Early-Onset Type 2 Diabetes 2

Understanding the drivers and consequences of early-onset type 2 diabetes

Lee-Ling Lim, Sophie Jones, Justin Cirhuza Cikomola, Marie-France Hivert, Shivani Misra

Early-onset type 2 diabetes (defined as type 2 diabetes diagnosed in people aged <40 years) is increasingly prevalent with substantial health and socioeconomic implications. Unlike late-onset type 2 diabetes, early-onset type 2 diabetes is a high-risk and aggressive phenotype, with accelerated pancreatic β-cell decline and greater insulin resistance due to the rising rate of obesity. People with early-onset type 2 diabetes have higher rates of macrovascular and microvascular complications with increased health-care use and premature mortality (due to cardiovascular and non-cardiovascular complications) than do people with late-onset type 2 diabetes. Emerging evidence also suggests that people with early-onset type 2 diabetes face an increased risk of complications in reproductive health (eg, during periconception and postpartum periods), metabolic-associated steatotic liver disease, mental health (eg, diabetes distress, depression, anxiety, and psychotic disorders), and some cancers, creating additional challenges in managing multiple long-term conditions. In this Series paper, we highlight the consequences of early-onset type 2 diabetes and the key driver for these risks—long duration of exposure to hyperglycaemia, with its effects amplified by younger age at type 2 diabetes diagnosis and interactions with other cardiometabolic risk factors. Recognising these adverse risks associated with early-onset type 2 diabetes is crucial for guiding the development and implementation of a more focused and integrated life-course approach to mitigate its long-term effect on individuals, communities, and health-care systems globally. However, substantial research gaps remain that must be addressed, particularly in diverse populations.

Introduction

Early-onset type 2 diabetes (type 2 diabetes diagnosed in people aged <40 years) is an increasing global health concern.[1,2] Its rising incidence parallels global trends in obesity prevalence,[3] urbanisation, and socioeconomic changes that, having predominantly affected older adults in the past, now increasingly affect children and younger adults. Early-onset type 2 diabetes emerges during crucial life stages, with substantial effects on education, employment, reproductive health, and long-term wellbeing. The observed aggressive clinical trajectory,[4,5] rapid progression to complications,[6–8] and shorter life expectancy,[9] pose a substantial burden on health-care systems.

In the first paper in this Series,[10] we explored the epidemiology and risk factors contributing to the rising incidence of early-onset type 2 diabetes. It often emerges as a direct consequence of early-onset obesity;[11] however, in the presence of additional risk factors,[12,13] the disease can manifest even without marked obesity.[1,14] In particular, Asian ethnicities develop early-onset type 2 diabetes at lower bodyweight than White people, reflecting differences in adiposity, diet, physical activity, or modifiers of disease risk including β-cell function.[13,14]

The burden of complications from early-onset type 2 diabetes diverges substantially from that of late-onset disease. Aside from the reduction in life expectancy (the life expectancy of people with early-onset diabetes, diagnosed aged ~30 years, is 15 years less than that of people without diabetes), a key concern is the early emergence of complications.[6] The risk of developing multiple comorbidities is higher in early-onset type 2 diabetes compared with late-onset type 2 diabetes, and these conditions might interact to accelerate disease progression.[1,11] Alongside typical microvascular and macrovascular complications, mental health conditions are more common in early-onset type 2 diabetes, further impacting quality of life.[8] Reproductive health is another major concern, with worse perinatal outcomes in type 2

Search strategy and selection criteria

We searched PubMed, EMBASE, and Web of Science, for publications in English from database inception to March 22, 2025. We used the search terms: "early-onset", "young-onset", or "youth-onset" in combination with "diabetes mellitus" or "type 2 diabetes", alone and in combination with the terms "complications", "mortality", "death", "pregnancy", "reproduction", "steatotic liver disease", "fatty liver disease", "non-alcoholic liver disease", "non-alcoholic steatohepatitis", "cancer", "malignancy", or "mental health". We selected randomised controlled trials and observational (eg, cross-sectional, retrospective, or prospective cohort) studies published between Jan 1, 2020, and March 22, 2025, but did not exclude commonly referenced and landmark publications published earlier that had a substantial effect on practice. We also searched the reference lists of articles identified and selected those we judged to be relevant. Review articles are cited to provide readers with more details and references that are outside of the scope of this Series paper.

Lancet 2025; 405: 2327–40

Published Online
June 23, 2025
https://doi.org/10.1016/S0140-6736(25)01012-8

This is the second in a Series of three papers about early-onset type 2 diabetes. All papers in the Series are available at thelancet.com/series-do/early-onset-diabetes

Department of Medicine, Faculty of Medicine, Universiti Malaya, Kuala Lumpur, Malaysia (Prof L-L Lim PhD); **Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong Special Administrative Region, China** (Prof L-L Lim PhD); **Asia Diabetes Foundation, Hong Kong Special Administrative Region, China** (Prof L-L Lim PhD); **Baker Heart and Diabetes Institute, Melbourne, VIC, Australia** (Prof L-L Lim PhD); **Department of Metabolism, Digestion and Reproduction, Imperial College London, London, UK** (S Jones BMBCh, S Misra PhD); **Department of Internal Medicine, Faculty of Medicine, Catholic University of Bukavu, Bukavu, Democratic Republic of the Congo** (Prof J C Cikomola PhD); **Department of Population Medicine, Division of Chronic Disease Research Across the Lifecourse, Harvard Pilgrim Health Care Institute, Harvard Medical School, Harvard University, Boston, MA, USA** (Prof M-F Hivert MD); **Diabetes Unit, Massachusetts General Hospital, Boston, MA, USA** (Prof M-F Hivert MD); **Department of Diabetes and Endocrinology, St Mary's Hospital, Imperial College Healthcare NHS Trust, London, UK** (S Misra PhD)

Correspondence to:
Prof Lee-Ling Lim, Department of Medicine, Faculty of Medicine, Universiti Malaya, Kuala Lumpur 50603, Malaysia
leeling.lim@ummc.edu.my

diabetes pregnancies than in type 1 diabetes pregnancies.[15]

The factors underlying the increased complication burden and reduced life expectancy from early-onset type 2 diabetes remain unclear. Although longer duration—and, therefore, greater cumulative glycaemic exposure—seems a logical explanation, data suggest a more complex picture. A more aggressive disease phenotype, early clustering of cardiometabolic risk factors, low health-care engagement in young adults, and inadequately designed models of care, could all be contributing factors. These factors remain underexplored but are crucial to improving outcomes in this vulnerable population.

In this Series paper, we review the epidemiology of complications from early-onset type 2 diabetes, summarising the evidence on established microvascular and macrovascular risks, reproductive health impacts, the burden of multiple long-term conditions, and emerging concerns that can compound morbidity and premature mortality. We also examine key drivers of complication risk, highlight windows for intervention, identify major research gaps, and draw on both paediatric and adult data to provide a comprehensive overview.

Established complications

Evidence for the association between early-onset type 2 diabetes and a higher risk of complications, first emerged from cross-sectional studies comparing early-onset type 2 diabetes to age-matched type 1 diabetes.[16] Although in the last two decades general trends suggest reductions in the incidence of cardiovascular events, kidney failure, lower-extremity amputations, and overall mortality in late-onset type 2 diabetes, these improvements have largely bypassed younger adults.[17–21] Surveillance data from the USA suggested that, between 1995 and 2015, complication rates worsened among individuals aged 18–44 years.[18] The scale of this issue is illustrated by the TODAY study, a North American prospective study of youth diagnosed with type 2 diabetes (diagnosed aged <20 years); by a mean age of 26 years, 80% of participants had developed at least one microvascular complication.[22]

Herein, we examine why early-onset type 2 diabetes is often considered more severe than late-onset type 2 diabetes and type 1 diabetes (figure 1), focusing on evidence for higher incidence of complications and faster progression to their development.

