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The burden of type 2 diabetes: are we doing enough?

P Zimmet

SUMMARY

Increasing levels of obesity, arising from energy-rich diets and sedentary lifestyles, are driving a global pandemic of type 2 diabetes. The prevalence of type 2 diabetes worldwide is set to increase from its present level of 150 million, to 225 million by the end of the decade and to as many as 300 million by 2025. Shocking as they are, these figures represent only clinically diagnosed diabetes, and many more cases of diabetes remain undiagnosed and untreated. In addition, up to one-quarter of western populations have impaired glucose tolerance or the dysmetabolic syndrome, which are considered to represent pre-diabetic states. Type 2 diabetes is appearing increasingly in children and adolescents, and the frequency of diagnosis of paediatric type 2 diabetes is outstripping that of type 1 diabetes in some areas. The long-term complications associated with type 2 diabetes carries a crushing burden of morbidity and mortality, and most type 2 diabetic patients die prematurely from a cardiovascular event. Diabetic patients are more than twice as costly to manage as non-diabetic patients, due mainly to the high costs associated with management of diabetic complications. Indeed, diabetes care already accounts for about 2-7% of the total national health care budgets of western European countries. Controlling the type 2 diabetes epidemic will require changes to the structure of healthcare delivery. Well-resourced interventions will be required, with effective co-ordination between all levels of government, health care agencies, multidisciplinary health care teams, professional organisations, and patient advocacy groups. Above all, intervention is needed today.

Key-words: Type 2 diabetes · Health economics · Cardiovascular disease · Quality of life · Diabetic complications.

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Today we are seeing a paradox in global public health. In recent decades, we have seen the re-emergence of communicable diseases such as tuberculosis, and a new group including HIV/AIDS, Ebola virus and, most recently, the devastating epidemic of severe acute respiratory syndrome (SARS). In addition, there is still a global crisis resulting from widespread malnutrition. However, against this background, we are seeing a dramatic rise in prevalence of chronic non-communicable diseases such as type 2 diabetes, cardiovascular diseases, hypertension and obesity in developed and developing nations.

There were already signals that diabetes was to become the epidemic of the 21st century in the early 1970s. At this time, Bennett and his colleagues discovered an extraordinarily high prevalence of type 2 diabetes in the Pima Indians of the USA [1], and we reported on the equally high rates of diabetes in the Micronesian population of Nauru and other Pacific island communities [2, 3]. Over subsequent decades, numerous reports have highlighted the high prevalence of type 2 diabetes in a number of other populations including native Americans, Afro-Americans, and Mexican Americans in the USA [4-7], native Canadians [8], Australian Aborigines and Torres Strait islanders [9], and Polynesians in New Zealand [10, 11].

Prevalence of diabetes

The prevalence of type 2 diabetes is rising relentlessly around the world *(Fig 1)*. Current estimates suggest that, globally, the number of persons with diabetes will rise from 151 million in the year 2000, to 221 million by the year 2010, and to 300 million by 2025 [12, 13]. This rise is predicted to occur in virtually every nation, with the greatest increases expected in developing countries. Type 2 diabetes will account for nine patients in every ten of these diagnoses. This explosive increase in the prevalence of type 2 diabetes, and the consequences of its complications and associated disorders, represents the greatest health care challenge facing the world today [14].

The highest rates of type 2 diabetes occur in native Americans and Pacific islanders, followed by Hispanics or Mexican Americans, people originating from the Indian subcontinent, South East Asians and African Americans [12, 13]. In addition, a relatively high prevalence has been reported from some of the Middle East Arab states [15, 16], and from disadvantaged minorities in the developed countries, including Australia's indigenous population [17, 18]. Type 2 diabetes affects up to 40% of adults in native American and Pacific island populations [1, 2, 19, 20] and the years 1976 to 1988 saw an increase from 11.4% to 14.3% in the prevalence of diabetes among people age 40-74 years in the USA [21]. In China, a prevalence figure of 2.5%, from a 1994 survey of 224,251 subjects aged 25-74 from all parts of the country, was about three-fold higher than prevalence estimates from a decade before [22]. The type 2 diabetes prevalence in an urban south Indian population among individuals aged over 20 years rose from 8.3% in 1989 to 11.6% in 1995 [23], while in Denmark, a 38% rise in diabetes prevalence has been reported over a 22-year period [24]. In our recent national study in Australia, 7.4% of adults were found to have diabetes compared to an estimated 3.4% in 1981 [18].

