Epidemiology of diabetes

Nita Gandhi Forouhi
Nicholas J Wareham

Abstract

The rising disease burden of diabetes mellitus globally is a major public health priority, placing unsustainable demands on individuals, their carers, health systems and society. The latest estimates show that there was a global prevalence of 425 million people with diabetes in 2017, which is expected to rise to 629 million by 2045. This is fuelled by the global rise in the prevalence of obesity and unhealthy behaviours including poor diets and physical inactivity; these are in turn promoted by wider societal determinants, including changes in nutrition in a global context (the so-called 'nutrition transition'). The aetiological classification of diabetes principally separates diabetes mellitus into two main types, type 1 and type 2, with type 2 diabetes accounting for most (>85%) of the total diabetes mellitus prevalence. Both of the common forms of diabetes can lead to multisystem complications of microvascular endpoints, including retinopathy, nephropathy and neuropathy, and macrovascular endpoints, including ischaemic heart disease, stroke and peripheral vascular disease. The aetiology of type 1 diabetes is still incompletely understood. The role of modifiable factors in the causation of type 2 diabetes is better understood, making prevention a realistic public health goal.

Keywords Aetiology; diagnosis; epidemiology; MRCP; prevention; screening; type 1 diabetes; type 2 diabetes

Key points

- The clinical and public health burden of diabetes mellitus is high, and rising globally
- The two main types of diabetes mellitus are type 1 and type 2, but other forms are also recognized
- The epidemiology of diabetes shows distinct patterns of distribution by age, sex, ethnic group and rural or urban area of residence; this varies markedly between type 1 and type 2 diabetes
- Genetic and behavioural risk factors, and the interplay between them, are important in the aetiology of diabetes
- Progress has been made in understanding the modifiable factors in the aetiology of type 2 diabetes, which has opened up opportunities for prevention

Types of diabetes

Diabetes mellitus is a complex metabolic condition, the classification and diagnosis of which has been the subject of intense scrutiny over decades. There is a broad consensus on four categories: type 1 diabetes, type 2 diabetes, hyperglycaemia in pregnancy (including gestational diabetes) and diabetes that has a specific aetiology which may be genetic (monogenic forms such as maturity onset diabetes of the young) or secondary to drugs, pancreatic factors or other illnesses. Together, type 1 and type 2 diabetes account for the major burden of diabetes.

Type 1 diabetes

The acute onset of type 1 diabetes mellitus and its rapid presentation to medical attention facilitates accurate registering of new cases. Provided ascertainment can be verified, these data can be combined with population denominator data to give age-specific and sex-specific incidences.

Geographical variation

International Diabetes Federation (IDF) estimates from 2017 indicate that >96,000 new cases of type 1 diabetes are diagnosed globally per year in children and adolescents aged <15 years. The countries with the top 10 highest burden by number are USA, India, Brazil, China, the UK, the Russian Federation, Algeria, Saudi Arabia, Nigeria and Germany, accounting for nearly 60% of all new cases. The incidence of type 1 diabetes in children varies nearly 400-fold between countries (Figure 1), with age-adjusted incidence rates ranging from 0.1 per 100,000 per year in parts of Venezuela and China to 37.8 in Sardinia and 40.9 per 100,000/year in Finland.[1] The incidence also varies within countries: for instance, China has a 12-fold variation by region (0.13–1.61 per 100,000). In general, countries in Europe and North America have a high or intermediate incidence, the incidence in Africa is generally intermediate, and that in Asia is low, with the notable exception of Kuwait.

