The worldwide epidemiology of type 2 diabetes mellitus—present and future perspectives

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Abstract | Over the past three decades, the number of people with diabetes mellitus has more than doubled globally, making it one of the most important public health challenges to all nations. Type 2 diabetes mellitus (T2DM) and prediabetes are increasingly observed among children, adolescents and younger adults. The causes of the epidemic of T2DM are embedded in a very complex group of genetic and epigenetic systems interacting within an equally complex societal framework that determines behavior and environmental influences. This complexity is reflected in the diverse topics discussed in this Review. In the past few years considerable emphasis has been placed on the effect of the intrauterine environment in the epidemic of T2DM, particularly in the early onset of T2DM and obesity. Prevention of T2DM is a 'whole-of-life' task and requires an integrated approach operating from the origin of the disease. Future research is necessary to better understand the potential role of remaining factors, such as genetic predisposition and maternal environment, to help shape prevention programs. The potential effect on global diabetes surveillance of using HbA_{1c} rather than glucose values in the diagnosis of T2DM is also discussed.

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Introduction

The global prevalence of diabetes mellitus is rapidly increasing as a result of population ageing, urbanization and associated lifestyle changes.[1] The number of people with diabetes mellitus worldwide has more than doubled over the past three decades.[2] In 2010, an estimated 285 million people worldwide had diabetes mellitus,[3] 90% of whom had type 2 diabetes mellitus (T2DM).[1] The number of people globally with diabetes mellitus is projected to rise to 439 million by 2030, which represents 7.7% of the total adult population of the world aged 20–79 years (Figure 1a,b).[3] This Review explores current trends in the epidemic of T2DM and the associated major risk factors (Box 1). In particular, the proposed role of genetic and epigenetic predispositions in the T2DM epidemic is discussed and the potential effect on global diabetes surveillance of the use of HbA_{1c} rather than glucose values as an alternative diagnostic approach is addressed.

New trends in the T2DM epidemic

T2DM was relatively rare in developing countries some decades ago; for example, the prevalence of the disease was <1% in China in 1980.[4] However, higher rates observed in Asian Indian and Chinese populations in Mauritius,[5] as well as in Asian immigrants in Western countries[6,7] strongly predicted the potential epidemic of T2DM that has now emerged in mainland China and India.

The major burden of diabetes mellitus is now taking place in developing rather than in developed countries. 80% of cases of diabetes mellitus worldwide live in less developed countries and areas.[3] Asia has emerged as the 'diabetes epicenter' in the world, as a result of rapid economic development, urbanization and nutrition transition over a relatively short period of time.[4] Among the 10 countries with the largest numbers of people predicted to have diabetes mellitus in 2030, five are in Asia (China, India, Pakistan, Indonesia and Bangladesh).[3] In particular, the latest figures derived from a national survey in China between 2007 and 2008 suggest that China has overtaken India and become the global epicenter of the diabetes epidemic with more than 92 million adults (9.7% of the total population) with diabetes mellitus and another 148.2 million adults (15.5% of the total population) with prediabetes, which includes individuals with impaired glucose tolerance (IGT) and/or impaired fasting glucose (IFG).[8] In addition to Asia, the Gulf region in the Middle East[3] and Africa[9,10] are other hot spots for diabetes mellitus. A higher prevalence of diabetes mellitus in immigrants from the Middle East living in Sweden than in native Swedes has also been reported.[11]

Compared with developed countries, the proportion of young to middle-aged individuals with T2DM is higher in developing countries.[3] Furthermore, T2DM is not necessarily less prevalent in rural than in urban areas of developing countries, as is generally believed. The rural–urban difference in prevalence is predicted to narrow owing to urbanization, rural to urban migration and its associated lifestyle changes. A study from India showed a significant increase in diabetes mellitus prevalence in both urban (from 13.9% in 2000 to 18.2% in 2006) and rural areas (from 6.4% in 2000 to 9.2% in 2006).[12] Similar findings have been reported from other Asian countries.[4]

