6.4 Diabetes

See Background Paper 6.4 (BP6_4DM.pdf)

Background

Diabetes and diabetes-related illnesses place an enormous burden on the health care systems of countries throughout the world. In 2008, diabetes accounted for about 2% of the burden of disease (DALYs) in the WHO European Region and about 1.5% worldwide. At the global level, diabetes accounted for 2% of all deaths – about the same as in the EU27. In 2012, there were an estimated 370 million people with diabetes worldwide and nearly 5 million deaths due to diabetes and diabetes-related illnesses (see Appendix 6.4.1).

Over time diabetes can damage the heart, blood vessels, eyes, kidneys and nerves. The disease is a considerable cause of premature mortality. Due to increases in life expectancy, urbanization, rates of overweight and obesity, and the prevalence of diabetes. The disease burden for diabetes is likely to worsen, particularly in low- and middle-income countries.

There are primarily two types of diabetes. Type 1 diabetes is an autoimmune disease in which the pancreas can no longer produce insulin. As a result, the body cannot control blood sugar levels. The key characteristics of type 1 diabetes are its onset mostly in young people and the extremely wide global variation in the incidence of the disease. There is a comprehensive lack of knowledge about the cause of this disease, and it remains an epidemiological puzzle. The overall standardized incidence varies from 0.1:100 000 per year in the Zunyi region of China to more than 40:100 000 per year in Finland. Type 1 diabetes appears to be on the increase in almost all populations. In Europe, the incidence of (childhood onset) type 1 diabetes continues to rise but the increase is not necessarily uniform. This pattern of change suggests that key risk exposures differ over time in different European countries.

Type 2 diabetes (previously called adult onset) is a metabolic disorder in which the body gradually becomes insensitive to the action of insulin with decreased beta cell mass and progressive beta cell failure so that blood sugar control is also compromised. Overall, the prevalence of type 2 diabetes dominates the total diabetes burden. In developed countries, most people with diabetes are aged over 60 years, while in developing countries the disease mainly affects people of working age (40 to 60 years).

Developments since 2004

The most recent global projections for diabetes are far higher than predictions made around the time of the 2004 Priority Medicines Report. In 2012, of the estimated 370 million people affected by diabetes worldwide, about half live in the Western Pacific, South Asia, and Eastern Mediterranean regions. See Appendix 6.4.1 and Figure 6.4.1
below (created from recent data assembled by the International Diabetes Federation (IDF) at Appendix 6.4.2). The IDF regions are not coincident with WHO regions.

**Figure 6.4.1: Median Regional Diabetes Prevalence (%)**

Source: Adapted from recent data assembled by the International Diabetes Federation (IDF): Appendix 6.4.2 at IDFAtlas5E_Detailed_Estimates.xls

Note: WP: Western Pacific; SACA: South and Central America; AFR: Africa; MENA: Middle East and North Africa; NAC: North America and Caribbean; SEA: Southeast Asia; EUR: Europe

It is estimated that from 2012 to 2030 the total number of people with diabetes worldwide will increase by about 180 million (from 371.33 million to 551.87 million). This dramatic increase of 48% from 2012, at an annual growth of 2.7%, is twice the annual growth of the total global adult population. Of this global increase, 42% is projected to occur in India and China alone. In low- and middle-income countries, adult diabetes numbers are likely to increase by over 60% from 2012 to 2030, compared to 20% in developed countries, while the total adult populations are expected to increase by 36% and 2% respectively.

With increasing levels of obesity among children, there is an alarming trend for juveniles to develop type 2 diabetes. Predictions from the United States suggest that within 10 years, normal adult onset type 2 diabetes might become the most common form of newly diagnosed diabetes in adolescent youth.
Remaining challenges

In view of the burden and associated costs of diabetes, the ongoing epidemic represents a major public health problem requiring effective control. There is currently a large gap between the prevalence of diabetes and treatment rates, with an estimated 30% to 50% of diabetes cases remaining undiagnosed and therefore untreated.4

People with type 1 diabetes require lifelong insulin replacement and face the additional complications of diabetes-related diseases. At present, there is no real ability to provide effective, long-term, tight blood sugar control through insulin replacement therapy. Moreover, insulin requires refrigeration and this creates an access problem in many low- and middle-income countries. Primary prevention of the disease may depend on the determination of autoantibody combinations conferring a high risk of progression to diabetes, which typically become established within the first three years of life. Therefore, ideally, primary prevention should be attempted as early in life as possible (i.e. soon after birth).8 Safety is the major criterion for any form of primary prevention, since only a small percentage of those at risk would be expected to develop diabetes. Meanwhile, metabolic testing of young people with type 1 diabetes can identify those at imminent risk of progression, which helps to stage the disease process. Major studies have demonstrated the feasibility of large scale controlled trials in antibody-positive first degree relatives of those with diagnosed type 1 diabetes, but the logistics are difficult and the number of interventions that can be tested is very limited.9