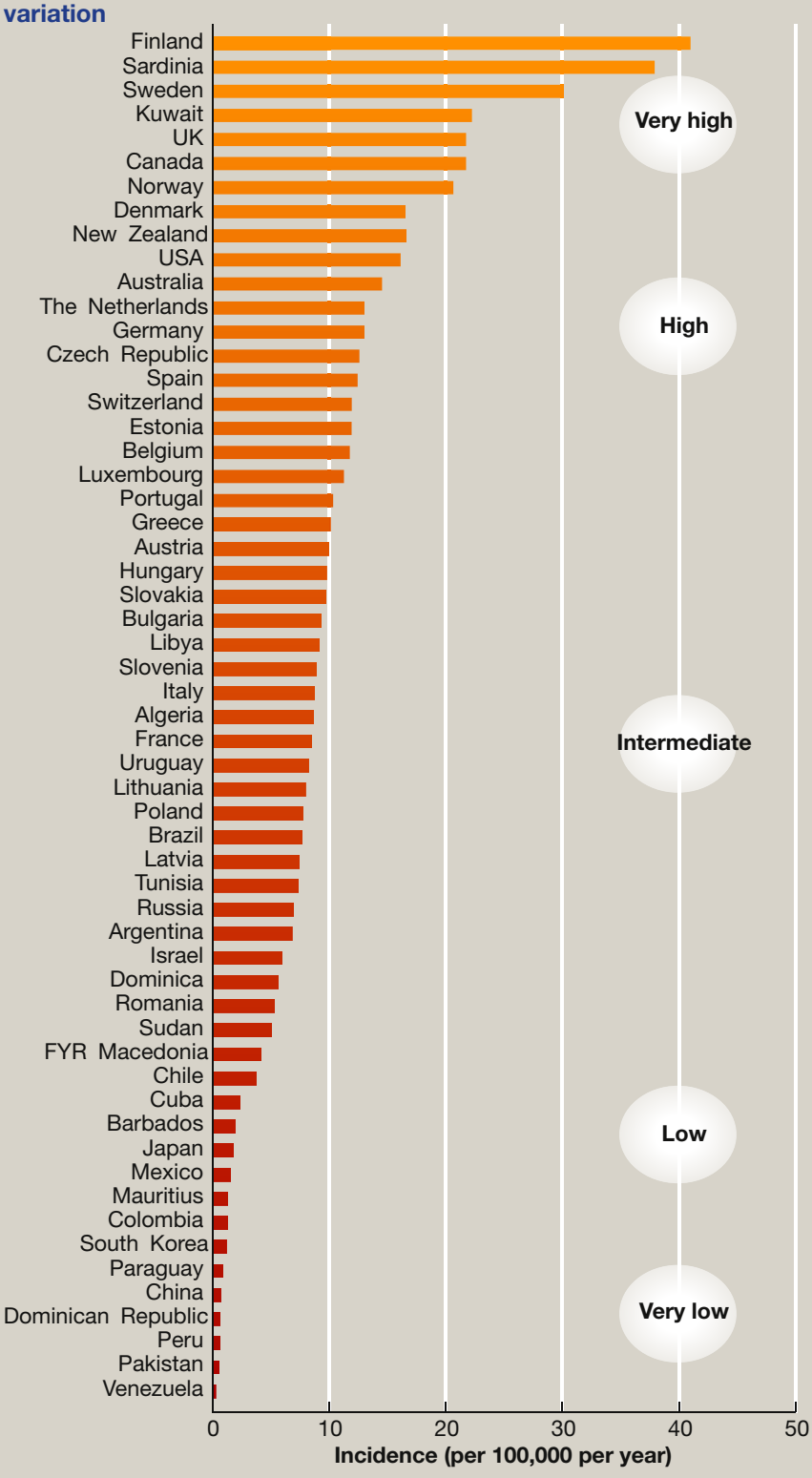
Variation with age, sex and ethnicity

Type 1 diabetes can occur at any age but is rare in the first year of life. In most populations, the incidence steadily increases with age up to puberty, and is higher among those aged <15 years than among 15–29-year-olds. There are no population-based incidence data for ages >35 years. Overall, there is a male excess among young adults. Among children, there is a slight male excess in high-incidence countries, while the opposite is seen in low-incidence countries, but the differences are small. Mirroring the geographical pattern, the incidence is higher in populations of European origin than in non-Europeans.