Our studies in Mauritius have provided a future guide to the magnitude of the global diabetes epidemic [25]. The population of this nation are Asian Indian, Creole (Black) and Chinese, and these three ethnic groups account for over 66%

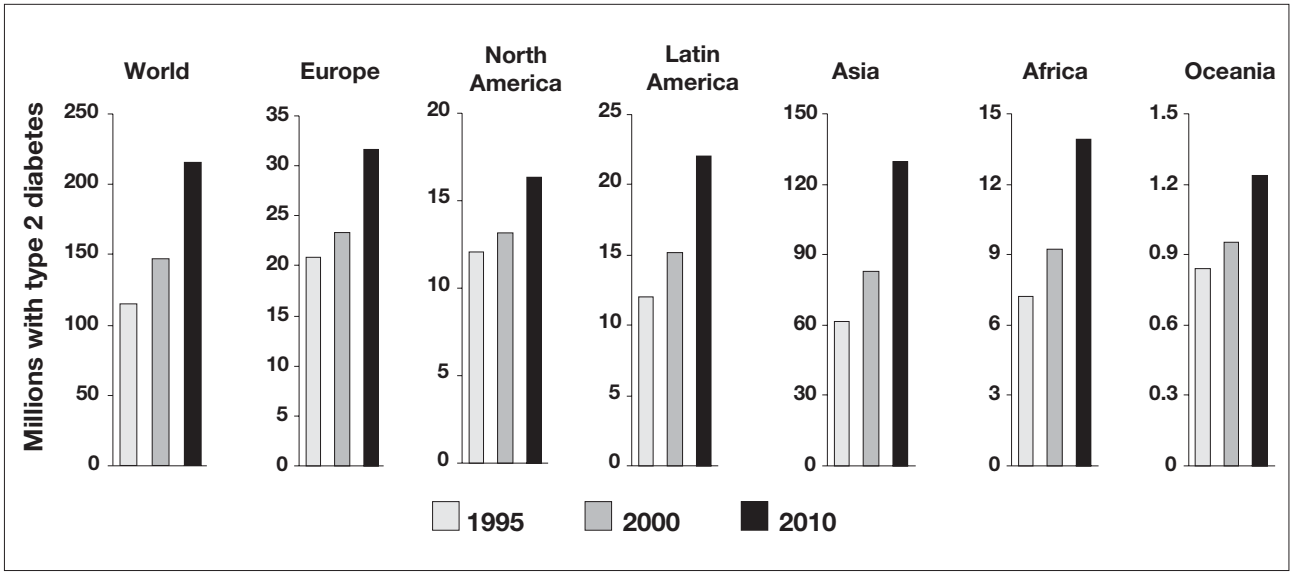


Figure 1
Increasing prevalence of type 2 diabetes by region [12].

of the world's population. Mauritians have a high diabetes prevalence [26] and a 40% secular increase occurred between 1987 and 1992 in Mauritian Asian Indians and Creoles [27, 28]. The Mauritian Chinese share this high prevalence [26]. Data showing that the prevalence of type 2 diabetes doubled between 1984 and 1992 in Singaporean Chinese, together with the high prevalence in Taiwan [29, 30], provide an alarming indicator of the magnitude of the anticipated epidemic in the People's Republic of China (PRC) [25]. In the PRC, the prevalence of type 2 diabetes was, until recently, less than 1% [31], but recent studies show a three-fold increase in prevalence in certain areas of China within the last two decades [22]. If China has just 50% of the prevalence of diabetes in Taiwan, the number of individuals with diabetes will increase dramatically from 8 million in 1996 to well over 35 million by 2010.

Diabetes prevalence is currently estimated at 6.2% in the developed world, and forecast to rise to 7.6% by 2025 [13]. Developing countries are starting from a lower baseline, at 3.5%, but this is set to increase by more than a third, to 4.9%, in 2025. The lower overall prevalence in developing countries conceals considerable heterogeneity between individual nations. In Latin American countries, the crude prevalence of type 2 diabetes for 2000 ranges from 1.2% in Chile to 8.2% in Argentina [32] and in Africa from 0.7% in Tanzania to 10.0% in the Northern Sudan [33]. In Asia, the overall prevalence is low in some countries, such as Bangladesh (roughly 1-2%), but higher in others, such as Pakistan (4-7%) [12, 13]. The Pacific islands bear an especially heavy burden of diabetes, as described above, with an estimated prevalence of 7% in Kiribati, 8% in the Cook islands, 11% in Fiji, and 24% in Nauru [13].

