OPINION

Diabetes mellitus statistics on prevalence and mortality: facts and fallacies

Paul Zimmet, K. George Alberti, Dianna J. Magliano and Peter H. Bennett

Abstract | Diabetes mellitus is one of the most important public health challenges of the twenty-first century. Until the past decade, it has been seriously underrated as a global health threat. Major gaps exist in efforts to comprehend the burden nationally and globally, especially in developing nations, due to a lack of accurate data for monitoring and surveillance. Early attempts to obtain accurate data, discussed in this article, seem to have been cast aside so, at present, these needs remain unmet. Existing international efforts to assemble information fall far short of requirements. Current estimates are imprecise, only providing a rough picture, and probably underestimate the disease burden. The methodologies that are currently used, and that are discussed in this Perspectives article, are inadequate for providing a complete and accurate assessment of the prevalence of diabetes mellitus. International consensus on uniform standards and criteria for reporting national data on diabetes mellitus prevalence as well as for common complications of diabetes mellitus and mortality need to be developed.

Diabetes mellitus is one of the largest epidemics the world has faced, both in developed and developing nations. Diabetes mellitus is a syndrome currently recognized and classified as a group of diseases characterized by signs and symptoms of chronic hyperglycaemia. Type 2 diabetes mellitus (T2DM), type 1 diabetes mellitus (T1DM) and gestational diabetes mellitus are by far the most frequent forms, but other specific types exist that are much less common[1]. This Perspectives article focuses primarily on T2DM, the type mainly responsible for the current global epidemic of this disease[2].

Globally, the number of people with T2DM has more than doubled during the past 20 years. The latest global estimate from the International Diabetes Federation (IDF) is that in 2015 there were 415 million people with diabetes mellitus and that by 2040 the number will be 642 million[3]. The NCD Risk Factor Collaboration and the WHO gave a similar estimate of 422 million in 2014 (REFS 4,5). Numerous studies continue to confirm large increases in prevalence over time[2]. Until a decade ago, and despite calls from the international diabetes community to address the prevention of diabetes mellitus as a global public health epidemic, many international health agencies and national governments had given fairly low priority to the increasing frequencies of diabetes mellitus and other noncommunicable diseases (NCDs). Funding for the prevention and control of NCDs (including diabetes mellitus) had been, and generally has remained, a low priority compared with that for the control of communicable diseases[2].

Against this background, in 2006, the United Nations (UN) General Assembly unanimously passed Resolution 61/225 (REF. 6). This resolution called for diabetes mellitus to be recognized as an international public health challenge and for each nation to target prevention and control of the emerging threat. Furthermore, in 2011, the UN General Assembly made a political declaration on the prevention and control of NCDs[7], which was followed by a call by the World Health Assembly to reduce avoidable mortality from NCDs by 25% by 2025 (REF. 8). Although these calls were welcomed, the practicalities of attaining such targets are fraught with difficulties — including that of defining diabetes mellitus, its complications and prediabetes to enable estimation of the burden of T2DM and its complications both nationally and globally.

Historical view — definitions

Published in 1978, the late Kelly West's book 'Epidemiology of Diabetes and its Vascular Lesions' (REF. 9) provided the impetus for increased attention to the epidemiology of diabetes mellitus and the need to define internationally accepted diagnostic criteria. This book foresaw the emergence of epidemiology as a major area of diabetes mellitus research — diabetes mellitus epidemiology was coming of age. West's book brought together almost all the contributions (clinical and population-based) on the subject of diabetes mellitus epidemiology up to that time. In particular, it highlighted the many gaps in our knowledge, particularly the difficulties of comparing studies.

Kelly West was prophetic in predicting some of the issues that are under critical (and sometimes not so critical) debate today, particularly in respect to classification and criteria of diabetes mellitus and its complications. One resounding question that he asked was "What is diabetes?" West was a great proponent of standardization of diagnostic criteria and he reported polling 20 international diabetologists on their views of the appropriate diagnostic criteria. He developed some hypothetical blood glucose results and circulated them to the group 40 years ago. Even these experts showed great disparity on the diagnoses — West received at least 10 different sets of criteria from these 'experts' (REF. 10)!