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Competing interests
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Among Chinese individuals aged 35–74 years, between 2001–2002 and 2006, the rural prevalence of diabetes mellitus increased from 5.3% to 14.2% in men and from 8.9% to 13.8% in women, compared with an increase in urban regions in men from 11.3% to 19.2% and in women from 11.3% to 16.1%.[13]

T2DM and prediabetes in youth

T2DM, traditionally considered a metabolic disorder exclusively of adults, has become more common not only in young adults but also in adolescents and, occasionally, in children.[14] For example, the crude prevalence of T2DM among North American youth aged 10–19 years in 2001 was estimated to be 42 cases per 100,000 youth.[15] T2DM constitutes an increasing percentage of all incident cases of pediatric diabetes mellitus, with less than 4% reported two decades ago and up to more than 80% of new-onset cases among adolescents in some ethnic groups, such as American Indian, Asian and Pacific Islander populations.[16,17]

The prevalence and incidence of T2DM in youth varies dramatically by ethnicity, with higher rates observed among high-risk ethnic groups, such as Native American and Australian Indigenous populations, and African American, Hispanic, Pacific Islander and Asian populations.[15,17] For example, the incidence of T2DM in youth is six times higher in Australian Indigenous individuals than in the general population.[18] In the SEARCH for Diabetes in Youth Study in the USA, a higher incidence rate was observed among youths aged 15–19 years in minority populations (17.0 to 49.4 per 100,000 person-years) compared with 5.6 per 100,000 person-years in non-Hispanic whites.[17] Further analyses from the same study suggest that the contributions of genetic and/or environmental factors to early-onset of T2DM may differ in various ethnic groups.[19]

In addition to the rising prevalence of T2DM in youth, the trend of prediabetes among adolescents is increasing. On the basis of the latest data from the US National Health and Nutrition Examination Survey (NHANES), a 87.1% increase in prevalence of IFG has occurred, from 7% in 1999–2000 to 13.1% in 2005–2006, among US adolescents aged 12–19 years.[20,21] Furthermore, an estimated 16.1% of US adolescents had IFG and/or IGT in 2005–2006.[21] The prevalence of prediabetes is even higher in pediatric populations who have other risk factors, such as obesity, hyperinsulinemia or a family history of diabetes mellitus.[21–23] The continuous increase in the prevalence of obesity in youth in Asian countries, such as China and India, portends to increasing numbers of individuals developing T2DM at younger ages if no effective intervention strategies slow down the obesity epidemic.[24]

The fall in the age of onset of T2DM[25] and the unfavorable metabolic control in youth with the disease[26] will substantially influence the future burden of T2DM. Youth with T2DM represent a population at increased risk of development of early complications, and the occurrence of lifelong chronic complications is likely to be higher in this age group owing to the long duration of the disease.

Key points

- The prevalence of type 2 diabetes mellitus (T2DM) and prediabetes has been rapidly rising worldwide over the past three decades, particularly in developing countries
- In addition to the early onset of T2DM in young adults, an increasing trend of T2DM and prediabetes is noticeable among children and adolescents
- The epidemic of T2DM is attributable to a mixture of genetic and epigenetic predispositions and a variety of behavioral and environmental risk factors
- An integrated approach, taking into account genetic and epigenetic determinants, is required for the effective prevention of T2DM beginning from the start of life