Nita Gandhi Forouhi *MB BS BMedSci PhD MRCP FFPH is a Programme Leader, Professor and Honorary Public Health Physician at the MRC Epidemiology Unit, University of Cambridge, UK. Competing interests: none declared.*

Nicholas J Wareham *MB BS PhD FRCP FFPH is the Director of the MRC Epidemiology Unit, and co-Director of the Institute of Metabolic Science, University of Cambridge and Honorary Consultant, Addenbrooke's Hospital, Cambridge, UK. Competing interests: none declared.*

Age-standardized incidence of type 1 diabetes in children under 14 years of age (per 100,000 per year) showing marked geographic variation



Countries are arranged in descending order according to the incidence.
Note that several countries also display within-country variation in incidence.
From Incidence and trends of childhood type 1 diabetes worldwide 1990–1999. The DIAMOND Project Group*Diabet Med* 2006;**23:** 857–66.
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Figure 1

Temporal variation

The incidence of type 1 diabetes has been rising, with average increases of around 3.0% per year worldwide. The relative magnitude of increase is generally greater in low-incidence countries. The most pronounced increase is in the youngest age group (0–4 years). The incidence of type 1 diabetes also varies with season, being highest in autumn and winter.

Aetiological factors

Genetic susceptibility is important but not sufficient in the causation of type 1 diabetes. Environmental factors have a more important role in progression from islet autoimmunity to overt disease, possibly because improved living standards have reduced exposure to microorganisms, leading to increased autoimmunity. Despite research efforts, no single environmental factor has been proven to be causally related to type 1 diabetes. However, associations have been described or hypothesized for early social mixing, viral infections, vaccinations, drugs, toxins, intrauterine factors, and dietary and nutritional factors such as exclusive breastfeeding and delayed introduction of cow's milk. Vitamin D deficiency has been implicated by some observational and genetics studies, and a role of omega-3 fatty acids has also been suggested.

Type 2 diabetes

The slow onset of type 2 diabetes, and its usual presentation without the acute metabolic disturbance seen in type 1 diabetes, means that the true time of onset is difficult to determine. There is usually a long (3–7-year) pre-detection period during which glucose levels are elevated but often not diagnosed clinically. Depending on the setting, a substantial proportion of the total number of cases in a population at a given time may be undiagnosed. Globally, approximately half (50%) of the people aged 20–79 years with diabetes are unaware of their disease, though this proportion varies by world region and opportunities for systematic or opportunistic screening, ranging between a third undiagnosed overall in high-income countries, to more than 75% undiagnosed in low-income countries (IDF Atlas data, 2017).

Diagnosis of type 2 diabetes

Because the ratio of detected to undetected cases can vary by population and over time, epidemiological research aimed at defining the true prevalence of type 2 diabetes has relied on studies in which the presence and absence of disease are defined by a biochemical test for blood glucose level. Diagnostic criteria were previously limited to the use of blood glucose measures during a 75 g oral glucose tolerance test (OGTT), with the World Health Organization (WHO) defining diabetes as a fasting glucose $\geq$7.0 mmol/litre and/or a 2-hour post–challenge glucose of $\geq$11.1 mmol/litre.

The WHO and other agencies such as the American Diabetes Association have recently also approved the use of glycated haemoglobin (HbA_{1c}) for the diagnosis of diabetes, with a cut-off of 48 mmol/mol (6.5%). This test has the benefit of not requiring a fasted sample, but the availability of standardized laboratories and the cost are considerations in some contexts. The interpretation of HbA_{1c} test results should take account of anaemia, renal impairment and, for some HbA_{1c} tests, haemoglobinopathies. Whatever method is used to diagnose diabetes clinically, the diagnosis should be confirmed with repeat testing using the same method.

Variation in prevalence by geographical location, ethnicity, age and sex

Around 425 million people worldwide (approximately 9% of adults aged 20–79 years) were estimated to have diabetes in 2017 (IDF estimates). Figure 2 shows the age-standardized prevalence of type 2 diabetes and impaired glucose tolerance (IGT, defined as a 2-hour glucose of 7.8–11.1 mmol/litre). As in type 1 diabetes, there is marked geographical variation, but the pattern is different. The prevalence is lowest in rural areas of developing countries, generally intermediate in developed countries, and highest in certain ethnic groups, particularly those that have adopted Western lifestyle patterns. Populations with the highest prevalence have a high prevalence of obesity.

