9 Diabetes

Burden, epidemiology and priority interventions

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Diabetes is one of the biggest challenges facing society in the 21st century. In the past three decades the prevalence of type-2 diabetes (T2D), which is closely related to obesity, has risen dramatically in almost all countries.[1] A number of interventions are available to control all forms of diabetes and for the prevention of T2D.

Definitions

Diabetes mellitus is a chronic, metabolic disease characterized by elevated levels of blood glucose. Over time the high glucose levels and the associated metabolic disorders can lead to serious damage to the heart, blood vessels, eyes, kidneys and nerves. The different types of diabetes and their characteristics are shown in Box 9.1. Around 95% of all cases are T2D.

BOX 9.1 TYPES OF DIABETES (ADAPTED AND SIMPLIFIED FROM THE WHO CLASSIFICATION)[2]

Type-1 diabetes (T1D). The immune system attacks and destroys the cells in the pancreas that produces insulin. Persons with T1D must take insulin every day to stay alive. Although T1D often develops at an early age, T1D can appear at any age. There are no known measures to prevent this form of diabetes. Without prompt diagnosis and treatment, T1D is rapidly fatal. The incidence of T1D may be underestimated in areas with deficient health services where deaths from T1D may go unrecognized.

Type-2 diabetes (T2D). The body does not produce enough insulin to maintain normal glucose levels. In nearly all cases of T2D, there is 'insulin resistance', meaning that the pancreas must produce increasingly higher amounts of insulin to 'force' blood glucose to enter into body cells. T2D and insulin resistance largely occur in response to

DOI: 10.4324/9781003306689-11

increased adipose tissue. T2D develops most often in middle-aged and older people but also increasingly in young adults and adolescents who are overweight or obese.

Gestational diabetes. This form of diabetes develops during pregnancy and disappears after giving birth. It appears in the second or third trimester and is more common in women with a high body mass index (BMI). Gestational diabetes can affect the pregnancy for both the foetus and the mother. Women with gestational diabetes have a greater risk of developing T2D later in life. T1D and T2D can also be diagnosed during pregnancy.

Other causes of diabetes. Less common causes of diabetes include inherited monogenic diabetes and disease of the pancreas (cystic fibrosis-related diabetes, pancreatitis). Elevated levels of blood glucose can also be seen in acute or chronic diseases.

Diagnosis of diabetes is based on one of the following:

- Fasting plasma glucose ≥7.0 mmol/l.
- Two-hour post-glucose-load plasma glucose ≥11.1 mmol/l after a 75 g oral glucose tolerance test (variations are often used for gestational diabetes).
- HbA1c ≥48 mmol/mol (≥6.5%).
- A random blood glucose ≥11.1 mmol/l in the presence of signs and symptoms.

Pre-diabetes is a term often used to describe moderately elevated levels of blood glucose (but blood insulin level is generally already substantially increased), which is associated with metabolic complications and a higher risk of progression to T2D. Its prevalence in the population can be two or three times higher than that of diabetes. There is no universally accepted definition of 'pre-diabetes' since the attribution of the diagnostic label has different implications for preventive action in different countries. Generally, it is based on one of the following criteria:

- Fasting plasma glucose ≥6.1 to <7.0 mmol/l according to WHO or ≥5.5 to <7.0 mmol/l according to the American Diabetic Association (ADA).
- Two-hour post-load plasma glucose ≥7.8 to <11.1 mmol/l after a 75 g oral glucose tolerance test.
- HbA1c ≥42 to <48 mmol/mol (6.0–<6.5%) in most countries or 5.7–6.4% according to ADA.

Disease burden

More than 500 million adults have diabetes, of whom 80% live in low- and middle-income countries, in line with the larger proportion of people living in these countries.[3]

Table 9.1 Mortality attributable to diabetes and high fasting blood glucose (IHME)

	Global		*HICs*		*Upper-MICs*		*Lower-MICs*		*LICs*	
	1990	*2019*	*1990*	*2019*	*1990*	*2019*	*1990*	*2019*	*1990*	*2019*
Diabetes as a direct cause of death										
Proportion of all deaths (%)	1.4	2.7	2.1	2.3	1.4	2.6	1.2	3.3	1.0	1.9
Age-standardized mortality rates (per 100,000)	18	20	14	10	15	16	36	34	24	33
High blood glucose as a risk for other diseases										
Proportion of all deaths (%)	6.2	11.5	11.3	12.8	6.7	11.9	4.3	11.8	2.6	5.7
Age-standardized mortality rates (per 100,000)	84	83	75	54	83	76	93	123	101	107