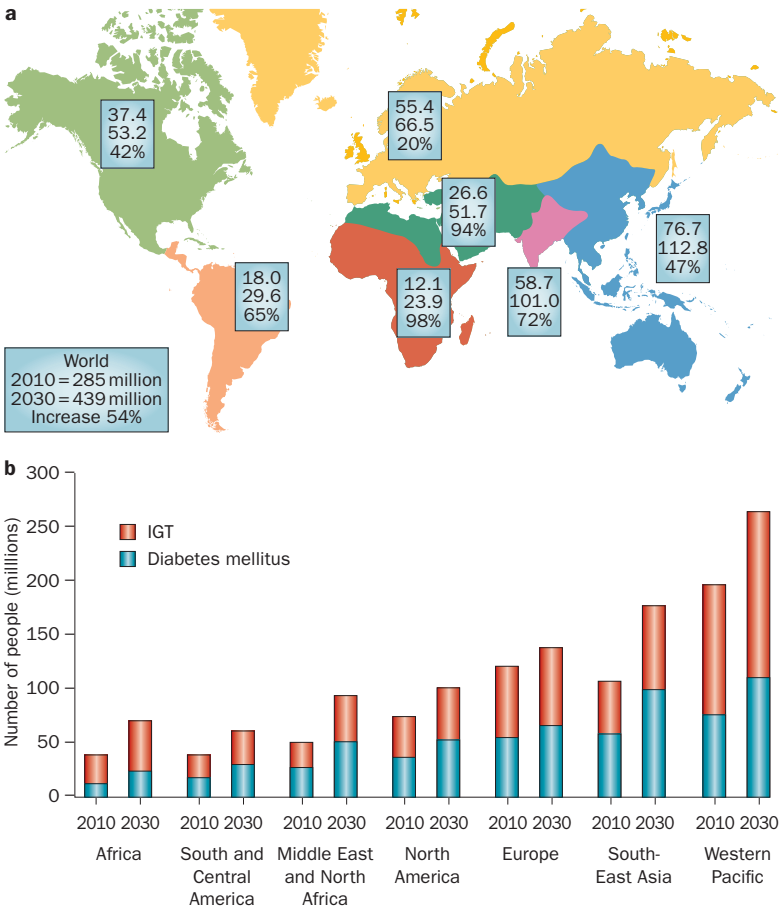

Figure 1 | Global projections for the diabetes epidemic: 2010–2030. **a** | In each box, the top and middle values represent the number of people with diabetes mellitus (in millions) in each of seven world regions (depicted with different colors) for 2010 and 2030, respectively; the bottom value is the percentage increase from 2010 to 2030. The number of people globally with diabetes mellitus is projected to rise from 285 million in 2010 to 439 million by 2030, a 54% increase. **b** | The number of people with diabetes mellitus and IGT (in millions) by region among adults aged 20–79 years for the years 2010 and 2030. Data courtesy of the International Diabetes Federation Diabetes Atlas.[114] Abbreviation: IGT, impaired glucose tolerance.

Risk factors for T2DM: new insights

Overweight and obesity

The global epidemic of T2DM is tied to rising rates of overweight and obesity in adults as well as in youth. The prevalence of overweight (BMI of 25–30 kg/m^2) or

Box 1 | Modifiable and nonmodifiable risk factors for T2DM

Modifiable risk factors

- Overweight or obesity
- Physical inactivity
- Sedentary behavior
- Dietary factors
- Smoking
- Previously identified glucose tolerance (IGT and/or IFG)
- Abnormal lipids (elevated triglycerides, low HDL cholesterol levels)
- Hypertension
- Inflammation
- Intrauterine environment

Non-modifiable risk factors

- Age
- Sex
- Ethnicity
- Family history of T2DM
- History of gestational diabetes
- Polycystic ovary syndrome

Abbreviations: IFG, impaired fasting glucose; IGT, impaired glucose tolerance; T2DM, type 2 diabetes mellitus.

obesity (BMI of ≥30 kg/m^2) in the world's adult population is predicted to rise from 33% in 2005 to 57.8% in 2030, if recent secular trends of obesity continue.[27] Overweight or obesity are the single most important predictors of T2DM,[28] and the effect of obesity on lifetime risk of T2DM is stronger in younger adults.[29] Moreover, in the European Prospective Investigation into Cancer and Nutrition–Potsdam Study, weight gain in early adulthood (25–40 years) was found to be associated with a higher risk and earlier onset of T2DM than was weight gain after the age of 40 years.[30]