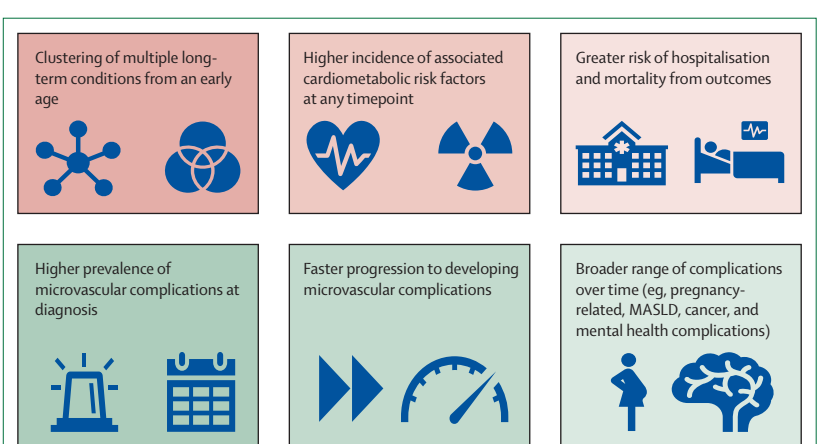

Figure 1: **Features of early-onset type 2 diabetes complications that highlight disease severity, compared with type 1 diabetes and late-onset type 2 diabetes**
MASLD=metabolic-associated steatotic liver disease.

Macrovascular and microvascular complications

Early-onset type 2 diabetes versus type 1 diabetes

Evidence has shown that people with early-onset type 2 diabetes have higher incidence and faster onset of complications than age-matched people with type 1 diabetes of the same disease duration. In a pooled analysis of the SEARCH and TODAY studies, two prospective adolescent studies in North America, complication burden was compared between 644 youth (mean age at diabetes diagnosis 13·2 [SD 2·1] years in the TODAY study and 14·3 [SD 2·7] in the SEARCH study) with type 2 diabetes and 546 with duration-matched type 1 diabetes. After 10–15 years of follow-up, youth with type 2 diabetes had higher rates of microvascular events. For example, the risk of any microvascular complication was 5·65 events per 1000 person-years in youth with type 2 diabetes versus 2·19 in those with type 1 diabetes.[23] Microvascular events also occurred earlier in youth with type 2 diabetes (starting 8 years after diabetes diagnosis) than in youth with type 1 diabetes (starting around 10 years after diagnosis).[23] Table 1 shows individual complications. In the same study, the incidence of any kidney event in youth with type 2 diabetes was 0·62, but notably, neither chronic kidney disease nor end-stage kidney disease events developed in youth with type 1 diabetes within 10–13 years of follow-up.[23] Given the few chronic kidney disease events and insufficient statistical power, larger cohort studies with a longer follow-up duration are needed.

Data from other countries reinforce this pattern, albeit with higher incidence rates and variations in outcome ascertainment methods. In India, a retrospective study compared incidence rates of complications in 90 clinic attendees with early-onset type 2 diabetes (mean age at diagnosis 21·6 years; SD 3·6) with those in 108 people with type 1 diabetes (mean age at diagnosis 17·1 years; SD 4·2).[24] Although the two groups were not studied from baseline, after a mean duration of approximately 10 years, the incidence rates of ischaemic heart disease, retinopathy, and neuropathy were higher in people with early-onset type 2 diabetes than in people with type 1 diabetes; however, incidence rates of chronic kidney disease were lower in people with early-onset type 2 diabetes (table 1).[24] In Hong Kong, a prospective registry study compared 209 people with type 1 diabetes (mean age at diagnosis 19·5 years; SD 10·6) with 1478 young

adults with type 2 diabetes and overweight (mean age at diabetes diagnosis 33·0 years; SD 5·9).[25] After a median follow-up of 9·3 years, those with early-onset type 2 diabetes reported higher incidence rates for cardiovascular disease and end-stage kidney disease than for those reported in people with type 1 diabetes (table 1).[25]

	Sample size and study design	Comparator group	Method of ascertainment of complications	Risk of microvascular complications	Risk of macrovascular complications	Risk of hospitalisation or mortality
Early-onset type 2 diabetes *vs* type 1 diabetes						
TODAY study and SEARCH study pooled analysis[23]	644 youth with type 2 diabetes (mean age at diagnosis 13·2 [SD 2·1] years for TODAY and 14·3 [2·7] years for SEARCH) and 546 youth with type 1 diabetes; prospective study with follow-up for 10–15 years	Youth with duration-matched type 1 diabetes	Self-reported complications with event adjudications with medical records	Event rates (events per 1000 person-years) for type 2 diabetes *vs* type 1 diabetes: 5·65 *vs* 2·19 for any microvascular event; 4·0 *vs* 1·1 for any ophthalmological event; 2·12 *vs* 1·11 for any neuropathy event; 0·62 *vs* 0 for any kidney event	Event rates (events per 1000 person-years) for type 2 diabetes *vs* type 1 diabetes:3·25 *vs* 0·78 for any macrovascular event; 2·12 *vs* 0·31 for any cardiac event; 0·50 *vs* 0·16 for any cerebrovascular event; 0·99 *vs* 0·31 for any vascular event or procedure	Not reported
Young diab study[24]	90 adults with type 2 diabetes and 108 adults with type 1 diabetes, all diagnosed aged 10–25 years; median follow-up of 5 years	Adults with type 1 diabetes	Clinical and laboratory assessment	Event rates (events per 1000 person-years) for type 2 diabetes *vs* type 1 diabetes: 78·0 *vs* 77·4 for retinopathy;13·9 *vs* 7·8 for neuropathy; 58·8 *vs* 62·0 for nephropathy	Event rates (events per 1000 person-years) for type 2 diabetes *vs* type 1 diabetes: 5·4 *vs* 1·2 for IHD; 2·0 *vs* 2·7 for PVD	Not reported
HKDR[25]	1478 adults with type 2 diabetes (overweight; mean age at diagnosis 33·0 [SD 5·9] years), 636 adults with type 2 diabetes (normal weight; mean age at diagnosis 32·8 [6·2] years), and 209 adults with type 1 diabetes (mean age at diagnosis 19·6 [10·6] years); prospective study with 9 years follow-up	Adults with type 1 diabetes	ICD-9 coded hospital discharge diagnoses	Event rates (per 1000 person-years) for type 2 diabetes (overweight) *vs* type 2 diabetes (normal weight) *vs* type 1 diabetes: 8·4 *vs* 6·4 *vs* 2·2 for ESKD	Event rates (per 1000 person-years) for type 2 diabetes (overweight) *vs* type 2 diabetes (normal weight) *vs* type 1 diabetes: 9·6 *vs* 5·1 *vs* 0·6 for CVD	Not reported
Early-onset type 2 diabetes *vs* late-onset type 2 diabetes						
Indigenous Americans of the Southwest[26]	96 adults (median age at baseline 25·0 [IQR 25·0–48·7]) with early-onset type 2 diabetes and 1760 with late-onset type 2 diabetes; prospective study	Adults with age-matched late-onset type 2 diabetes	ICD-9 coded hospital discharge diagnoses	Event rates (events per 1000 person-years) for early-onset *vs* late-onset type 2 diabetes: 25·0 *vs* 5·4 for ESKD	Not reported	Event rates (events per 1000 person-years) for early-onset *vs* late-onset type 2 diabetes: 18·6 (3·0–34·2) *vs* 12·7 (10·5–14.9) for all-cause mortality; 5·3 (0·0–15.6) *vs* 1·1 (0·7–1·5) for cardiovascular mortality; 3·1 (0·4–6·2) *vs* 1·4 (0·9–1·8) for diabetic nephropathy; and 6·9 (0–17·5) *vs* 0·9 (0·4–1·3) for infection
Kaiser Permanente Northwest[27]	1600 people with newly diagnosed, early-onset type 2 diabetes (diagnosed aged <45 years) and 6244 people with late-onset type 2 diabetes (diagnosed aged ≥45 years); prospective study with a mean follow-up of 3·9 years	Diabetes-free, age-matched, and sex-matched controls	ICD-9 coded hospital discharge diagnoses, laboratory and pharmacy records	Not reported	HR for early-onset *vs* late-onset type 2 diabetes: 7·9 (4·8–13·0) and 3·8 (3·4–4·2) for any macrovascular complication; 14·0 (6·2–31·4) and 3·7 (3·2–4·2) for MI; 30·1 (6·0–152·1) and 3·1 (2·7–3·7) for stroke; 3·6 (1·7–7·9) and 4·2 (3·5–5·1) for PVD	Not reported