Diabetes was the direct (immediate) cause (e.g. diabetic renal disease, diabetic coma) of 0.7 million deaths (1.4%) in 1990 and 1.5 million, globally, in 2019 (2.7%) (Table 9.1, estimates from IHME). As a risk factor (e.g. high blood glucose increases the risk of CVD by two to four times[4]), high blood glucose (including moderately elevated glucose defining 'pre-diabetes') accounted for 6.5 million deaths (11.5% of all deaths in 2019 globally), an increase from 2.9 million in 1990. The percentage of deaths attributable to high blood glucose increased in all regions between 1990 and 2019, with a steeper increase in low- and middle-income countries, a twofold increase, than in high-income countries (HICs), partly owing to aging populations. The age-standardized mortality rates attributable to high blood glucose (which are not influenced by the age distribution of the populations compared) were lower in HICs and upper-middle-income countries (where rates decreased over time) than in low- and middle-income countries (where rates increased), partly reflecting a steeper increase in the prevalence of T2D and poorer blood glucose control in low- and middle-income countries than HICs.[5]

According to IHME, the following proportions of T2D mortality were attributable to modifiable risk factors globally in 2019: increased body mass index 42%, dietary risks (low fruit, high red/processed meat, low whole grain, high sugar-sweetened drinks) 26%, ambient and household air pollution 20%, tobacco use 16%, low physical activity 8%.

Consequences of diabetes

Very high blood glucose concentration results in acute symptoms of polyuria (excessive urination), thirst, loss of weight, hunger and tiredness, the classic way that those with T1D first present. If T1D is untreated, diabetic ketoacidosis, coma and death follow.

Over many years, elevated blood glucose in T1D and T2D affects the inner linings of both large (macrovascular damage) and small arteries (microvascular damage). Microvascular damage can result in blindness and kidney failure and destroys the sensory nerves, particularly in the lower limbs, which makes injury a major risk. Healing of injuries and wounds is less effective in patients with diabetes, and this, coupled with vascular impairment, can lead to ulceration and persistent infection which may require amputation. Macrovascular complications of diabetes include ischaemic heart disease (IHD), stroke and peripheral arterial disease. Diabetes is also associated with increased susceptibility to infections and more serious complications from infections.[6]

Diabetogenic environment

This concept of a diabetogenic environment is essentially the same as that for the obesogenic environment described in Chapter 10 on obesity. This has resulted in the current high and increasing levels in nearly all countries of 'diabesity', the combined 'epidemic' of obesity and T2D.

Interventions at the population level

Tackling the diabetogenic environment requires the same sorts of macro-policy interventions across multiple sectors as described for the obesogenic environment (Chapter 10, Box 3). Tackling the diabetogenic environment also requires behaviour change at scale as well as whole-of-government (e.g. legal, fiscal and regulatory policies to address the commercial determinants of NCDs) and whole-of-society (e.g. civil society and the private sector) actions. These issues are considered in more detail in other chapters.

Screening

Although it is unclear if systematic testing of blood glucose in the entire population is cost-effective,[7] opportunistic testing of high-risk individuals has been shown to be cost-effective in some settings for detecting diabetes and pre-diabetes and reducing their associated disease burden,[8] and, for example, the US Preventive Services Task Force recommends that overweight or obese adults aged 35–70 years are screened for diabetes and pre-diabetes.[9]

Interventions at the individual level

Risk factor reduction. Weight control is central to the management of T2D and pre-diabetes.[10] For diabetic patients who are overweight or obese, intensive weight management (e.g. loss of >10 kg) markedly improves blood glucose and associated metabolic risk factors[11] and can even result in remission to a non-diabetic state in a significant proportion of patients.[12] Interventions targeting weight control at the individual level are described in Chapter 10 on obesity,

including the extreme but highly effective 'bariatric surgery'.[13] Encouraging physical activity, quitting smoking and reducing alcohol consumption are also important. WHO best buys include advice on healthy lifestyles and medical treatment of risk factors among individuals with high CVD risk.

Pharmacologic treatment for T1D. Insulin is the cornerstone of treatment. However, insulin is not sufficiently available or affordable in many settings, resulting in an increased risk of death. Good glycaemic control can be achieved with fastidious attention to insulin dosing and tight monitoring of blood glucose (including self-monitoring). Newer biosimilar products (insulin analogues, such as glargine which is included in the WHO Essential Medicines List) may help achieve tighter glycaemic control but at a much higher cost.[14,15] Newer devices, ranging from fairly inexpensive pens that make injections easier, to complex and very expensive automated insulin delivery systems, are increasingly available to support patients in strengthening their ability to monitor and control blood glucose levels more effectively.[16]