Factors driving the global epidemic of type 2 diabetes

Increased rates of obesity due to low levels of physical activity and high-energy diets are driving this global epidemic [14]. For example, between 1990 and 1998, the average body weight of men and women in the USA increased by 3.4 kg and 3.9 kg, respectively, while the prevalence of diabetes increased from 4.9% to 6.5% [34]. Obesity, particularly abdominal obesity, promotes the development of insulin resistance and the dysmetabolic syndrome (also known as the "metabolic syndrome", or "syndrome X") and, ultimately, type 2 diabetes [35-38]. Approximately one quarter of the population of the developed world are already believed to have the dysmetabolic syndrome [36, 39].

Impaired glucose tolerance or impaired fasting glucose develop in response to worsening insulin resistance before the clinical diagnosis of type 2 diabetes is made, and signify an increased risk of developing type 2 diabetes [40]. Between 10% and 25% of western populations may already have IGT [21, 41]. For example, the Australian Diabetes, Obesity and Lifestyle Study (AusDiab) recently surveyed the glycaemic status of a population of 11,247 adults [18]. The overall prevalence of diabetes was 7.4%, but the combined prevalence of impaired fasting glucose or impaired glucose tolerance was more than twice as high, at 16.4%. These glucose-intolerant, but non-diabetic, individuals represent a reservoir of potential new diabetes cases. Approximately 4-9% of individuals with impaired glucose tolerance go on to develop type 2 diabetes each year [42].

Demographic, social and cultural factors profoundly influence the prevalence of diabetes in a developing nation, as shown by recent studies in India. The overall prevalence of diabetes in that country was estimated at 4.0% in the year 2000 [13]. However, a survey in Madras, an urban area of southern India, showed that the prevalence of diabetes had risen by 40% between 1988-1989 and 1994-1995, and by a further 16% in the year 2000 [25, 43]. Increasing urbanisation and sedentary work was significantly associated with this increased prevalence [44, 45]. Indeed, 12% of urban residents, and only 2% of rural residents were found to have type 2 diabetes in this survey. South Asians who migrate to developed nations face a similar increase in the risk of developing diabetes [46, 47]. A greater tendency to insulin resistance is already evident in children of south Asian descent in the UK, which is associated with a steeply rising incidence of type 2 diabetes [48, 49]. The impact of urbanisation on diabetes prevalence in India is consistent with experience from other cultures, such as Australian Aborigines, Pacific islanders and native Americans [17, 50]. Global estimates predict that the ratio of people with diabetes in urban and rural areas in the developing world will rise from 1.5-fold, at present, to more than 3-fold in 2025 [13]. Other socio-economic factors, particularly poverty, also increase the risk of type 2 diabetes [51].

Undiagnosed diabetes

Patients with a diagnosis of diabetes represent the tip of the iceberg, and a large number of patients with undiagnosed diabetes may also be at risk of adverse clinical outcomes. In the AusDiab study, there was one undiagnosed case for every known case of diabetes [18]. An observational study carried out in an apparently healthy, elderly (70-79 years) population in the US revealed that 8% of the 3,075 participants had undiagnosed diabetes. Higher estimates have been observed in patients with a previous MI (12%; [52]) or awaiting coronary angioplasty (17.9%; [53]). A study in the UK, which surveyed 553 subjects without known diabetes in an impoverished urban area, illustrates how genetic and socioeconomic factors combine to amplify the problem of undiagnosed diabetes [54]. The age-adjusted prevalence of diabetes in this population was high in subjects of south Asian or African-Caribbean descent (33% and 22%, respectively), as would be expected from earlier studies. However, the age-adjusted prevalence of type 2 diabetes was unexpectedly high (20%) in subjects of European descent. Similarly, data from the Third US National Health and Nutrition Examination Survey suggested that the adult prevalence of undiagnosed type 2 diabetes nationwide was 2.7%, though this concealed wide vari-

ations between men and women and between ethnic groups [21]. For example, the prevalence of undiagnosed diabetes among middle-aged (50-59 years) Mexican-American men and women was 12.9% and 7.5%, respectively, compared with 3.3% and 5.8%, respectively, for the general population within this age range.