The concept of being metabolically obese despite a normal weight has been proposed to explain the high risk of T2DM in some normal-weight individuals.[31] Studies have shown that the incidence of T2DM is higher among individuals with normal weight but with insulin resistance or the metabolic syndrome than in overweight individuals who do not have insulin resistance or the metabolic syndrome.[32,33]

The 'metabolically obese' phenotype might also explain the mismatch between the rates of obesity and T2DM in Asia.[34] Although the prevalence of overweight or obesity is generally lower in most Asian than white populations, Asian individuals tend to develop T2DM at a lower BMI level than Europids,[34] and the risk of T2DM tends to be higher in Asian populations compared with people of Europid origin for any given BMI levels.[35] Asian individuals are more likely to have a higher fat percentage[36] or visceral adiposity[37,38] at a given BMI or waist circumference than Europids. Data from the Obesity in Asia Collaboration, which includes information on >263,000 individuals from 21 studies in the Asia-Pacific region, have shown that measures of central adiposity, such as waist circumference, have a stronger association with prevalent T2DM than BMI.[35]

Visceral adiposity is an independent risk factor for insulin resistance, T2DM and other cardiovascular risk factors.[39] Some investigators argue that nonalcoholic fatty liver disease (NAFLD), a phenotype of ectopic fat accumulation in the liver, is a better indicator of T2DM risk than excessive accumulation of visceral adipose tissue.[40] NAFLD is found to have a stronger association with peripheral insulin resistance than abdominal fat content.[41] In a meta-analysis of 21 cohort studies, ultrasonography-diagnosed NAFLD and associated elevation in its surrogate markers, such as alanine aminotransferase and γ-glutamyl-transferase, are consistently found to independently predict the development of T2DM.[42] Moreover, Taylor has proposed that ectopic fat deposition in the liver and islets underlies the development of hepatic insulin resistance and β-cell dysfunction.[43]

Developmental origins of T2DM

Intrauterine development is a critical and sensitive period during which an adverse intrauterine milieu can affect fetal development by modifying epigenetic gene expression. Epigenetic modifications have been defined as heritable alterations in gene expression that are not associated with changes in DNA sequence, but instead involve DNA methylation and histone modification.[44–46]

Low birth weight has been consistently found to be associated with an increased risk of the development of T2DM in later life. In a meta-analysis that included 28 populations from different ethnicities, a 1 kg increase in birth weight was associated with a 20% risk reduction of T2DM.[47] Low birth weight due to nutritional deprivation *in utero* influences later susceptibility to obesity, T2DM and other metabolic abnormalities through the acquisition of a 'thrifty phenotype'; the thrifty phenotype hypothesis postulates that poor fetal and infant nutrition lead to permanent changes in glucose metabolism.[48] The link between fetal malnutrition and later T2DM risk in humans is elegantly illustrated by the observations from the Dutch Hunger Famine birth cohort study, which reported that adults who had been exposed to famine during fetal life had a worse glucose tolerance status than unexposed individuals.[49] Similar findings have been replicated in populations from other regions that have suffered nutritional hardship, such as the Chinese Famine (1959–1961) Study.[50]

Fetal undernutrition is proposed to predispose individuals to insulin resistance[49,51,52] and reduced β-cell mass and function,[53] which in turn increases their susceptibility to the development of T2DM in later life. The risk of T2DM owing to inadequate fetal nutrition is likely to be exacerbated in people who are exposed to an affluent nutritional environment in adult life and who have excess and rapid weight gain in early adulthood.[49,50,54] The role of mismatch between intrauterine and adult life environment in this proposed mechanism might explain the current diabetes epidemic in some developing countries. For example, in Cambodia, where severe undernutrition occurred during the political upheaval some three decades ago, economic development and

improved nutrition have coincided with the emergence of T2DM at prevalence rates comparable with those of developed nations.[55]

Instead of a simple reverse relationship between birth weight and the risk of T2DM, a few studies, such as those in Pima Indians,[51] Taiwanese schoolchildren[56] and Australians,[57] have suggested a U-shaped or reversed J-shaped association between birth weight and T2DM, in which high birth weights (>4.0 kg) are also associated with an elevated risk of T2DM. Exposure to intrauterine hyperglycemia predisposes the fetus to produce additional insulin, which acts as a fetal growth hormone leading to excess fetal growth. Abnormal glucose tolerance during pregnancy is, therefore, a two-edged sword, because it predisposes both mother and offspring to the development of obesity, the metabolic syndrome and T2DM in later life.