It is hypothesized that genetic susceptibility to obesity would be disadvantageous in times of food abundance, but advantageous when food is scarce, driving its persistence by natural selection. This 'thrifty genotype' hypothesis is supported by evidence of gene–environment interaction: individuals who migrate from low-prevalence areas to developed countries have an increased risk of type 2 diabetes. For instance, type 2 diabetes is up to 4- to 6-fold more prevalent in immigrant South Asians and African-Caribbean individuals in the UK compared with white European populations. There is a small sex difference in the global numbers of people with diabetes, with about 17 million more men than women estimated to have diabetes in 2017. The prevalence increases sharply with age in both sexes.

Incidence and temporal variation

The annual incidence is approximately 6.7–7 per 1000 per year in developed countries, when ascertained by self-report (USA data) or studies using serial glucose tolerance testing (UK data). The incidence in individuals known to have IGT is about 10-fold greater than in those with normal glucose tolerance. The risk of future progression to diabetes is also greater in those with other hyperglycaemic states, including gestational diabetes mellitus. US data show a near 5-fold increase of diagnosed diabetes, from 5.5 million persons in 1980 to 23.4 million in 2015. This increase mirrors the increasing prevalence of obesity. Worldwide, there is a projected increase in the prevalence of diabetes in adults from 425 million (8.8%) in 2017 to 629 million (10.1%) in 2045. Estimates of prevalence in developing countries show even more marked increases, particularly in areas where populations are rapidly adopting Western lifestyles.

The increase in prevalence of obesity in childhood has led to the appearance of type 2 diabetes in children and young adults, particularly those in highly susceptible ethnic groups. US data show an average annual increase in incidence of type 2 diabetes among youth (age 10–19 years) of 4.8% over 2002–2012, but the annual rate of increase in incidence was markedly higher among youth of Native American (8.9%), black (6.3%), Hispanic (3.1%) and Asian or Pacific islander (8.5%) origin compared with white youth (0.6%).[2]