There is compelling evidence that undiagnosed diabetes is associated with cardiovascular risk factors characteristic of insulin resistance or the dysmetabolic syndrome, including hypertension and abdominal obesity [53-55]. The additional increases in metabolic dysfunction associated with westernisation and urbanisation of the developing world, as described above, can only exacerbate this problem in the future.

Diabetes in children

Type 2 diabetes mellitus in children, teenagers and adolescents is a serious new aspect of the type 2 diabetes epidemic and is an emerging public health problem of significant proportions [14]. While, globally, type 1 diabetes is still numerically the major form in children, it is likely that type 2 diabetes is set to be the predominant form within 10 years in many ethnic groups and potentially in Europid groups. Type 2 diabetes has already been reported in children from Japan, the United States, Pacific islands, Hong Kong, Australia and the United Kingdom [14].

The prevalence of type 2 diabetes in the general population of the USA has been estimated at 4.1/1000 12-19 year olds [56]. Dabelea *et al.* have studied Pima Indian children since the late 1960s, and have demonstrated rising rates of glucose intolerance with time and age, as well as a female preponderance [57]. From 1967-76 to 1987-96, the prevalence of type 2 diabetes has markedly increased from 2.4% in males and 2.7% in females to 3.8% in males and 5.3% in females. Diagnoses of type 2 diabetes now outnumber diagnoses of type 1 diabetes by 4:1 in children in parts of Japan and China, compared with a ratio of about 1:3 of total diagnoses of diabetes in urban USA centres [58, 59]. Obesity and insulin resistance are driving this explosion of paediatric diabetes, as in adults [60].

Burden of type 2 diabetes

Cardiovascular morbidity and mortality

A diagnosis of diabetes has a profound impact on life expectancy, and a patient diagnosed with type 2 diabetes in middle age (40-49 years) stands to lose as much as 10 years of life expectancy [61]. Given the close association between type 2 diabetes and the cardiovascular risk factors constituting the dysmetabolic syndrome, it is not surprising that most type 2 diabetic patients ultimately die from a cardiovascular cause [62]. Indeed, type 2 diabetes confers the same degree of risk of premature death as a previous myocardial infarction in a non-diabetic subject [63].

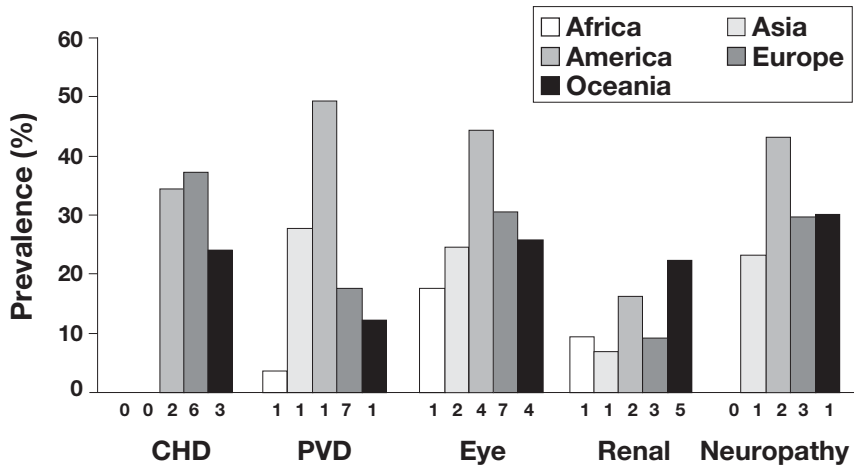
A substantial proportion of type 2 diabetic patients already have diabetic complications at the time of diagnosis of diabetes. For example, retinopathy, peripheral neuropathy and proteinuria were present in 35%, 12% and 2%, respectively, of the newly-diagnosed patients in the UK Prospective Diabetes Study (UKPDS) at baseline [64]. The Cost of Diabetes in Europe - Type 2 (CODE-2) study has investigated the prevalence of diabetic complications in a randomly selected cohort of type 2 diabetic patients. Less than half (41%) of the German cohort of 2,701 patients (mean age 67 years) did not have diabetic complications, while 23% had at least two, and 3% had at least three complications [65]. Cardiovascular complications were present in 43% of patients, cerebrovascular complications in 12%, and neuropathy or diabetic foot syndrome, retinopathy and nephropathy were present in 23%, 11% and 6% of patients, respectively. The CODE-2 data are consistent with previous estimates of the prevalence of coronary heart disease and other complications in type 2 diabetic patients in various countries *(Fig 2)*.