Women with gestational diabetes mellitus have a more than sevenfold increased risk of subsequently developing T2DM compared with women who experience a normoglycemic pregnancy.[58] Exposure to intrauterine hyperglycemia is an important determinant of diabetes mellitus in adult offspring in addition to genetic susceptibility and independent of maternal diabetes type.[59–62] Fetal exposures to maternal hyperglycemia lead to increased overall and abdominal obesity in youth[63] and predispose to an earlier onset of T2DM.[64] Furthermore, a strong association between maternal glycemia during pregnancy and risk of T2DM in Pima Indian offspring was observed even among mothers who had a normal range for glucose tolerance during pregnancy.[65]

Given the earlier onset of T2DM in female offspring with intrauterine exposure to hyperglycemia and the increasing prevalence of T2DM that predates pregnancy[66] or gestational diabetes,[67,68] it is essential that the vicious cycle of diabetes begetting diabetes over generations is broken. This intergenerational cycle of T2DM highlights the importance and need for effective prevention or intervention strategies to improve the management of glucose tolerance during pregnancy.

Genetic susceptibility

T2DM is a complex, multifactorial disease fuelled by interactions between multiple susceptible genetic loci and various environmental and behavioral factors (Box 1). Disparity in the risk of T2DM between different ethnic groups after controlling for diverse environmental attributes indicates a genetic predisposition in the development of T2DM. For example, the common variants of the *TCF7L2* gene are significantly associated with risk of T2DM, with a pooled odds ratio of 1.46 for the rs7903146 variant.[69] However, substantial differences exist in the locations of risk allele and frequencies of occurrence of particular risk alleles across different ethnic groups.[4]

Despite multiple genetic loci being associated with the risk of T2DM, the discriminative ability of genetic scores based on a number of risk alleles is unsatisfactory.[70] Furthermore, the addition of risk alleles only slightly improved the prediction of future T2DM compared with risk models based on clinical risk factors or family history of T2DM (commonly considered to represent heritable genetic risk).[71–77] However, the use of genetic markers might be a much more valuable addition in children and younger adults, as other commonly used phenotypic risk factors such as family history or hypertension may not yet be expressed. A report from the Framingham Offspring study with 34 years of follow-up showed that knowledge of common genetic variation appropriately improved T2DM risk reclassification after accounting for common clinical risk factors among people <50 years of age but not older people.[78] In addition, the cost of potential use of genetic testing would be another important practical issue in the evaluation of its value, particularly in the countries and areas with limited budgets for health care.

Diabetes genetic testing can be used not only to ascertain an individual's risk but also to motivate high-risk individuals to change their lifestyle and adhere to necessary preventive measures prior to the onset of clinical phenotypes. Some evidence suggests that genetic factors interact with the environment to affect risk of T2DM. In the Health Professionals Follow-up Study, a Western dietary pattern characterized by high consumptions of red and processed meats as well as refined foods, was significantly associated with an elevated risk of T2DM among men with a high genetic risk score but not among those with a low genetic risk score.[79] Furthermore, findings from the Finnish Diabetes Prevention Study suggest that individual tailoring of lifestyle interventions based on genetic predisposition may maximize the benefits of the interventions.[80]

In the US Diabetes Prevention Program[81] and Finnish Diabetes Prevention Study,[82] lifestyle intervention significantly reduced the risk of T2DM among high-risk participants as determined by genetic polymorphisms. However, direct evidence that perception of T2DM genetic risk improves the motivation level of high-risk individuals towards behavioral change is scarce. In a survey from 152 patients without T2DM, over 70% of patients reported that an appraisal of high-risk status would motivate them much more to adhere to healthy lifestyle changes.[83] On the other hand, concerns also exist that less motivated individuals would use the low-risk assessment results to further reduce their engagement in health prevention. Interviews with 22 overweight individuals with high phenotypic risk of T2DM suggested that individuals' knowledge and healthy behaviors prior to genetic testing would lead to a positive response of genetic testing results.[84]