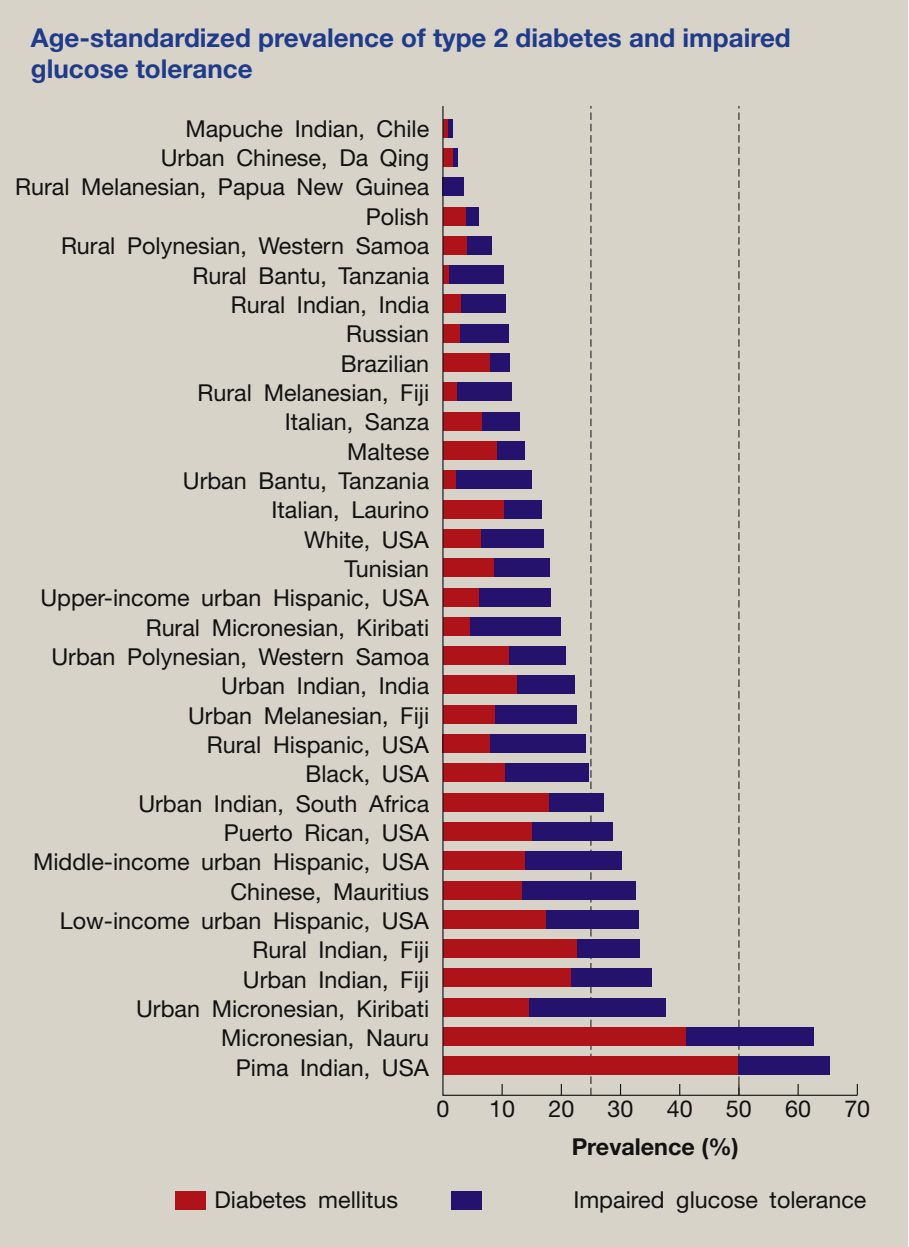

Figure 2

Aetiological factors

The main pathophysiological defects leading to type 2 diabetes are insulin resistance and a relative insulin secretory defect. The main aetiological risk factors are age, obesity, family history, ethnicity, physical inactivity and diet. Much progress has been made in understanding dietary risk factors, particularly the critical importance of overall dietary quality: the risk-raising impact of diets characterized by high consumption of red and processed meat, sugar-sweetened beverages and refined carbohydrate sources; the risk-reducing impact of fruit and vegetables; some types of dairy products such as yoghurt; and overall healthy eating patterns including higher sources of foods rich in polyunsaturated fats, fibre and whole-grain products, legumes and nuts.[3] Novel strategies to use nutritional biomarkers in tissues such as blood, which supplement information from self-report dietary assessment methods, are paving the way for a more detailed understanding of the association between diet and diabetes. The role of wider societal determinants, including nutrition transition in a global context, is also now recognized as a key driver of dietary intakes.

Although the heritability of type 2 diabetes is high (30–70%) and >400 genetic variants related to diabetes risk have now been identified,[4] the individual effects of genetic variants are modest; even when combined into a genetic score, known genes contribute little to prediction of diabetes. Phenotype-based risk models provide greater discrimination for diabetes. The current conclusion is that genetic variants provide important insights into the biological pathways and pathogenesis of diabetes, but

not its prediction. It is likely that interactions between behavioural and genetic factors provide an explanation for the risk of type 2 diabetes, but demonstrating such an interaction is challenging.

Prevention and screening

Primary prevention

Randomized clinical trials in several countries have provided evidence that, in high-risk individuals with IGT, progression to type 2 diabetes can be reduced by intensive lifestyle intervention with diet or physical activity, or with drug therapy using glucose-lowering agents such as metformin. In addition to their clinical effectiveness, there is now also evidence for the cost-effectiveness of these interventions. The challenges that remain are to determine how high-risk individuals should be identified, and how lifestyle changes in terms of healthier diet and regular physical activity can be sustained in real-world settings.

As in many areas of primary prevention, high-risk approaches can be effective for the individuals included in the programmes but have a limited impact on the public health burden of diabetes. Complementary approaches that seek to make small shifts in the population distribution of dietary and physical activity behaviours are required. Such approaches make relatively little difference to risk at the individual level, but have a major impact on the public health burden of diabetes when that risk reduction is summated across large numbers of people in the population. The future challenge involves finding ways of integrating high-risk and population approaches to prevention, and balancing relative investment in the two strategies.