(Table 1 continues on next page)

	Sample size and study design	Comparator group	Method of ascertainment of complications	Risk of microvascular complications	Risk of macrovascular complications	Risk of hospitalisation or mortality
(Continued from previous page)						
Swedish National Diabetes Register[28]	7253 adults with early-onset type 2 diabetes (diagnosed aged <40 years) and 115 412 with late-onset type 2 diabetes (diagnosed aged ≥40 years) without previous CVD; prospective study with a median follow-up of 5·6 years	Diabetes-free, age-matched, and sex-matched controls	ICD-9 and ICD-10 coded hospital discharge diagnoses and linkage to the death registry	Not reported	HR for those diagnosed aged <40 years *vs* those diagnosed aged 61–70 years: 3·52 (3·10–3·99) and 1·42 (1·37–1·47) for CVD; 4·33 (3·82–4·91) and 1·70 (1·65–1·76) for IHD; 3·41 (2·88–4·04) and 1·46 (1·40–1·53) for MI; 3·58 (2·97–4·32) and 1·38 (1·32–1·44) for stroke; 4·77 (3·86–5·89) and 1·71 (1·63–1·79) for heart failure	HR for those diagnosed aged <40 years *vs* those diagnosed aged 61–70 years: 2·05 (1·81–2·33) and 1·13 (1·09–1·16) for all-cause mortality; 2·72 (2·13–3·48) and 1·00 (0·95–1·06) for cardiovascular mortality; 1·95 (1·68–2·25) and 1·18 (1·14–1·22) for non-cardiovascular mortality
HKDSD and HKDR[8]	HKDSD: 21 032 people with early-onset type 2 diabetes (diagnosed aged 20–39 years) and 401 876 people with late-onset type 2 diabetes (diagnosed aged 40–75 years). HKDR: 3566 people with early-onset type 2 diabetes (diagnosed aged 20–39 years) and 17 320 with late-onset type 2 diabetes (diagnosed aged 40–75 years). Prospective study (HKDSD median follow-up 6·1 years and HKDR median follow-up 10·6 years)	Adults with late-onset type 2 diabetes	ICD-9 coded hospital discharge diagnoses and linked to the death registry	Not reported	Not reported	Association of age of type 2 diabetes onset (34 years *vs* 54 years) on hospitalisation rate at age 60 years (RR): 6·7 (4·2–10·6) for renal complications; 2·1 (1·8–2·5) for cardiovascular complications; 1·7 (1·4–2·1) for infection
Australian National Diabetes Services Scheme[29]	113 090 people with early-onset type 2 diabetes (diagnosed aged 10–39 years) and 999 292 people with late-onset type 2 diabetes (diagnosed aged ≥40 years); prospective study with a median follow-up of about 7 years	Adults with late-onset type 2 diabetes (10-year age bands), diabetes duration-matched	Linked to the dialysis and transplant registry, and death registry	Event rates (events per 1000 person-years) for diagnosis aged 30–39 years *vs* diagnosis aged 50–59 years, for diabetes duration 20–24 years; 4·83 (4·07–5·74) *vs* 2·48 (2·16–2·84) for ESKD	Not reported	Not reported
HKDSD and HKDR[30]	HKDSD: 17 478 people with early-onset type 2 diabetes (diagnosed aged 20–39 years) and 419 266 people with late-onset type 2 diabetes (diagnosed aged ≥40 years). HKDR: 2566 people with early-onset type 2 diabetes (diagnosed aged 20–39 years) and 14 413 with late-onset type 2 diabetes (diagnosed aged ≥40 years). Prospective study with a median follow-up of 5–6 years	Adults with late-onset type 2 diabetes aged ≥70 years	ICD-9 coded hospital discharge diagnoses and linked to the death registry	HR for CKD: 1·37 (1·13–1·65) in adults with diabetes diagnosed aged 20–29 years *vs* 1·15 (1·08–1·22) in adults with diabetes diagnosed aged 60–69 years	Not reported	Not reported

(Table 1 continues on next page)

	Sample size and study design	Comparator group	Method of ascertainment of complications	Risk of microvascular complications	Risk of macrovascular complications	Risk of hospitalisation or mortality
(Continued from previous page)						
ICES[31]	73 054 people with early-onset type 2 diabetes (diagnosed aged 20–39 years) and 669 999 people with late-onset type 2 diabetes (diagnosed aged ≥40 years); retrospective population-based study with a median follow-up of 8·9 years	Diabetes-free matched controls	Diagnostic codes	Not reported	Not reported	HR for heart failure hospitalisation: 6·49 (5·38–7·84) in adults with diabetes diagnosed aged 20–39 years and 1·27 (1·24–1·29) in adults with diabetes diagnosed aged >70 years
UK Biobank[32]	799 adults with early-onset type 2 diabetes (diagnosed aged 15–39 years) and 18 528 with late-onset type 2 diabetes (diagnosed aged ≥40 years); prospective study with a median follow-up of 13·9 years	Adults with late-onset type 2 diabetes who were diagnosed aged ≥40 years	ICD-9 and ICD-10 coded hospital discharge diagnoses and self-reported data	Proportion of people with incident complications at follow-up (early-onset *vs* late-onset): 22·4% *vs* 29·5% for CKD; 1·5% *vs* 1·1% for ESKD	Proportion of people with incident complications at follow-up (early-onset *vs* late-onset): 12·5% *vs* 13·5% for MI; 3·9% *vs* 5·2% for stroke; 9·6% *vs* 12·1% for heart failure	Not reported
UKPDS 30-year follow-up[33]	429 adults with early-onset type 2 diabetes (diagnosed aged <40 years) and 4121 with late-onset type 2 diabetes (diagnosed aged ≥40 years); prospective study	Adults with late-onset type 2 diabetes	Diagnostic codes and linked to the death registry	Event rates (events per 1000 person-years) for early-onset *vs* late-onset type 2 diabetes: 18·0 (13·8–22·1) *vs* 11·7 (10·7–12·7) for microvascular disease	Event rates (events per 1000 person-years) for early-onset *vs* late-onset type 2 diabetes: 12·0 (8·81–15·2) *vs* 22·7 (21·4–24·1) for MACE; 10·6 (7·59–13·5) *vs* 17·0 (15·8–18·1) for MI; 1·27 (0·25–2·30) *vs* 6·51 (5·80–7·21) for stroke; 1·97 (0·67–3·27) *vs* 2·04 (1·66–2·43) for PVD; 38·0 (31·9–44·1) *vs* 57·8 (55·5–60·1) for any diabetes-related endpoint	Event rates (events per 1000 person-years) for early-onset *vs* late-onset type 2 diabetes: 12·0 (8·8–15·1) *vs* 27·3 (25·9–28·7) for all-cause death; 6·57 (4·20–8·94) *vs* 15·0 (13·9–16·0) for diabetes-related death