Other lifestyle and environmental risk factors

Apart from overweight and obesity, genetic and epigenetic factors and other major factors (Box 1), a number of novel factors have been identified to be independently associated with the risk of T2DM, such as sleeping disorders,[85] depression[86] and antidepressant medication use.[87] Some studies have also suggested a potential role of environmental toxins, such as endocrine disruptors (for example, bisphenol A)[88] and particulate matter in air pollution, in the development of T2DM.[89,90]

Table 1 | Accuracy of using HbA_{1c} ≥6.5% for detecting undiagnosed diabetes as defined by OGTT

Study	Study period	Age (years)	Newly diagnosed diabetes by OGTT (%)	Newly diagnosed diabetes by HbA_{1c} ≥6.5% (%)	Probability (sensitivity) of having HbA_{1c} ≥6.5% among diabetes cases defined by OGTT (%)	Specificity of using HbA_{1c} ≥6.5% for detecting diabetes cases defined by OGTT (%)
Qingdao, China[99]	2006	35–74	11.9	10.8	28.0 (men), 21.9 (women)	90.5 (men), 91.2 (women)
Shanghai, China[107]	2007–2008	≥20	6.2	3.1	50.5	98.1
Inter99, Denmark[100]	1999–2001	46.2±7.9	4.2	6.7	42.6	NA
Whitehall II, UK[100]	2002–2004	60.5±5.9	3.7	1.0	25.0	NA
The Australian Diabetes, Obesity and Lifestyle Study, Australia[100]	1999–2000	≥25	4.0	0.7	17.0	NA
Inuit Health in Transition Study, Greenland[100]	2005–2009	44.1±14.6	7.0	3.9	29.6	NA
Kenya[100]	2005–2006	37.6±10.6	3.4	1.4	20.0	NA
Chennai Urban Rural Epidemiology Study, India[100]	2001–2004	38.8±12.6	10.2	12.9	78.0	NA
NHANES, USA[101]	2003–2006	≥20	5.1	1.6	25.5	95.6
New Hoorn Study, Netherland[102]	2006–2007	40–65	4.0	1.0	24.0	99.0
Minority Americans, USA[103]	1995–1999, 1997–2000	54.2	15.5	8.9	40.0	96.8
Screening for Impaired Glucose Tolerance Study, USA[104]	2005–2008	≥18	4.6	2.2	33.3	99.3
Non-Hispanic white or black adults in NHANES III, USA[104]	1988–1994	>40	7.6	2.8	37.9	98.5
Non-Hispanic white or black adults in NHANES 2005–2006, USA[104]	2005–2006	≥18	5.2	1.8	29.2	99.6
Telde Study, Spain[105]	NA	≥30	6.4	2.9	38.7	99.6
Leicester Ethnic Atherosclerosis and Diabetes Risk study, UK[106]	2002–2004, 2004–2008	40–75	3.3	5.8	69.7	NA

Abbreviations: NA, not available; NHANES, National Health and Nutrition Examination Survey; OGTT, oral glucose tolerance test.

Move to HbA_{1c} for diabetes diagnosis

Plasma (or blood or serum) glucose concentrations have been used in the diagnosis of T2DM and, therefore, estimates of T2DM prevalence and incidence have been primarily dependent on glucose measures. In the past few years, HbA_{1c}, a measure of average glycemia over the previous 8–12 weeks[91] has been recommended as an alternative means for the diagnosis of T2DM by the American Diabetes Association (ADA)[92] and the WHO.[93] Among individuals without T2DM, increasing HbA_{1c} level is associated with not only future risk of T2DM[94] but also a substantially increased risk of incident cardiovascular events and deaths.[95,96]