The prognosis of type 2 diabetes in patients who already have diabetic complications is extremely poor. A retrospective review of 126 patients referred to a combined diabetes-renal clinic showed that their median survival was only 61 months [66]. Similarly, odds ratios for all-cause and cardiovascular mortality in 104 Finnish type 2 diabetes patients with diabetic retinopathy were 5.1 and 5.6, respectively, compared with non-diabetic control subjects [67].

Burden on society

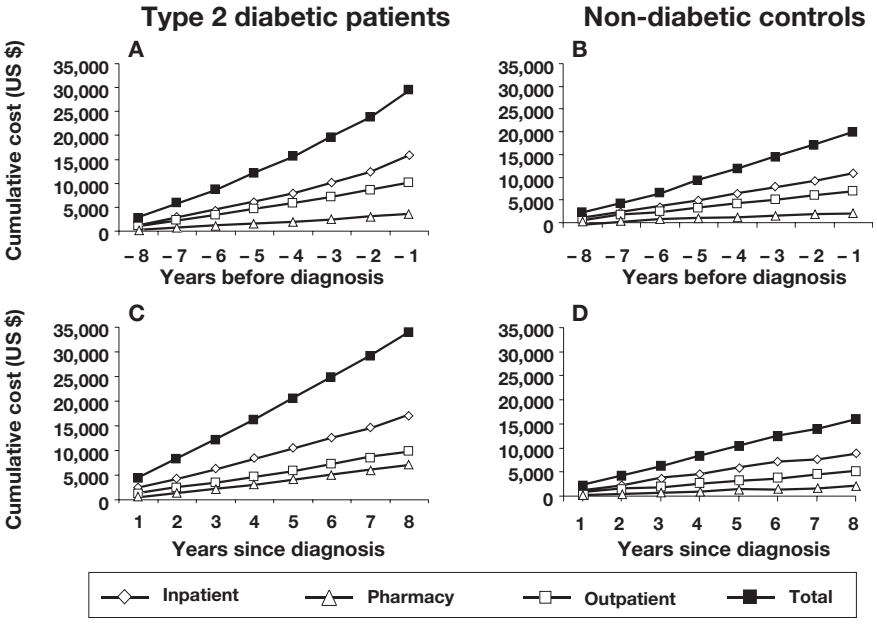
Diabetes is expensive to manage, and the per capita costs of managing a diabetic patient are 2-4-fold higher than for a non-diabetic patient [68]. However, the additional cost burden associated with type 2 diabetes begins long before diabetes is diagnosed. Analysis of data from a managed care organisation in the USA showed that the cumulative costs associated with inpatient, outpatient and pharmacy provision for patients with type 2 diabetes were higher, on average, than those incurred by control subjects matched for gender and age for each of the 8 years preceding diagnosis of diabetes [69]. By the time of diagnosis, the total cost of treatment was $9,643 higher for a diabetic patient, compared with a control subject *(Fig 3)*. Costs for the 8 years following diagnosis were higher in diabetic subjects, as would be expected, with a total difference in average total costs of $18,057 between a type 2 diabetic patient and a matched control subject *(Fig 3)* [70].

Most of the cost of managing type 2 diabetes is associated with the management of diabetes-related complications, especially where hospital treatment is required. The UKPDS performed separate health economic evaluations, based on the main cohort, who were managed with conventional diet-based treatment or intensive glycaemic management with a sulphonylurea or insulin [71], and on overweight patients, who were managed with diet or with intensive metformin-based treatment [72]. The total costs incurred during 11 years of follow-up are shown in *Table I*. Managing complications



Columns show the average of estimates of the prevalence of individual complications for adults with type 2 diabetes presented by Amos *et al.* [12]. Numbers beneath columns show the number of estimates used in each case. CHD: coronary heart disease; PVD: peripheral vascular disease.