Event rates and HR or RR with 95% CI are quoted for comparing early-onset type 2 diabetes with either type 2 diabetes or late-onset type 2 diabetes, as stated. CHD=coronary heart disease. CVD=cardiovascular disease. ESKD=end-stage kidney disease. HKDR=Hong Kong Diabetes Registry. HKDSD=Hong Kong Diabetes Surveillance Database. HR=hazard ratio. ICES=Institute for Clinical Evaluative Sciences. IHD=ischaemic heart disease. MACE=major adverse cardiovascular events. MI=myocardial infarction. PVD=peripheral vascular disease. RR=rate ratio. UKPDS=UK Prospective Diabetes Study.

Table 1: **Summary of key studies comparing complication burden in early-onset type 2 diabetes**

In all three studies outlined, the prevalence of baseline complications was higher in early-onset type 2 diabetes than in type 1 diabetes. For example, in the prospective Hong Kong registry study, microalbuminuria was present at baseline in 34 (16·3%) people with type 1 diabetes and in 359 (24·3%) people with early-onset type 2 diabetes (p<0·001).[25]

The incidence rates of both macrovascular and microvascular complications reported in Asian populations with early-onset type 2 diabetes are much higher than in North Americans. Aside from ethnic variations in susceptibility to the development of complications,[34] these findings could reflect differences in study design. For example, the Indian and Hong Kong cohorts were older compared with the North American cohort at baseline and could have had a more prolonged period with undiagnosed diabetes. Additionally, there could have been under-reporting of events in the prospective SEARCH and TODAY studies (North American) that relied on participant recall and medical record adjudication, compared with clinical or laboratory assessment and diagnostic coding linkage in the two Asian studies.[6,22]

These comparisons with duration-matched type 1 diabetes suggest that diabetes duration alone does not explain the higher incidence and earlier onset of complications. Contributing factors are discussed later in this Series paper.[6,22,24]

Early-onset type 2 diabetes versus late-onset type 2 diabetes

The early onset of some complications, and increased lifetime risk of others, in early-onset type 2 diabetes is also evident when compared with late-onset type 2 diabetes. This association persists even when accounting for duration and is more than the expected age-related increase for some outcomes.

In the TODAY study (mean age at baseline of 14 years), the baseline prevalence of any microvascular complication was 9·0%, progressing rapidly to a cumulative incidence of 50·0% by 9 years of follow-up

and 80·1% by 15 years of follow-up.[22] For kidney disease (ie, moderately increased albuminuria), the baseline prevalence was 8·0%, and the cumulative incidence at 15 years of follow up was 54·8%.[22] By contrast, in the UK Prospective Diabetes Study (UKPDS) of type 2 diabetes (mean age at diagnosis 50·2 years; SD 8·0), the prevalence of moderately increased albuminuria 10 years after diagnosis was 25%.[35] The same cumulative incidence was reached 10 years earlier in the TODAY study (15 years after diagnosis in the TODAY study *vs* 25 years in UKPDS), reflecting annual rates of 3·7% in early-onset versus 2·2% in late-onset type 2 diabetes.[35] A similar comparison between UKPDS and TODAY for retinopathy showed 264 (22%) of 1216 UKPDS participants developed retinopathy after 6 years of follow-up versus 202 (50%) of 404 by 7 years of follow-up in the TODAY study.[22,36]

A prospective study of Indigenous Americans of the Southwest revealed an additional important insight that, even within the early-onset age group, people diagnosed at younger ages had worse outcomes.[37] The sex-adjusted incidence rate of end-stage kidney disease in Indigenous Americans who were diagnosed when they were younger than 20 years was 8·4 times (95% CI 1·5–46·0) higher than those diagnosed aged 25–34 years, 5 times (2·2–11·3) higher than those diagnosed aged 35–44 years, and 4 times (1·2–13·6) higher than those with late-onset diabetes diagnosed aged 45–54 years.[26] Studies of end-stage kidney disease and chronic kidney disease in Australia and Hong Kong have also shown higher rates in people with early-onset type 2 diabetes than in people with late-onset disease, independent of diabetes duration (table 1).[29,30] A Hong Kong study importantly highlighted a graded response across age strata, with an attenuation of risk as age at diabetes diagnosis increased, which was independent of cardiometabolic risk factors, previous comorbidities, and medication use.[30]

A similar graded response for cardiovascular outcomes was observed in an analysis of the Swedish National Diabetes Register, which grouped adults with type 2 diabetes into bands for age at diagnosis, incorporating those younger than 40 years as a single group.[28] Compared with people without type 2 diabetes, the hazard ratios (HRs) for complications in those younger than 40 years at diagnosis were higher over a median follow-up of 5·6 years: 4·33 (95% CI 3·82–4·91) for ischaemic heart disease, 3·58 (2·97–4·32) for stroke, and 4·77 (3·86–5·89) for heart failure (adjusted for age, sex, and duration), with an incremental decline in HR for every decade increase in age at diagnosis.[28] Similar findings were reported from the USA Kaiser Permanente Northwest cohort (table 1).[27]

Is it the age at diabetes diagnosis or duration of diabetes that affects risk?

Disentangling the relative effects of age at diagnosis from duration is challenging as they are co-linear, but some studies have tried to address this issue. In 2024, the UKPDS study published 30-year outcomes according to age at diagnosis, with the longest follow-up time—median 17·5 years—of any of the studies discussed previously.[33] The incidence of microvascular complications was higher in early-onset type 2 diabetes (18·0 events per 1000 person-years; 95% CI 13·8–22·1) compared with those with late-onset type 2 diabetes (11·7 [10·7–12·7]), but incidence of macrovascular complications (ie, myocardial infarction, stroke, and peripheral vascular disease) was lower in early-onset type 2 diabetes (table 1).[33] However, when restricted to 5-year incidence, at any given age, microvascular complications and myocardial infarction were higher in the early-onset type 2 diabetes age group.[33] This shows that age at type 2 diabetes diagnosis contributes substantially to the risk of complications, even after matching for duration of diabetes in the analysis.