Important milestones in diabetes mellitus epidemiology were the international workshop convened in April 1978 by the US National Diabetes Data Group (NDDG), of the NIH, USA[11], followed by a conference held by the Kroc Foundation

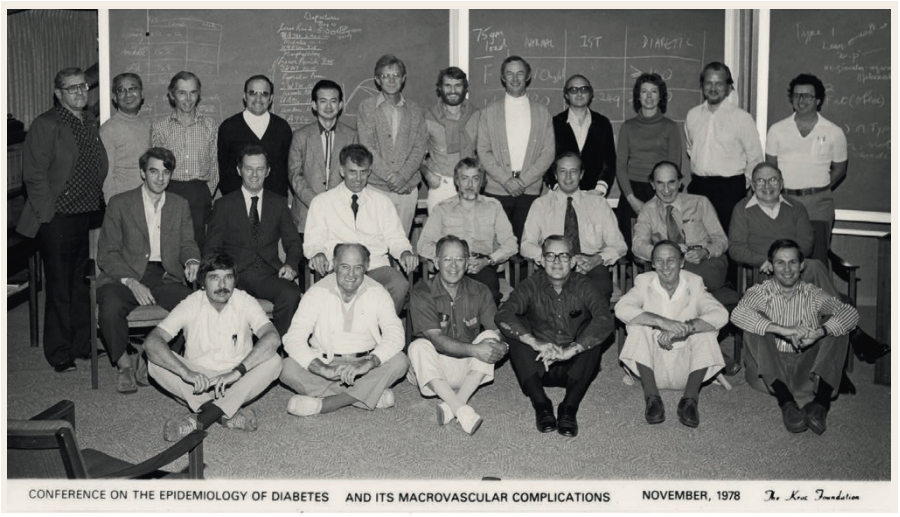

Figure 1 | **Attendees at the historic 1978 Kroc Foundation Conference at the McDonald Ranch in the Santa Ynez Valley, California, USA[12].** Front row left to right: Chuck Lawrence, Edward White, Robert L. Kroc, Kelly West, Jack Medalie, Peter Wilson. Middle row left to right: Richard Cooper, John O'Sullivan, Timothy A. Welborn, R. John Jarrett, Peter H. Bennett, Harry Keen, Reuben Andres. Back row left to right: William B. Kannel, Ryoso Kawate, Geoffrey Rose, Walter Garey, E. Miki, Peter Amacher, Morten Christy, Donald McMillan, Paul Zimmet, Maureen Harris, Kalevi Pyörälä, Robert Murphy. Republished with permission of American Diabetes Association, from *Diabetes Care* **2**, 63–249 (1979); permission conveyed through Copyright Clearance Center, Inc.

at the McDonald Ranch in the Santa Ynez Valley, near Santa Barbara, California, USA (FIG. 1). Proceedings of the Kroc conference were published in *Diabetes Care* in March 1979 (REF. 12) and contain extensive debate on issues of classification, diagnostic criteria and appropriate methodology for diabetes mellitus epidemiological studies. Later that year, following these meetings, the WHO convened its Second Expert Committee on Diabetes[13].

The NDDG[11] and WHO Expert Committee[13] reports made recommendations on the classification and criteria for diabetes mellitus and associated categories of glucose intolerance. In particular, they recommended standardization of methodologies for epidemiology studies in diverse populations to facilitate comparisons within and between national and ethnic populations. Such studies were regarded as having the capacity to provide direction for research into the possible genetic and environmental determinants and biochemical mechanisms underlying T1DM and T2DM, as well as being able to provide important information on geographic, social, cultural, behavioural and economic risk factors. The WHO recommendations[13] became the first widely recognized international criteria for the classification and diagnosis of diabetes mellitus and the newly introduced risk category of impaired glucose tolerance (IGT). These recommendations were soon adopted and were used in both clinical and epidemiological research. However, in the past 15 years, there has been a renewed and continuing international debate, and considerable confusion, regarding how best to define and classify diabetes mellitus and other categories of dysglycaemia[14].