Figure 2
Prevalence of diabetic complications.



Costs for the 8 years before and after diagnosis are in 1983 and 1998 $US, respectively.

Figure 3
Cumulative costs of managing a type 2 diabetic patient and an age- and gender-matched control subject in a managed care organisation over a period of 8 years before (A and B) or after (C and D) the diagnosis of diabetes [69, 70].

accounted for about two-thirds of the total costs in the diet-treated group of the main cohort, and about three quarters of the costs in diet-treated overweight patients. Complications accounted for more than half of the total costs during follow-up even after intensive glycaemic management with a sulphonylurea or insulin (main cohort) or metformin (overweight cohort), which significantly reduced the incidence of microvascular and macrovascular complications, respectively [64, 73].

Comparing the health economic costs between countries is difficult, because of variations in the costs of services and standard clinical practice, and variations in how data are presented. However, in general terms, the cost of managing complications drives the overall treatment costs in most countries. *Fig 4* compares the average annual costs of managing a type 2 diabetic patient across Europe: in most countries, costs arising from hospital treatment (mainly associated with the management of complications) were markedly greater than out-of-

Table I
Total costs (in UK £) associated with type 2 diabetes and its management during 11 years of follow-up in the UK Prospective Diabetes Study [71, 72].

	Lean patients		Overweight patients	
	Diet-treated	Intensive management (sulphonylurea or insulin)	Diet-treated	Intensive management (metformin)
Routine treatment	3,655	4,350	2,157	3,242
Management of complications				
In hospital	4,266	3,494	4,632	3,317
Out of hospital	1,666	1,631	1,324	1,288
Specialist eye and/or renal care	283	133	51	36
Total cost of managing complications	6,215	5,258	6,007	4,642
Overall total (clinical trial)	9,869	9,608	NA	NA
Overall total (standard practice costs)	7,871	8,349	8,165	7,883
% of costs due to complications	63	55	74	59

Data are from separate analyses, from the perspective of a healthcare purchaser. All costs are undiscounted direct costs and are in UK £ (1997 values). Additional costs for specialist care were for eye or renal care in lean patients and eye care in overweight patients. The analysis in lean patients presented individual costs from the clinical trial setting and adjusted the total for the routine community care setting; the analysis in obese patients presented all costs after adjustment for the routine care setting, hence NA (= not available) for trial costs for overweight patients. The percentage of costs due to complications was calculated using trial costs for lean patients and standard practice costs for overweight patients, for the same reason.