In contrast to the aforementioned studies that show that age at diagnosis (independent of diabetes duration) is associated with higher risk of myocardial infarction, heart failure, stroke, and chronic kidney disease, a 2024 analysis of UK Biobank participants did not report an independent effect of age at diagnosis. Participants with early-onset type 2 diabetes in UK Biobank had a median age of 36·1 years at diagnosis (IQR 31·5–38·5); this cohort might have under-represented the youngest age groups within the early-onset bracket, who have the highest risk of the aforementioned complications.[32] However, more studies are needed, with longer follow-up time. A meta-analysis of 26 observational cohorts involving 1·3 million people from North America, Europe, and Asia Pacific showcased a continuum of risk; every 1-year decrease in age at diabetes diagnosis had an odds ratio (OR) of 1·05 (95% CI 1·04–1·06) for microvascular complications and 1·03 (1·02–1·04) for macrovascular complications, independent of current age and duration.[7]

Overall, macrovascular complications appear to increase with type 2 diabetes duration. Longer-term studies that did not adjust for duration reported higher risk with late-onset type 2 diabetes, reflecting the age-related increase in cardiovascular disease. However, when adjusted for age or restricted to shorter follow-up periods, early-onset type 2 diabetes showed an excess of macrovascular risk, compared with late-onset disease. By contrast, microvascular complications consistently showed higher risk with younger age at diagnosis.[7] The underlying contributors to this higher burden of complications are manifold and discussed later in this Series paper.[26,38]

Hospitalisations

Rates of hospital admission for kidney disease, cardiovascular disease, heart failure, infections, mental

health conditions, and all-cause admissions are consistently higher among people with early-onset type 2 diabetes (table 1).[8,31] These findings underscore the broader clinical burden associated with early-onset disease, extending beyond the predominantly cardiovascular-related admissions typically observed in late-onset type 2 diabetes. The occurrence of such hospitalisations in younger, working-age populations is particularly concerning, given the potential implications for long-term morbidity and socioeconomic impact.

Mortality

Although there is evidence for a higher risk of complications in early-onset type 2 diabetes than in late-onset disease, whether it translates into an increased mortality risk must be assessed. In Indigenous Americans of the Southwest, people with type 2 diabetes diagnosed when they were younger than 20 years had a higher rate of all-cause mortality (18·6 per 1000 person-years [95% CI 3·0–34·2]) and cardiovascular mortality (5·3; 0·0–15·6]), than for those diagnosed at ages 20–55 years (all-cause mortality rate of 12·7 [10·5–14·9] and cardiovascular mortality rate of 1·1 [0·7–1·5]).[26] The observation of this inverse association between age at diagnosis and mortality risk has been reproduced in numerous studies.[28,33,39]

In studies using the Swedish National Diabetes Register, compared with matched diabetes-free controls, people with early-onset type 2 diabetes had an HR of 2·05 (95% CI 1·81–2·33) for all-cause mortality, 2·72 (2·13–3·48) for cardiovascular mortality, and 1·95 (1·68–2·25) for non-cardiovascular mortality.[28] The Emerging Risk Factors Collaboration showed a linear dose–response relationship between earlier age at type 2 diabetes diagnosis and excess all-cause mortality. Each decade earlier at diagnosis was associated with a 3–4-year reduction in life expectancy. For example, individuals diagnosed at age 30 years died, on average, 14 years earlier than peers without diabetes, whereas those diagnosed aged 40 years died 10 years earlier and those diagnosed aged 50 years died 6 years earlier.[9]

The substantial reduction in life expectancy associated with early-onset type 2 diabetes is particularly concerning for low-income and middle-income countries or regions, where incidence is expected to rise (as discussed in the first paper in this Series).[10] In these settings, the working-age population is typically younger than in high-income countries, and diagnoses during economically productive years are likely to amplify the socioeconomic burden. In high-income countries or regions, the loss of life-years linked to early-onset type 2 diabetes is similar to that observed for cancer diagnosed before age 40 years; one study estimated reductions in life expectancy of approximately 11 years for cancer diagnosed in people younger than 40 years.[40]

Mechanisms underlying high complication and mortality rates in early-onset type 2 diabetes

Multiple reasons are likely to underpin the observed excess risk of diabetes-associated complications and mortality in early-onset type 2 diabetes (figure 2).

Effects of glycaemic burden and glycaemic escape

The observed faster decline in β-cell function in people with early-onset type 2 diabetes, a key feature of the pathophysiology of this disease,[41,42] results in a higher glycaemic burden (ie, an increase in glycated haemoglobin [HbA_{1c}] over time) and less glycaemic durability (ie, a shorter timeframe for treatment failure and escalation), compared with those with late-onset type 2 diabetes.

In the TODAY study, about 46% of the entire cohort showed deterioration in glycaemic control over time, with 59% of adolescents having HbA_{1c} of 8% or greater after 15 years of follow-up.[22] This progressive glycaemic trajectory has also been reported in other populations. An observational study of the Swedish National Diabetes Register showed a 0·5% HbA_{1c} difference over 8 years between people with type 2 diabetes diagnosed aged 18–44 years (mean HbA_{1c} at baseline 6·9%; SD 1·3%) and those diagnosed when they were older than 75 years (mean HbA_{1c} at baseline 6·6%; SD 0·9%).[43] In the

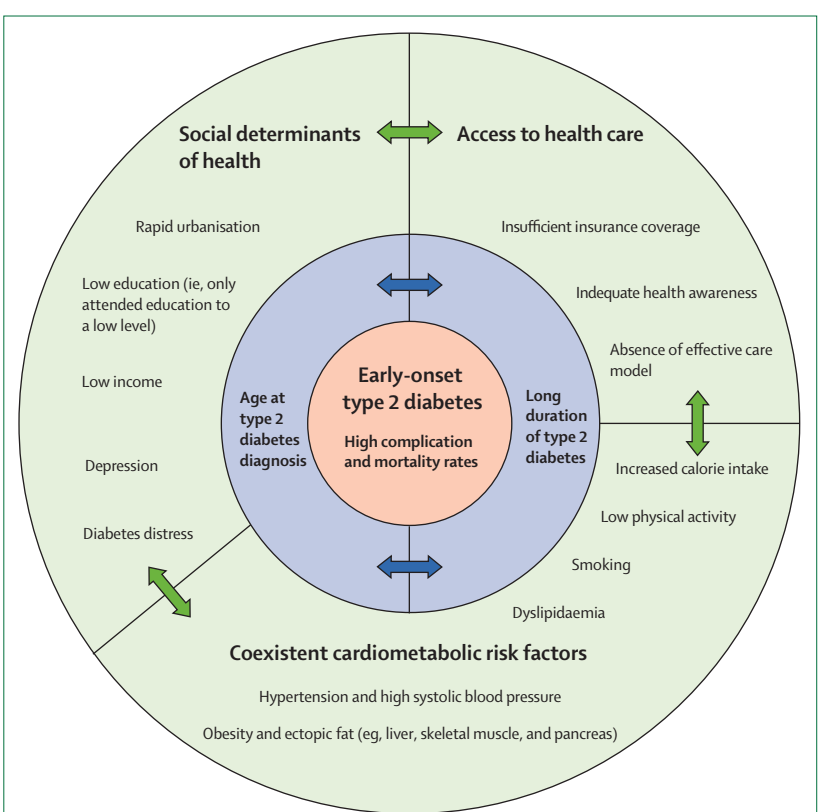

Figure 2: **Mechanisms underlying the increased risks of complications and mortality in early-onset type 2 diabetes**

30-year UKPDS follow-up study, people with early-onset type 2 diabetes (diagnosed aged 25–35 years) had greater cumulative glycaemic exposure, even at diagnosis itself, than did those diagnosed aged 56–65 years.[33]

In the Joint Asia Diabetes Evaluation (JADE) study (consisting of data from nine regions), compared with people with late-onset type 2 diabetes, those with early-onset type 2 diabetes reported a lower rate of treatment target attainment; less than 10% of people with early-onset disease attained all three targets on glycaemia, blood pressure, and LDL cholesterol.[44] Whether this lack of attainment of treatment targets (also highlighted in other datasets[45]) reflects therapeutic inertia, or whether it is unavoidable due to the disease trajectory, remains unknown. In Hong Kong, early diagnosis was associated with more rapid glycaemic deterioration (annually, HbA_{1c} increased by 0·08% in those diagnosed aged 20 years whereas this increase was 0·02% in those diagnosed aged 50 years) and reduced efficacy of glucose-lowering therapies.[46]