Secondary prevention: screening

Screening for type 2 diabetes was proposed in the hope that early detection and treatment would reduce long-term burden. This was tested for cardiovascular outcomes among individuals with screen-detected diabetes in ADDITION (Anglo-Danish-Dutch Study of Intensive Treatment In People with Screen Detected Diabetes in Primary Care), a primary care-based trial of intensive multifactorial treatment compared with routine care. This trial has shown the following: that screening for diabetes is feasible, with little short- or long-term adverse psychological impact; that cardiovascular risk factors (blood pressure, cholesterol, smoking, weight) improve after screen detection of diabetes, even among those being given routine general practice care; but that, at the population level, invitation of high-risk individuals to screening is not associated with a reduction in all-cause or diabetes-related mortality over 10 years.[5]

Uncertainties remain concerning optimal strategies to increase uptake of screening, deliver care to screen-detected patients and manage those who screen negative but are at high risk of diabetes and cardiovascular disease; the overall cost-effectiveness of screening programmes is also uncertain. Rather than screening whole populations for diabetes, primary care teams should focus efforts on earlier detection, lifestyle advice and intensive treatment of risk factors among individuals at high risk of diabetes and cardiovascular disease. In some settings, such as the UK, this is offered within the vascular health check programme in primary care.

New horizons

There is continuing interest in opportunities for the personalized prevention and management of diabetes. Whether such personalization will best be achieved through genetic or phenotypic approaches, or a combination, is the subject of ongoing research. Further refinement of the classification of type 2 diabetes into heterogeneous subgroups has also been proposed as a strategy to help differentiate people with differing disease progression trajectories. ◆

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TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online here.

Question 1

A 32-year-old woman presented with tiredness and increased thirst. She was otherwise well and was not pregnant. She was of South-Asian Bangladeshi origin and living in London.
Clinical examination was normal. Her body mass index was 25 kg/m^2.

Investigations

- Haemoglobin 130 g/litre (115–165), with no abnormal haemoglobin detected

Which test would be the best to exclude a diagnosis of diabetes?

A Urinalysis for glucose
B Either one of fasting glucose, or an oral glucose tolerance test, or a glycated haemoglobin (HbA_{1c}) test
C Both an oral glucose tolerance test and HbA_{1c} test should be done, as neither is sufficient on its own
D Not the HbA_{1c} test as this test should not be used in some ethnic groups
E Only an oral glucose tolerance test

Question 2

A 58-year-old man presented with non-specific tiredness. He was otherwise well, was a life-long non-smoker and consumed alcohol infrequently in moderate amounts. He was white British and worked in an office as a clerk.
On clinical examination, he was obese, with a body mass index of 32 kg/m^2. Blood pressure was 120/80 mmHg.

Investigations

- Haemoglobin 155 g/litre (130–180)
- HbA_{1c} 50 mmol/mol (20–42); 6.7% (4.0–6.0)

What is the most appropriate next step in management?

A. Repeat the HbA_{1c} in 1 year's time
B. Perform an oral glucose tolerance test
C. Start him on oral antidiabetic medication immediately.
D. Confirm diagnosis of diabetes with a repeat HbA_{1c} test, and if confirmed, start sulphonylurea therapy
E. Confirm diabetes diagnosis with a repeat HbA_{1c} test, give lifestyle advice and review him in 3 months

Question 3

At a meeting for medical students that you attended, a second-year medical student gave a talk on various aspects of type 1 diabetes that he had understood from his self-study.

Which one of the medical student's statements would you agree with?

A. The incidence of type 1 diabetes has been stable over the last 20 years or so
B. In those aged over 35 years, the incidence of type 1 diabetes is on the decline
C. Various environmental factors may play an important part in the aetiology of type 1 diabetes
D. The incidence rates of type 1 diabetes vary substantially by country, but within a country the incidence rates are usually very similar in different regions because of shared factors
E. Type 1 diabetes generally has a greater incidence in spring and summer