The cut-off of HbA_{1c} of ≥6.5% for the diagnosis of diabetes mellitus, as recommended by the ADA and WHO, was derived based on the association between HbA_{1c} and prevalent retinopathy.[97] The decision to use this threshold was based on data from the DETECT-2 project, which pooled data from ~45,000 participants from five countries and showed a narrow threshold range for HbA_{1c} at which risk of diabetes-specific retinopathy (moderate nonproliferative and more severe retinopathy) increases significantly.[98]

Although HbA_{1c} is a convenient diagnostic test, as it can be performed in the nonfasting state and has greater preanalytic stability and less biological perturbations compared with fasting or 2 h post-load glucose testing, the discordant diagnosis of diabetes mellitus with the use of HbA_{1c} and glucose criteria is concerning (Table 1).[99–107] Research conducted in the USA and India indicates a substantially overlapping distribution of HbA_{1c} level among individuals with different glucose tolerance status.[108,109] Furthermore, of the 16 studies that have reported the prevalence of undiagnosed diabetes mellitus detected by either HbA_{1c} ≥6.5% or oral glucose tolerance test (OGTT), 13 have found that HbA_{1c} criteria lead to a lower prevalence of undiagnosed diabetes mellitus than OGTT criteria. HbA_{1c} criteria have high specificity (>90%) in detecting diabetes mellitus as defined by OGTT. However, the probability of having an HbA_{1c} ≥6.5% among cases of diabetes mellitus based on OGTT criteria varies dramatically across ethnicities (from 17.0% among Australians to 78.0% in Asian Indians).[99–107]

A number of studies have proposed alternative HbA_{1c} cut-off points for detecting undiagnosed diabetes mellitus and suggested the potential use of ethnic-specific

cut points. However, these alternative thresholds are primarily suggested on the basis of the sensitivity and specificity values for comparisons with glucose-defined diabetes mellitus cases, rather than on the basis of the association of different HbA_{1c} values and long-term diabetes complications.[107,109,110] The International Expert Committee report on the role of HbA_{1c} in the diagnosis of diabetes mellitus in 2009 states that "establishing identical prevalences should not be the goal in defining a new means of diagnosing diabetes. The ultimate goal is to identify individuals at risk for diabetes complications so that they can be treated".[97] Among individuals with normal glucose levels, elevated HbA_{1c} levels are associated with less favorable cardiovascular risk profiles, such as with older age, abdominal obesity and dyslipidemia.[108] Interestingly, the Danish arm of the ADDITION trial (Anglo-Danish-Dutch Study of Intensive Treatment of People with Screen Detected Type 2 Diabetes in Primary Care) has shown that the combined use of HbA_{1c} ≥6.0% with cardiovascular risk assessment could identify a similar proportion of people who might benefit from preventive interventions (96.7%) as those detected using glucose measures in combination with cardiovascular risk assessment (97.6%).[111]

In addition to the use of HbA_{1c} as an alternative diagnostic option, the ADA has also proposed that persons with an HbA_{1c} of 5.7–6.4% should be classified as being at high risk of diabetes mellitus, requiring lifestyle or pharmacological interventions.[92] However, this criterion dramatically reduces the number of people identified to be at high risk compared with glucose measures.[101,104,112] No statement on a specific HbA_{1c} threshold for the presence of intermediate hyperglycemia has been released from the WHO.[93] The selection of a threshold at which to initiate preventive strategies should take into account not only the sensitivity and specificity but also the cost and feasibility of the program in the target population.

Whilst considerable improvement in assay standardization of HbA_{1c} has occurred, the cost and availability of HbA_{1c} would be another concern for the wide adoption of the measure as a diagnostic approach. Finally, the potential shift to the use of HbA_{1c} as diagnostic criteria would lead to a different prevalence estimate, because a remarkable discrepancy in diabetes prevalence defined by glucose measures and HbA_{1c} exists. This change would have a considerable effect on the capacity to compare longitudinal changes in populations in future studies given the different methods used to diagnose diabetes mellitus—namely, glucose before and now HbA_{1c}. A recommendation that diabetes prevalence be defined both by HbA_{1c} and glucose criteria for a period of time is, therefore, appropriate as it will enable comparison of national and international historical data.