Taken together, high glycaemic burden, risk of glycaemic escape, and high complications at baseline likely synergistically increase the risk of both microvascular and macrovascular complications in early-onset type 2 diabetes. The importance of early and sustained glycaemic control has been established through landmark glucose-lowering trials (ie, UKPDS, ADVANCE, ACCORD, and VADT);[47–50] these trials, and their extension studies, have shown microvascular benefits, although macrovascular benefits might not be immediate. Therefore, a crucial approach for treatment of early-onset type 2 diabetes is early, aggressive glucose lowering (as discussed in the third paper in this Series).[51,52]

Effects of coexistent cardiometabolic and behavioural risk factors

The worsening trajectories of cardiometabolic risk factors in people with early-onset type 2 diabetes are notable in large, prospective cohorts worldwide. For example, in a study of the Swedish National Diabetes Register, people with type 2 diabetes who were diagnosed aged 18–44 years had higher BMI at baseline (33·4 kg/m²; SD 7·3), than those diagnosed when they were older than 75 years (28·3; SD 4·7).[43] Notably, the approximately 5 kg/m² difference in BMI was sustained over 8 years.[43] In a UK primary-care database, larger differences in systolic blood pressure between those with and without type 2 diabetes were consistently shown in younger age groups (adjusted mean difference 7 [95% CI 6–7] mm Hg for people aged 20–39 years), with a narrowing in systolic blood pressure in older age groups (–0·5 [–0·9 to –0·2] mm Hg for people aged ≥80 years).[53]

Data from Asia reinforce this adverse profile. In the JADE study, compared with people with late-onset type 2 diabetes (mean age at diagnosis 53·2 years; SD 8·9), people with early-onset type 2 diabetes (mean age at diagnosis 33·2 years; SD 5·4) showed higher rates of smoking (17% in people with early-onset disease *vs* 14% in people with late-onset disease), obesity (35% *vs* 26%), macroalbuminuria (14% *vs* 11%), and insulin use (24% *vs* 15%), but less use of renin-angiotensin system inhibitors (25% *vs* 29%) and statins (31% *vs* 37%).[44]

Amid rapid socioeconomic transitions, the burden of type 2 diabetes has increased more substantially in Asia than in Europe and North America.[54,55] The distinct Asian phenotype of early-onset type 2 diabetes is characterised by lower BMI at onset, greater β-cell dysfunction, ectopic fat in the liver and pancreas, and reduced skeletal muscle mass (as discussed in the first paper in this Series) compared to populations in Europe and North America.[41,42,54–56] This phenotype predisposes individuals to diabetes even in the presence of modest weight gain. This weight gain seems inevitable as societies shift from energetic rural lifestyles to urban environments, marked by reduced physical activity in combination with increased caloric intake and sedentary behaviours.[57–59] These changes are compounded by increasing rural-to-urban migration in Africa and Asia.[60,61]

The cardiometabolic characteristics described are independent risk factors for microvascular and macrovascular complications. Notably, adjustment for glycaemic control alone has minimal effect on cardiovascular risk, whereas further adjustment for BMI, blood pressure, and lipids substantially attenuates this risk,[25] highlighting the importance of cardiometabolic and behavioural factors,[25,42,62] and underscoring the need for aggressive risk factor management (as discussed in the third paper in this Series).[52,59]

Effects of societal determinants of health and access to health care

The little evidence for optimal care models, efficacy of interventions, and durability of interventions, are likely to compound therapeutic inertia and delay the optimisation of guideline-directed medical therapy among people with early-onset type 2 diabetes (as discussed in the third paper in this Series).[52] However, the rapid disease progression in early-onset type 2 diabetes could also relate to social determinants of health, including socioeconomic deprivation, which can make self-management practices challenging.[14,63,64]

In the TODAY study, 82% of youth with type 2 diabetes had low socioeconomic status, diabetes distress was associated with an OR of 2·72 (95% CI 1·37–3·58) for suboptimal glycaemic control (HbA_{1c} ≥8% [64 mmol/mol]), and better self-management support was associated with improved glycaemia (0·60; 0·41–0·88).[65] The proportion of youth with type 2 diabetes with depression significantly increased from 12·6% (at baseline) to 17·6% (after 6 years of follow-up), and the proportion with poor health-related quality of life increased from 13·1% (at baseline) to 16·7% (after 6 years of follow-up).[66] These social determinants of health were more common in females and those with low

socioeconomic status, with a risk of retinopathy progression OR of 1·75 (1·16–2·64) in females and 1·80 (1·14–2·84) in people with low socioeconomic status.[66]

People with early-onset type 2 diabetes could have difficulties in self-management due to competing priorities and poor health literacy that could affect treatment adherence and treatment target attainment, and result in delay in seeking care and loss to follow-up.[44,45,54] Timely access to appropriate specialists and integrated health-care services is another important determinant for managing chronic diseases, and was highlighted in a qualitative study seeking feedback from people living with early-onset type 2 diabetes regarding unmet needs.[67–69] In the TODAY study, lack of health-care coverage was associated with higher HbA_{1c}; it was also associated with fewer outpatient visits with a community diabetes health-care provider.[70] These data highlight the need for tailored health-care delivery models to effectively prevent complications and premature mortality in people with early-onset type 2 diabetes.

Effects of genetic and epigenetic factors

Genetic susceptibility and in-utero fetal programming from exposure to maternal obesity and diabetes could have a part to play in the observed complication burden from early-onset type 2 diabetes, but these associations have not been proven to be causal.[14,63,64,71] Genetic variants associated with type 2 diabetes could directly or indirectly increase the risks of microvascular and macrovascular complications.[72,73] In the WHO Multinational Study of Vascular Disease in Diabetes,[74] after a mean follow-up of 9·5 years, Indigenous Americans of the Southwest with early-onset type 2 diabetes (diagnosed aged <30 years) had a higher age-adjusted incidence rate of albuminuria, proteinuria, and kidney failure, compared with the Asian and European populations with the same age at type 2 diabetes diagnosis.[75] These differing complication rates also reflect intercountry and interethnic variations in cardiometabolic risk factors, management, and potential genetic influences.

Emerging complications

People with early-onset type 2 diabetes are increasingly facing a dual burden of established and emerging complications. Herein, we focus on key emerging complications in reproductive health, metabolic-associated steatotic liver disease, cancers, and mental health.

Reproductive health

Data from the last 5 years have highlighted poor preconception care and pregnancy outcomes in women with type 2 diabetes. Females of reproductive age with type 2 diabetes were less likely to receive preconception care than those with type 1 diabetes.[76] Studies have reported that 10–20% of women with type 2 diabetes were using effective contraception (lower than those with type 1 diabetes or without diabetes).[77,78] This affects preconception care and pregnancy planning, increasing the risk of unplanned pregnancies and associated adverse maternal and fetal outcomes in women with type 2 diabetes.