Pharmacologic treatment for T2D. Metformin is inexpensive and is the drug of first-choice. Sulphonylureas, at least first generations, are no longer recommended as a first–line agent since they may cause weight gain. Insulin is often required when oral hypoglycaemic medications cannot reduce blood glucose sufficiently. However, insulin often increases body weight, which further increases insulin resistance. This highlights the opportunity that comes from newer treatments which, like metformin, reduce blood glucose but also impact favourably on body weight and prevent diabetes complications. GLP-1 analogues (glucagon-like peptide-1 receptor agonists, e.g. semaglutide, exenatide) reduce satiety (and thus lower body weight) and also reduce CVD risk. SGLT-2 inhibitors (sodium-glucose cotransporter-2 inhibitor, e.g. gliflozins) slow chronic kidney disease progression and reduce heart failure and CVD risk.[17,18] These treatments can be even more effective than insulin, and some of them also have the advantage of requiring less frequent administration.[19] Although expensive, their costs are decreasing, making them increasingly cost-effective, even in low- and middle-income countries.[20] As many patients with T2D have comorbidities, and given that diabetes is a strong risk factor for developing CVD, additional drugs, for example, to control BP and lower blood cholesterol, are most often also required[21] (see Chapters 6 on CVD, 36 on high-risk approaches and 20 on cholesterol). Guidelines and protocols for the management of T2D are widely available.[22,23,24]

Follow-up

Patients with diabetes need to be able to access care to prevent and manage acute and long-term complications. Hypoglycaemia (often a result of treatment) and hyperglycaemia (which can result from insufficient treatment, changes in diet or levels of physical activity or acute infection) can be life-threatening, so patients and those around them should be able to recognize hypo- or hyperglycaemic emergencies and how to manage these situations should be managed.

Patients should be supported to be assiduous in monitoring their blood glucose (including self-monitoring), regularly examining and examining their skin and feet, and using suitable footwear and bedding. Follow-up also involves diligent and rigorous long-term monitoring for: (i) eye disease (retinopathy, cataract and glaucoma), which should be done every two years at a minimum; (ii) kidney disease (through annual assessment, including measurement of serum creatinine and albuminuria); (iii) diabetic neuropathy (through annual assessment); and (iv) long-term macrovascular complications (IHD, cerebrovascular disease and peripheral vascular disease), which includes regular assessment and treatment of BP, blood lipids, smoking cessation and daily acetylsalicylic acid for patients who have had a CVD event and no history of major bleeding. Patient support groups are an important source of advice and support.

The importance of strong health services and systems

Effective long-term care requires partnerships between patients and multiple healthcare professionals, with both taking responsibility for managing the disease. As with all NCDs, optimal long-term care for patients with diabetes requires strong health services and systems (Chapter 42). However, evidence-based care for people with diabetes is sub-optimal in all countries, even the most well-off countries.[25] In addition, half of all adults across the world with T2D are undiagnosed, and large proportions of those diagnosed are untreated or insufficiently treated,[26] and these proportions are much higher in low- and middle-income countries.[27] Continuing lack of access to effective care, particularly access to insulin, highlights a range of deep systemic issues, including that: (i) three multinational companies control over 95% of the global insulin supply, although the inclusion of insulin in the WHO Prequalification of Medicines Programme is an opportunity to facilitate entry of new companies into the market; (ii) many governments lack policies on the selection, procurement, supply, pricing and reimbursement of insulin; (iii) mark-ups in the supply chain affect the final price to the consumer; (iv) expenses related to diabetes often require out of pocket payments; and (v) the organization of diabetes management within the healthcare system often affects patient access to insulin.[28]

Targets and indicators in the WHO Global NCD Action Plan

Target	To halt the rise in diabetes and obesity between 2010 and 2025. (Combining diabetes and obesity into one target emphasizes the strong relationship between the two).
Indicators	Age-standardized prevalence of overweight and obesity in persons aged 18+ years (respectively BMI ≥25 kg and ≥30 kg/m^2). Prevalence of overweight and obesity in adolescents (defined according to the WHO growth reference for children and adolescents).

Monitoring

Examination population surveys are useful to estimate the proportion of the population with diabetes/pre-diabetes and the proportion of those who are treated and adequately controlled. Indicators at health care level are also useful, including the proportion of patients treated/controlled for blood glucose, BP and blood lipids, frequency of exams to assess complications (e.g. eye, kidney or foot), and broader indicators, such as the presence and use of diabetes protocols, monitoring systems and availability of medicines.

In 2021, WHO launched the Global Diabetes Compact,[29] an initiative to bring partners together to improve access to equitable, comprehensive, affordable and quality treatment and care, as well as to support the prevention of T2D. The initiative also sets priority metrics and targets to serve as diabetes-related health objectives for all countries of the world to achieve by 2030.[30]

Notes

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