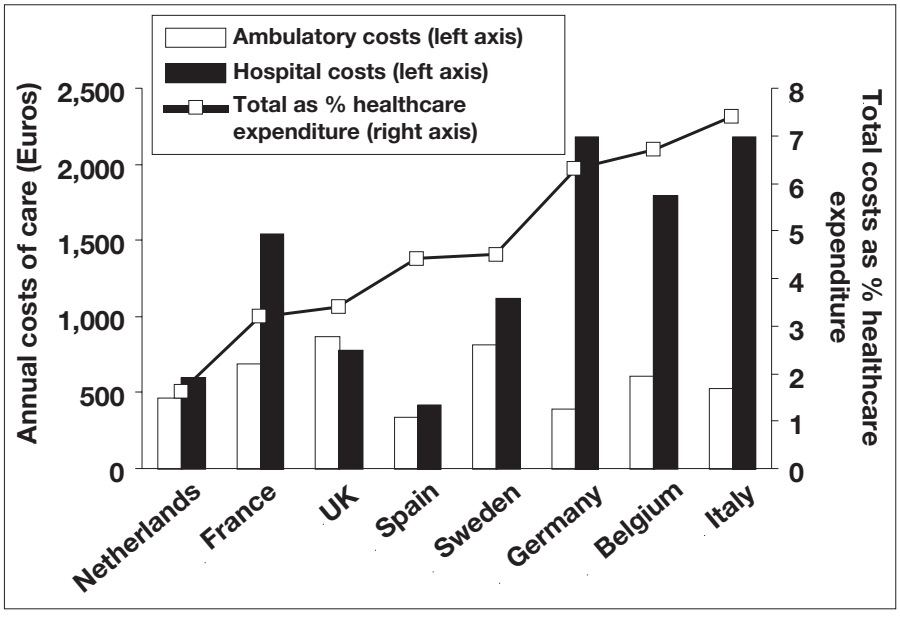
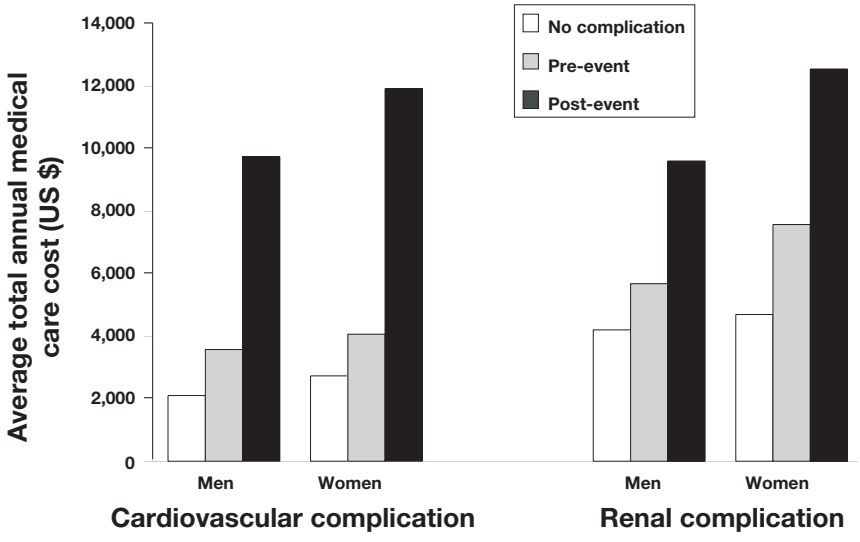


Figure 4
Direct medical costs per type 2 diabetic patient in some European countries in 1998 [51].

hospital (ambulatory) costs [51]. Data from the USA, from a model based on the interventions used in the UKPDS, show that the annual costs of managing complications in patients receiving diet-based therapy ($37,602) accounted for 78% of total direct costs of care ($48,343) [74]. A retrospective analysis of 11,768 patients within a managed care organisation in the USA compared the costs of diabetes management in type 2 diabetic patients with no evidence of significant cardiovascular or renal disease ("no complications"), in patients under treatment or investigation for risk factors for cardiovascular or renal conditions ("pre-event"), and in patients with a history of cardiovascular events or clinically significant renal dysfunction ("post-event") [75]. Direct costs were lowest in the "no complications" group *(Fig 5)*, and increased in the "pre-event" group for men and women. However, the greatest differences in costs were between the "pre-event" and "post-event" groups, with a greater than doubling of costs for patients who developed cardiovascular complications.



Costs are in 1993 prices from the perspective of a health care purchaser.
Patients were stratified as follows. No complication: patients in the analysis either had no history of cardiovascular or renal disease or treatment; pre-event: patients were under treatment with an antihypertensive drug, had made at least two visits to a cardiologist, or had had at least one positive test for microalbuminuria; post-event: patients had suffered at least one major cardiovascular event (e.g. myocardial infarction, stroke, revascularisation, or hospitalisation for congestive heart failure) or had documented clinical renal dysfunction indicated by high serum creatinine measurements.

Figure 5
Additional treatment costs arising from the development of cardiovascular or renal diabetic complications [75].

The high prevalence of type 2 diabetes means that the overall costs of managing the disease, including costs arising from managing diabetic complications, are high enough to place a substantial burden on national economies. The total direct healthcare expenditure on the management of diabetes in the USA in 1997 was $44 billion. Of this amount, only $7 billion was required for glycaemic management, with $36 billion required for the management of complications and other problems related to diabetes [76]. The total costs of managing type 2 diabetes in Europe already range between roughly 2% and 8% of national healthcare budgets in Europe *(Fig 4)*. The burden on some other economies is even higher. For example, diabetes care in Mexico accounts for 15% of the total healthcare budget, which equates to 0.8% of gross domestic product [77]. Moreover, the burden grows heavier as the global epidemic of type 2 diabetes evolves. Projections based on the UK diabetic population suggest that the total costs of managing type 2 diabetes will increase from £1.8 billion in 2000 to £2.2 billion by 2040, an increase of 24% [78] *(Fig 6)*.