In women with type 2 diabetes, studies have shown that stillbirths were 7–16 times more likely during pregnancy than in women without diabetes and women with gestational diabetes.[15] Neonatal or perinatal mortality is also more frequent in pregnant women with type 2 diabetes than in women without diabetes, with gestational diabetes, or with type 1 diabetes.[79] Pregnant women with type 2 diabetes also have a higher rate of pregnancy-related hypertensive disorders, preterm births, caesarean delivery, and newborns that are large for gestational age, than have women with gestational diabetes or women who do not have diabetes.[79] Newborns of people with type 2 diabetes are more likely to be affected by classic diabetes-related neonatal complications (such as hypoglycaemia, hypocalcaemia, hyperbilirubinaemia, and respiratory distress syndrome) and therefore, to require neonatal intensive care unit care.[15]

Women with type 2 diabetes entering pregnancy are more likely to have chronic hypertension but fewer microvascular complications than those with type 1 diabetes, likely due to shorter diabetes duration before pregnancy in some cohorts.[15] In the TODAY study, pregnancy outcomes were particularly concerning for those with early-onset type 2 diabetes, likely reflecting longer diabetes duration at conception, insufficient preconception care (only 23 [16%] of 141 reported counselling; 21 [15%] had ever used contraception before first pregnancy), and social determinants.[78] Among female TODAY participants, the average diabetes duration at conception was 8 years, with a mean HbA_{1c} of 8·7% (72 mmol/mol); outcomes included 25% unintended pregnancy loss (12·3% miscarriage, 3·7% stillbirth, and 9·3% unknown pregnancy loss) and a 33% rate of preterm birth beyond 20 weeks.[78]

Metabolic-associated steatotic liver disease

A global pooled analysis, published in 2024, showed that 65% of people with type 2 diabetes have metabolic-associated steatotic liver disease; however, prevalence in early-onset type 2 diabetes has not been systematically studied.[80] Several studies in youth have shown that metabolic-associated steatotic liver disease is a risk factor for progression to type 2 diabetes,[81,82] and two systematic reviews and meta-analyses of the prevalence of metabolic-associated steatotic liver disease in type 2 diabetes did not stratify by age.[80,83]

The co-existence of metabolic-associated steatotic liver disease and type 2 diabetes amplifies the risk of cardiovascular disease and death. In a South Korean population-based analysis, in people with stage 2 metabolic-associated steatotic liver disease and type 2 diabetes, the HR for progression to cardiovascular disease was 3·53 (95% CI 1·86–6·68) in people

aged 20–29 years, 2·57 (2·07–3·2) in people aged 30–39 years, and 1·40 (1·33–1·48) in people aged 70 years and older, compared with those without metabolic-associated steatotic liver disease.[84] These results show that although type 2 diabetes is a known risk factor for cardiovascular disease and death, the earlier manifestation of metabolic-associated steatotic liver disease further exacerbates the risk.

One study showed that children (mean age 12·6 years) were more likely to develop biopsy-proven steatohepatitis (the more progressive form of metabolic-associated steatotic liver disease) if they had prediabetes (OR 1·9; 95% CI 1·2–2·9) or type 2 diabetes (3·1; 1·5–6·2), than were children who had normoglycaemia.[85] Notably, there is an insufficient amount of direct comparative studies on liver-related events in early-onset and late-onset type 2 diabetes. The TODAY study reported a rate of 6·7 events per 1000 person-years for all liver, pancreas, and gallbladder events, but without further organ-specific stratification.[22] In a large-scale retrospective cohort study in Hong Kong, compared with people aged 60 years who did not have type 2 diabetes, prolonged diabetes duration was associated with an increased risk of liver-related events in people with type 2 diabetes and metabolic-associated steatotic liver disease.[86] The incidence rates were 2·26 for a diabetes duration of less than 5 years, 3·16 for 6–10 years, and 6·20 for more than 10 years.[86] However, more studies are needed to delineate any differential trajectories of liver-related and other organ-specific events between early-onset and late-onset type 2 diabetes. The scarcity of data on this important complication highlights methodological issues. For example, poor clinical coding for metabolic-associated steatotic liver disease and insufficient diagnostic accuracy of non-invasive tests (including Fibrosis-4 Index) in assessing advanced liver fibrosis, means that invasive liver biopsy is depended on for the diagnosis and longitudinal monitoring of liver-related events.[87,88]

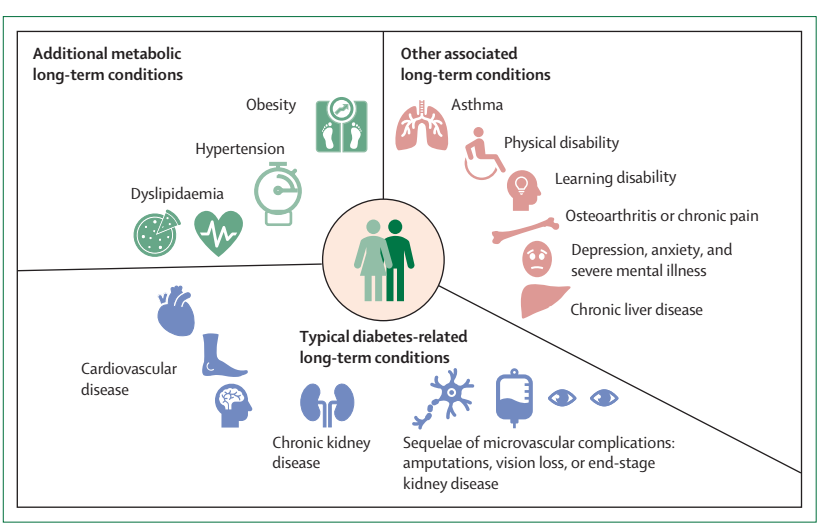

Figure 3: **Multiple long-term conditions associated with early-onset type 2 diabetes**
The conditions included are based on literature examined or included in a recent large primary-care database analysis in England.[92] The top five most prevalent conditions in those aged 20–49 years from the analysis were hypertension, cardiovascular disease, osteoarthritis, depression, and asthma.

Cancers

Recent large observational studies have reported associations between early-onset type 2 diabetes and cancer-related events.[89–91] In the Nurses' Health Study, type 2 diabetes diagnosed in people younger than 40 years was associated with a 2·5-times greater risk of diabetes-related cancers at age 40–50 years, after adjustment for confounders including BMI (HR 2·47, 95% CI 1·61–3·78). Type 2 diabetes diagnosed in people aged 40–50 years showed a weaker association (1·29, 1·10–1·52) with incident diabetes-related cancers in the following decade (at age 50–60 years), and even lower estimates in later decades.[90] In these analyses, the individual cancers driving most of the associations were renal and endometrial, and (to a lesser extent) colorectal, pancreatic, thyroid, and bladder.[90] In the large UK primary-care database, the relative risk of cancer-specific mortality comparing people with and without type 2 diabetes decreased with increasing age at diabetes diagnosis: HR 3·74 (95% CI 1·86–7·55) at age 16–27 years, which decreased to 1·28 (0·90–1·82) at age 32–35 years, and remained stable thereafter.[91]

The observed diabetes–cancer associations could be explained by shared risk factors such as obesity (figures 2, 3). Although many epidemiological studies adjusted for BMI, the associations persisted, suggesting other drivers such as chronic inflammation and hyperglycaemia.[93,94]

Mental health conditions

Early-onset type 2 diabetes is associated with a higher prevalence of diabetes distress, depression, and anxiety than late-onset type 2 diabetes. Two studies done in the younger type 2 diabetes population have reported rates of diabetes distress of 35% for mean age 32 years and 63% for mean age 35 years.[95,96] In the follow-up of the TODAY study (mean age 26 years, mean diabetes duration 12 years), 25% reported a high diabetes distress score, which was associated with higher HbA_{1c} at baseline and 1 year.[65]