Primary prevention of type 2 diabetes has always been centered on control of the energy economy of the body (i.e. achieving a negative calorie balance if weight loss is required and/or optimal intake of carbohydrates and lipids).10,11 Controlling obesity and increasing physical inactivity can prevent, or at least delay, the development of the disease in many genetically susceptible individuals. However, success in controlling these risk factors on a large scale has been limited. Efforts to control blood sugar levels in type 2 diabetes has become increasingly complex and, to some extent, controversial as there is still debate over how “flexible” or “tight” such control should be. With a widening array of pharmacological agents now available, there is growing concern about their potential adverse effects and uncertainties regarding the asserted benefits of aggressive glycemic control on macrovascular complications.12 In the long run, many patients with type 2 diabetes will require insulin therapy alone or in combination with other agents to maintain glucose control.

Although blood glucose lowering agents can assist in preventing the onset of type 2 diabetes, a significant percentage of patients do not achieve glucose or weight goals and develop complications. At present, there is an inability to prevent progressive loss of islet B-cell function/mass (affecting prevention and then progression of hyperglycemia). There is also an inability to manage the progressive ineffectiveness of glucose-lowering treatments over time, resulting in the need for multiple therapy (and usually insulin about 10 years after the onset of the disease).13
There are considerable gaps in our understanding of optimal applications of existing and new therapies, particularly since many patients will have coexisting conditions that require polypharmacy. The risk of possible drug interactions and the safety of new agents will remain of primary concern. The accumulated evidence for type 2 diabetes suggests that not everyone benefits from aggressive glucose management.\textsuperscript{14}

Diabetes is an example of a disease with an unmet global medical need and conforms to the "commonality of interest" principle of the Priority Medicines Project. The dramatic increases in diabetes that are projected over the next several decades require a global strategy for prevention, treatment and medicine development.

**Research needs**

The availability of heat-stable insulin, for use in developing countries with limited access to refrigeration, and for use by travellers, would be a major public health advance. Another major advance would be the development of glucose-responsive insulin. At present, all insulin treatments for people with diabetes release an amount of insulin at fixed times that is not in proportion to local blood glucose levels, in contrast to people without diabetes, in which the body secretes insulin in proportion to local blood glucose levels. A glucose-responsive insulin for people with diabetes could therefore be a transformative solution, vastly improving the quality of life of people with insulin-dependent diabetes.\textsuperscript{15,16}

In addition, there is a need for therapies directed at multiple risk factors for type 2 diabetes, such as dyslipidemia, hypertension and obesity. These have been a major focus of research and therapy. One possible future strategy is the fixed-dose combination ‘polypill’, whereby several risk factors are treated with a single capsule containing a combination of pharmaceuticals, which can be assembled in various ways. A second pharmacological strategy to reduce the problems associated with polypharmacy for patients with several risk factors is to develop single drugs that have multiple targets or modulate targets that affect several risk factors.

Research is also needed into effective delivery of preventive strategies to delay progression of the disease and its complications. This should integrate individual, clinical, system, and society-level approaches that span the full course of life.

- The evidence base for clinical and public health interventions needs to be expanded to include a much broader spectrum of disciplines including, for instance, experts in behavioural economics, systems dynamics, political science, and urban planning. Integration of surveillance, clinical and population-based epidemiology, health services research and economics is sorely needed.
- Large, long-term intervention studies are needed to identify effective strategies for reducing barriers to diabetes care and improving adherence to treatment and management regimens.
- The gap is large between scientific and technological progress and its implementation. Europe can help reduce this gap by championing international
efforts to assure that children and adolescents around the world do not suffer premature death and disability because their diabetes is mismanaged.

- Although effective preventive strategies exist for type 2 diabetes, the susceptibility genes identified so far do not provide predictive abilities strong enough to warrant genetic screening. Therefore continued research into genetic screening is needed.
- The safety, efficacy, and economic impact of self-adjusting closed-loop control systems are currently unknown and deserve further investigation.
- Translational research, which seeks to understand how advances can be adopted in community-based and often uncontrolled conditions (e.g. resource-poor environments) has received little attention in the diabetes field. Some of the important questions in translational research cannot be addressed in randomized trials.
- Community-based participatory research, issues related to lifestyle, diet, physical activity and cultural preferences should be explored.
- A diabetes registry that keeps track of glycosylated haemoglobin (A1C) values is one example of linking diabetes with key policy decisions. Such a registry was implemented in New York City.  

Substantial resources continue to be allocated to diabetes research by public and private funders. By 2019, the global market for diabetes is expected to be worth US$ 35 billion and the private sector is investing heavily. The pharmaceutical industry considers development of effective diabetes medications to be a major goal. The European Commission (EC), together with support from network organizations, has the opportunity to continue research on genetic and environmental factors in different population groups.

References


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