Prevention of T2DM

Individuals with blood glucose levels higher than normal but not high enough for a diagnosis of T2DM, such as those with IGT and/or IFG, are usually considered to have a high risk of future T2DM.[113] Global estimates suggest that the number of people with IGT will increase from 344 million in 2010 to 472 million in 2030 (Figure 1a),[114] which represents a large pool of people who are likely to develop T2DM in the near future.

Epidemiological studies have shown than nearly 90% of cases of incident T2DM can be attributed to five major lifestyle factors: diet, physical activity, smoking, overweight or obesity and alcohol consumption.[28,115] The importance of adoption of a healthier lifestyle is supported by robust data from diabetes prevention trials. Several major trials unequivocally show that intensive lifestyle interventions, specifically aimed at weight loss and increased physical activity in high-risk individuals, can prevent or at least delay the progression to overt T2DM by 50% and that they are as effective as pharmacological interventions.[116] Moreover, intensive lifestyle intervention in individuals with IGT is found to be most effective among those with a high baseline T2DM risk, as determined by the presence of multiple risk factors.[117]

A number of risk assessment tools for predicting incident T2DM, based on self-assessed, biological measures and even genetic markers, have been derived from different ethnicities,[118] and they provide a more practical and valuable approach for detecting those at risk of developing T2DM compared with universal population screening using a blood glucose test.[119] Some self-assessment tools and lifestyle intervention strategies have been incorporated into the diabetes screening and prevention program in the primary care setting in the past few years, such as the Finnish National Diabetes Prevention Program[120] and the DE-PLAN (Diabetes in Europe–Prevention using Lifestyle, Physical Activity and Nutritional Intervention) project.[121] The 1-year follow-up data from the last two studies strongly support the implementation of community-based lifestyle intervention programs in high-risk populations, which will complement the population-based approach,[122] such as provision of supportive environments for physical activity.

Conclusions

Over the last three decades, we have experienced a spectacular rise in the prevalence of obesity and T2DM in nearly every nation of the world and the resulting heavy health burden associated with these disorders and their related complications. The causes of the diabetes epidemic are embedded in an extremely complex combination of genetic and epigenetic predispositions interacting within an equally complex combination of societal factors that determine behavior and environmental risks.

On the other hand, considerable improvements in the detection of individuals with undiagnosed T2DM and effective interventions in high-risk populations have taken place. Furthermore, some evidence now suggests that the prevalence of obesity is going to be stable or level off in adults as well as in youth in some developed countries,[24] which might lead to the reduction of incident T2DM in these countries, as obesity remains a key driver of T2DM. However, a number of other factors are attributable to the diabetes epidemic other than obesity. They include fetal and early life nutrition status, as well

as some factors associated with rapid socioeconomic development, such as depression,[86] sleeping disorders[85] and environmental pollutants.[88]

Tackling and curbing the escalating diabetes epidemic has been a long and twisted journey, and it requires efforts from each level of society, including scientists, medical practitioners, public health professionals, health-care providers and policy-makers, and most importantly, the awareness of the general population. Further research is required to better understand the potential role of the remaining risk factors, such as fetal and genetic predisposition, to help shape prevention programs.

Review criteria

Articles were identified from searches in PubMed. The search terms used were "diabetes", "impaired glucose tolerance", "impaired fasting glucose", "glycated haemoglobin", "prevalence", "incidence", "epidemiology", "ethnicity", "gestational diabetes", "obesity", "birth weight" and "genetic susceptibility". Articles published between 1995 and 2011 were searched with a special focus on papers published since the year 2000. All articles identified were English-language, full-text papers. Additional references were selected from the reference lists of identified articles.

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Author contributions
All authors contributed equally to all aspect of article preparation.