Major depression, anxiety, and other mood-related psychiatric disorders are also common in early-onset type 2 diabetes. In a large population-based study from Sweden, compared with over 3 million people without type 2 diabetes, the approximately 8000 people with early-onset type 2 diabetes had an increased risk of having depression (HR 3·97; 95% CI 3·75–4·22), bipolar disorder (4·17; 3·68–4·73), anxiety (3·76; 3·54–3·99), and stress-related disorders (3·35; 3·11–3·61).[97] In the same study, psychiatric diagnoses were more common in relatives of people with early-onset type 2 diabetes, and familial coaggregation analysis and quantitative genetic modelling were supportive of shared genetics between type 2 diabetes and mental health conditions.[97] This

hypothesis is also supported by genome-wide association studies that have shown pleiotropic genes for type 2 diabetes and mood disorders.[98–100]

Conversely, as outlined in the first paper in this Series,[10] people experiencing mental health conditions are at increased risk of developing early-onset type 2 diabetes. Whether these findings reflect causation through the effects on lifestyle behaviours and BMI, adverse effects of psychotropic medications, or shared risk factors between early-onset type 2 diabetes and mental health conditions, remains to be explored.

Multiple long-term conditions

Multiple long-term conditions have typically manifested at older ages and diabetes is recognised as a key driver for their development.[101] One analysis of a large primary-care database involving greater than 46 million adults in England provided the first ever quantification of the burden and consequences of diabetes-associated multiple long-term conditions.[92] A third of the study population had diabetes and greater than three other conditions by age 50 years, almost double that of the general population.[92] The patterns of multiple long-term conditions also differed by age strata. In people older than 50 years, hypertension, depression, cancer, and ischaemic heart disease predominated, whereas in people aged 20–49 years, depression, serious mental health conditions, learning disabilities, and asthma were the most prevalent.[92] This study did not differentiate type 1 from type 2 diabetes. Figure 3 summarises key multiple long-term conditions in early-onset type 2 diabetes.

Early-onset type 2 diabetes has a greater effect on years of life lost due to multiple long-term conditions than late-onset type 2 diabetes. As a crude estimation, a person aged 40 years with diabetes and three other conditions lost approximately 14 years of life, compared with 8 years of life lost in a person aged 60 years with three other conditions.[92] These excess years of life lost could differ depending on the actual combinations of conditions, age at diabetes diagnosis, and current age, for which data has been scarce.[102] Preventing the development of multiple long-term conditions and associated frailty[103] presents an opportunity for improving outcomes in early-onset type 2 diabetes, as discussed in the third paper in this Series.[52]

Current gaps in knowledge and future research

Despite the increasing incidence of early-onset type 2 diabetes, much remains unknown about its cause, pathophysiology, differential complications, and disease trajectories. Table 2 summarises the key gaps in knowledge and future research priorities in these areas.

Conclusion

Early-onset type 2 diabetes is associated with a more aggressive disease trajectory, an earlier onset of complications, and a higher risk of developing multiple long-term conditions than is late-onset type 2 diabetes. Evidence supports the view that prolonged diabetes duration confers this substantially higher risk, especially when combined with younger age at diagnosis. These outcomes are further shaped by co-existing cardiometabolic risk factors, alongside poor social determinants of health and inequities in health-care access and engagement. However, more studies are needed to characterise early-onset type 2 diabetes across its age spectrum, to understand how phenotype affects complications outside of epidemiological studies.

The early emergence of microvascular, macrovascular, hepatic, reproductive, and psychological complications highlights the need for urgent prioritisation in care with tailored intervention strategies. A more nuanced understanding of disease heterogeneity, underlying mechanisms, and differential risks across diverse populations is needed. Importantly, early diagnosis offers a crucial window to intervene, yet current models

	Research priorities
The definition of early-onset type 2 diabetes is heterogeneous	To standardise the definition and reporting of early-onset type 2 diabetes; to investigate subtypes of early-onset type 2 diabetes for improved targeting of therapeutic approaches
The attributable risks of genetic susceptibility, epigenetic modifications, gut microbiome, and environmental risk factors (including pollution) in early-onset type 2 diabetes are not fully mapped	Big data and multiomics studies to identify molecular drivers and their interactions for the development and progression of early-onset type 2 diabetes
How insulin resistance developed during adolescence and puberty contributes to sex disparity in epidemiological studies and long-term complications is not well defined	Prospective studies following up adolescents diagnosed with type 2 diabetes into adulthood
Microvascular complications, particularly kidney disease, appear to be more aggressive in people with early-onset type 2 diabetes, but the mechanisms contributing to this progression are not well defined	Precision medicine approaches including deep phenotyping, multiomics profiling, imaging, and artificial intelligence studies to investigate the heterogeneity in risk of complications
Are there differences in more diverse and non-cardiovascular complications between early-onset type 2 diabetes, late-onset type 2 diabetes, and age-matched and sex-matched type 1 diabetes?	To evaluate differences in complications in large, multinational, multiethnic contemporary cohorts well characterised at baseline and with complete outcomes capture (eg, cancers, mental health conditions including psychotic disorders), and the emerging multiple long-term conditions
There is a scarcity of prospective data on the relationship (likely bidirectional) between early-onset type 2 diabetes and mental health conditions, and their pathophysiological processes	To evaluate the temporality and directionality of early-onset type 2 diabetes (ie, progression and complications) and mental health conditions, and their mechanistic pathways
Those with early-onset type 2 diabetes (especially youth diagnosed when they were aged <18 years) are likely to have parents with type 2 diabetes of long duration and complications, which could prevent adequate support for the younger patient with type 2 diabetes (due to poor physical health of the parent)	To develop intervention studies targeting multigenerations and families affected by type 2 diabetes
Challenges of optimal glycaemia management before, during, and after pregnancy	Implementation research to improve contraception, preconception care, and obstetric management in females with type 2 diabetes; investigations on the pathophysiology of severe perinatal complications (higher frequency perinatal and neonatal mortality than in people with pre-existing type 1 diabetes)

Table 2: **Key knowledge gaps and corresponding future research priorities in early-onset type 2 diabetes**

of care are often ill-equipped to meet the needs of younger people with type 2 diabetes. Addressing these challenges requires integrated, equitable, and multidisciplinary care approaches, supported by trans-sectoral action to tackle upstream determinants that continue to drive the increase in the incidence of early-onset type 2 diabetes.

Contributors

SM was responsible for the conceptualisation of all papers in this Series. L-LL, SJ, JCC, M-FH, and SM contributed content for the first draft of the manuscript. All authors critically reviewed the final draft of the manuscript for important intellectual content and agreed to be accountable for all aspects of the manuscript. L-LL and SM finalised the manuscript. All authors approved the final manuscript for publication.

Declaration of interests

L-LL has received research grants via her institution from Abbott Diabetes Care, AstraZeneca, and Novartis; and speaker honoraria from Abbott, AstraZeneca, Boehringer Ingelheim, Novo Nordisk, Roche Diabetes Care, and Zuellig Pharma. SM has received speaker honoraria from Lilly UK, Sanofi, and Menarini. All other authors declare no competing interests.

Acknowledgments

SM is funded by a Wellcome Trust Career Development Award (223024/Z/21/Z) and is supported by the UK National Institute for Health and Care Research Imperial Biomedical Research Centre. L-LL is supported by Universiti Malaya (IF024-2025). SJ is funded by a Medical Research Council Clinical Research Training Fellowship.

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