), loss of parental involvement, and inadequate communication between care providers.[113] Although whether people with early-onset type 2 diabetes are better managed in primary care or specialist settings is not clear, harmonising clinical care pathways will undoubtedly have value. Methods such as structured transition preparation programmes, workshops, and combination visits with paediatric and adult providers might be helpful but require further evaluation.[113] In addition, identification of particularly high-risk groups such as women of childbearing age is essential to ensure they receive adequate preconception care, contraception, and advice on deferring pregnancy if their disease is not optimally controlled or if they are taking potentially teratogenic medications is important. The involvement of multidisciplinary teams including psychologists to provide holistic care might be needed, but benefits of such interventions have not been evaluated in young people with type 2 diabetes, unlike those with type 1 diabetes, although evidence showcases there is a need.[75,114,115]

Should there be different treatment targets?

Given the high lifetime complication risk of type 2 diabetes, it is prudent to consider whether treating HbA_{1c}, cholesterol and blood pressure by targeting lower levels than current guidelines is warranted. However, such an approach has no evidence base, and it is worth noting that studies aiming to decrease HbA_{1c} to less than 6% (42 mmol/mol) in people with later-onset type 2 diabetes have been associated with higher incidence of hypoglycaemia because intensification of treatment was often achieved with use of sulphonylureas and insulin treatment.[116] These studies predate the arrival of GLP-1 receptor agonists and SGLT2i that have the potential to facilitate reaching tighter HbA_{1c} targets through weight reduction or weight-neutral strategies, without significant risk of hypoglycaemia. Further research is needed, and many people with early-onset type 2 diabetes do not reach current HbA_{1c} targets, let alone more intensive targets.[8]

Similarly, statin usage is routinely advised for primary prevention in adults with type 2 diabetes older than 40 years.[116,117] For young people with type 2 diabetes, there might have been a cumulative duration of 15–25 years of diabetes before reaching the 40 year age threshold at which statins are considered. Evidence is scarce as to the optimal time to initiate statins for primary prevention in younger adults, and risk calculators might not consider lifetime exposure, thus underestimating risk. The potential teratogenicity of statins and ACE inhibitors during pregnancy is another unresolved issue.[80]

Current guidelines for young people with type 2 diabetes[85,118,119] do not make specific recommendations around cardiovascular risk reduction and only advocate the use of SGLT-2 inhibitors for glycaemia and weight reduction. For adults with early-onset type 2 diabetes, standard guidelines apply;[117,120] however, modifications are

***Panel*: Research recommendations**

There remain a number of evidence gaps that can be addressed as priority areas in future research.

Investigating pathophysiology:

- Future studies with larger and more diverse samples, functional characterisation of candidate genes, and studies evaluating the interplay between lifestyle and genetic factors are needed to continue to understand the unique aspects of the genetics of early-onset type 2 diabetes in different ancestries.

Optimum management strategies for prevention of complications:

- In both young people and people in early adulthood, what medications (alone or in combination) achieve durable glycaemic control? Should treatment to tighter targets be recommended to mitigate future cardiovascular risk? Should disease-modifying therapies (weight-loss treatments) be deployed earlier in the treatment algorithms? Should combination therapies be deployed early, at diagnosis?

Remission approaches:

- What is the best approach for remission? Will protocols for very-low calorie diets result in durable remission? What are the mechanisms by which bariatric surgery achieves remission before weight loss in young adults? What are the long term consequences of bariatric surgery in young adults?

Prevention strategies:

- How preventable is the obesity epidemic in young people and young adults? Are lifestyle interventions successful, durable, and sufficient? Would pharmacotherapy help prevent progression from obesity to type 2 diabetes? What are the best preventive strategies in pregnant women with gestational diabetes or type 2 diabetes to prevent transgenerational incidence of dysglycaemia?

Pregnancy:

- How can women of childbearing age be supported before conception to reach better glycaemic control. Would continuous glucose monitoring improve glycaemic control during pregnancy and mitigate adverse neonatal outcomes?

suggested for individuals in whom weight reduction is prioritised or in whom lifetime cardiovascular risk is elevated.

Research gaps

Many research gaps exist from investigating pathophysiology to optimum treatment, prevention, and management during pregnancy (panel). A better understanding of disease heterogeneity is needed, so that glucose-lowering treatments can be targeted more effectively. Clinical trials that examine the best treatments to ensure durable glycaemic control and minimise risk of future cardiovascular disease are also required. In addition, a focus on prevention and remission strategies that work best in young people and determining how pregnancy outcomes can be improved (eg, through the use of technology), is also needed.