Are we doing enough?

National governments have either failed to recognise the future socioeconomic burden of type 2 diabetes or are ignoring it. The global epidemic of type 2 diabetes is already threatening healthcare budgets, and the burden will continue to increase. We should not forget that these prevalence figures relate to people with a clinical diagnosis of type 2 diabetes. Many more people have undiagnosed diabetes, and there is a vast reservoir of people with IGT, most of whom will develop diabetes eventually, and who are already at substantial risk of developing cardiovascular disease [40]. Increasing rates of obesity will place ever more people at risk of developing the dysmetabolic syndrome, type 2 diabetes, and cardiovascular disease. The increasing prevalence of type 2 diabetes in children and adolescents underlines the urgency of taking action.

The Diabetes Prevention Program has shown us that preventing type 2 diabetes with lifestyle interventions or with pharmacologic therapy is cost-effective in either the European or American settings [79, 80]. However, extending these benefits beyond the tightly-controlled structure of a randomised clinical trial will require an unprecedented degree of public health intervention. Educating the public on the dangers of obesity and glucose intolerance will certainly be important. Some steps in this direction have been made. For example, efforts are underway to improve the lifestyles of school-age children in Japan [81], and health workers in Philadelphia in the USA patrol the streets armed with weighing machines to spread the message of the dangers of obesity [82]. In Finland, a simple questionnaire is being used as a screening tool to identify citizens at risk of type 2 diabetes, who may benefit from further follow-up and intervention [83].

Mounting a successful challenge to the diabetes epidemic, however, will require major alterations to the structure of society. For example, the intervention in Finland is being

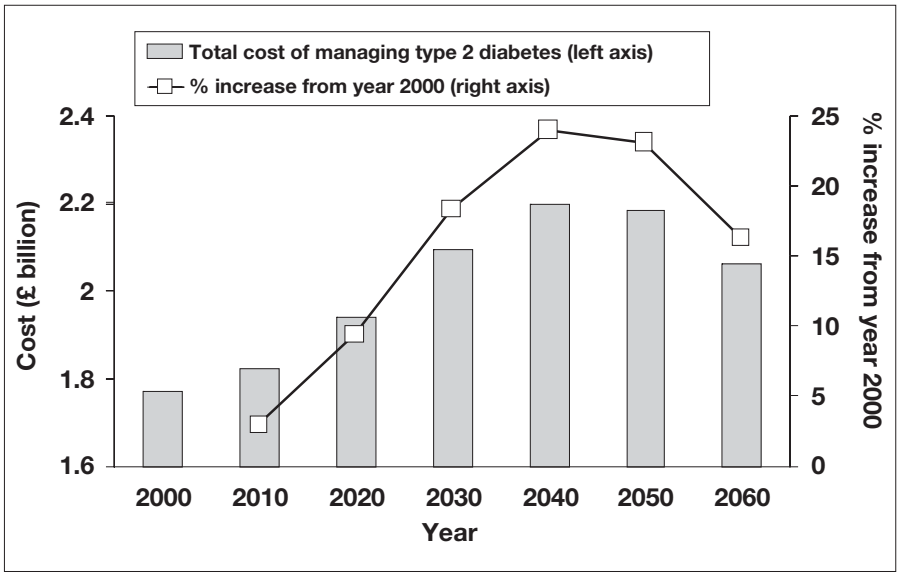


Figure 6
Projected total costs of managing type 2 diabetes in the UK [78].

mounted in collaboration with a broad range of governmental agencies and healthcare advocacy groups, as part of a broader strategy dating back several decades [84]. Support from the highest level of governments is also needed, as resources to mount diabetes prevention efforts must be made available, and changes to taxation and reimbursement structures relating to resources for people to improve their lifestyles would also certainly help in the longer term.

Conclusions

The rising tide of type 2 diabetes and its complications will place an increasingly heavy burden of morbidity and mortality on patients and their families for decades to come. Moreover, the expenditure required to manage these patients will stretch the healthcare systems even of the richest countries. All involved in the provision of healthcare, including the full range of healthcare professionals, professional societies, patient advocacy groups, healthcare agencies, or any level of government, bear a share of the responsibility for halting the diabetes epidemic. Above all, action is required immediately, if we are to stand any chance of success.

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