Prevention and global considerations

Four of five people with type 2 diabetes live in low-income and middle-income countries.[34] When considering how best to prevent and treat early-onset type 2 diabetes, a global approach is needed. The major modifiable risk factors are being overweight or living with obesity; therefore, population-level interventions that reverse or reduce obesity are likely to have the greatest success in prevention. The rise in obesity over the past decades is most noticeable in adolescents and young adults, and although the prevalence of type 2 diabetes is plateauing in many high-income countries, the age-standardised prevalence is increasing in Asia.[121]

The challenge in early adulthood is that although obesity prevalence is high, the proportion of people living with obesity who have type 2 diabetes is comparatively small. The evidence base to support diabetes screening in adolescents or young adults with obesity is poor and further studies are needed.[122] Some guidelines recommend screening youth with obesity with other morbitidies (eg, hypertension) for type 2 diabetes.[85] However, there is also evidence that trajectories from normoglycaemia to type 2 diabetes might be different in young people, making the window of opportunity to screen and prevent progression narrower than at later ages[46] and the cost-effectiveness unknown. One study in UK Bangladeshi and Pakistani populations showed that a polygenic score offered better prediction for the development of incident type 2 diabetes in adults younger than 40 years and women with a history of gestational diabetes, over and above clinical risk prediction; however, case numbers were small.[123] Further studies are needed to understand whether application of such scores could meaningfully reduce progression to type 2 diabetes, over and above standard approaches.

Lifestyle interventions have been undertaken in relatively small paediatric studies in people younger than 18 years with obesity;[124] a metanalysis of 24 studies found very-low calorie diets to be effective at reducing weight in the short term but no long-term follow-up has been undertaken.[125,126]

In the English national diabetes prevention programmes, 5% of referrals (77 797 referrals) were received for people younger than 40 years and mean weight reduction was 2·4 kg in those who completed the programme, but this weight reduction was the lowest across all age categories.[127] Behavioural interventions in young people showed better uptake in digital format.[128]

Search strategy and selection criteria

We searched PubMed and medRxiv from inception up until March 31, 2023 for publications in English, with the search terms including "type 2 diabetes" and "youth" or "young-onset" or "early-onset" or "paediatric" or "early-adulthood". We excluded articles related to subtypes other that type 2 diabetes and those that were not written in English.

An especially high-risk group for progression to early-onset type 2 diabetes is women who have had a previous pregnancy complicated by gestational diabetes.[129] A study done in Israel showed that the adjusted hazard ratio of progression to type 2 diabetes was 71·9 per 10 000 person-years (95% CI 66·0–78·3) in women with gestational diabetes.[130] There is an urgent need to improve prevention in women with a history of gestational diabetes given this substantial risk and because lifestyle interventions have been shown to be effective[131] but pragmatically difficult to implement.

Conclusion

The prevalence of early-onset type 2 diabetes in increasing across the world and carries substantial risks of morbidity, heralding future risk of multimorbidity. The complication trajectory for individuals with early-onset type 2 diabetes is likely to affect the productivity of this population, especially in middle-income and high-income countries, where incidence is highest. Although absolute numbers remain a small proportion of all cases of type 2 diabetes, it is perhaps of little surprise that the numbers of people with early-onset type 2 diabetes have increased, given its strong associations with sociocultural determinants of health, ethnic preponderance, rising obesity, and social deprivation. The differential risk factors driving the rise of the disease will require tailored approaches to treatment and prevention. There is an urgent need for major societal change to reduce obesity and for government-level public-health interventions.

The evidence base to respond with prevention, remission, and optimal treatment approaches is lagging behind the steep rise in cases; children, adolescents, and young adults are under-represented in all major studies of type 2 diabetes, as are participants from ethnic minority populations. These major hurdles must be overcome to derive a solid evidence base for the treatment of affected individuals. Although safe and highly efficacious treatments for type 2 diabetes exist, how these treatments should be deployed in younger age groups is unknown, and arguably current approaches are less effective given the adverse outcomes reported. A unified global approach with prioritisation of key research gaps, especially in early adulthood, is urgently needed if this vulnerable group is to be supported correctly.

Contributors

All authors contributed to the development of the review topics, wrote specific sections, edited drafts, and approved the final version of the manuscript. SM led the development and planning of the Review, edited all sections, and led the writing of the introduction, models of care and treatment targets, and conclusion. DJM and AL led the writing of the epidemiology section. SS, MJN, and JCF led the writing of the pathophysiology section. AL and CK led the writing of the complications section. CK, AG, SS, and KK led the writing of the management section.

Declaration of interests

SM is in receipt of an investigator-initiated grant from DexCom, has received speaker fees (donated to institution) from Sanofi for a scientific talk over which she had full control of the content, and serves as Trustee to the Diabetes Research and Wellness Foundation charity, UK. CK reports receiving personal fees from Abbott, Sanofi, and AstraZeneca. AL reports receiving funding from research contracts and grants from Amgen, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Lee Pharmaceutical, MSD, Novo Nordisk, Roche, Sanofi, Sugardown, and Takeda. JCF has received consulting honorarium from AstraZeneca and speaker fees from Novo Nordisk for a scientific talk over which he had full control of content. The spouse of JCF has received a consulting honorarium from Novartis. KK has acted as a consultant, speaker, or received grants for investigator-initiated studies for Astra Zeneca, Bayer, Novartis, Novo Nordisk, Sanofi-Aventis, Lilly, and Merck Sharp and Dohme, Boehringer Ingelheim, Oramed Pharmaceuticals, Roche, and Applied Therapeutics. All other authors declare no competing interests.

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