Classification and criteria

The first WHO Expert Committee on Diabetes Mellitus was convened in Geneva, Switzerland, in 1965 (REF. 15). The report includes one of the first attempts at international consensus on a classification of diabetes mellitus but its impact was minimal as interest in the epidemiology of diabetes mellitus was still in its infancy. Although a number of sets of nomenclature and diagnostic criteria were subsequently proposed for diabetes mellitus, no systematic uniform categorization existed until 1980, as discussed earlier. The contemporary classification of diabetes mellitus and other categories of glucose intolerance began with, and are still based largely on, those developed in 1979 by the NDDG[11] and the second WHO Expert Committee on Diabetes Mellitus in 1980 (REF. 13). The first major revision of the 1980 WHO classification was published in 1999 (REF. 16). This report, preceded by an American Diabetes Association (ADA) report[17], generated a new international classification and revised criteria. The fasting plasma glucose (FPG) threshold for diabetes mellitus diagnosis was lowered from 7.8 mmol/l to 7.0 mmol/l and a new category of abnormal glucose metabolism was introduced — impaired fasting glycaemia (IFG), which is defined as an FPG of 6.1–6.9 mmol/l, that is, fasting glycaemia above 'normal', but with levels not high enough to be diagnostic of diabetes mellitus.

Furthermore, the ADA report (but not the WHO report) recommended the use of FPG rather than the oral glucose tolerance test (OGTT) as the diagnostic test of choice both for clinical and epidemiologic purposes[17]. This recommendation was based on the inconvenience and cost of the OGTT as a result of the 2 h time interval and the number of blood tests involved. This practical yet controversial decision was pivotal in initiating a situation that has resulted in many researchers and countries now using the FPG as the standard procedure for diagnosing diabetes mellitus.

Further confusion emerged in 2003 when the ADA Expert Committee recommended that the threshold for identification of IFG be lowered from 6.1 mmol/l to 5.6 mmol/l (REF. 18). The 2006 WHO–IDF consultation group rejected this proposal[19] and has retained 6.1 mmol/l as the threshold for IFG to the present time. The various suggestions from NDDG and WHO Expert groups for diagnostic criteria for states of glucose intolerance from 1964 to 2009 are shown in TABLE 1.

Measuring levels of HbA_{1c} then emerged as a potentially attractive means to diagnose diabetes mellitus and other forms of dysglycaemia[20]. This measurement reflects glycaemia over the previous 2–3 months, shows less day to day variation than measures of FPG or 2 h post-load plasma glucose (2 h PG) and can be measured at any time of day. Use of HbA_{1c} levels for the diagnosis of diabetes mellitus was formally recommended by an International Expert Committee convened by the ADA in 2009 (REF. 20) and endorsed by the WHO in 2011 (REF. 21) with the criterion of HbA_{1c} ≥6.5% as diagnostic of diabetes mellitus. This recommendation comes with the caveat that HbA_{1c} can be used as a diagnostic test for diabetes mellitus providing that stringent quality assurance tests are in place. In addition, assays need to be standardized to criteria aligned to international reference values. An additional caveat is that the individuals tested do not have conditions that change the half-life of red blood cells, which could preclude its use as an accurate

Table 1 | **Diagnostic criteria (FPG and 2 h PG) cut-off points for diabetes mellitus and other dysglycaemic states between 1964 and 2011**

Criteria	Diabetes mellitus			IGT	IFG
	FPG (mmol/l)	2 h PG (mmol/l)	HbA_{1c} (%)	FPG; 2 h PG (mmol/l)	FPG (mmol/l)
1965 (WHO)	NA	7.2*	NA	NA	NA
1979 (NDDG)	7.8	11.1	NA	7.8–11.0	NA
1980 (WHO)	8.0	11.0	NA	8.0–10.9	NA
1985 (WHO)	7.8	11.1	NA	7.8–11.0	NA
1997 (ADA)	7.0	11.1	NA	7.8–11.1	6.1–6.9
1999 (WHO)	7.0	11.1	NA	7.8–11.1	6.1–6.9
2003 (ADA)	7.0	11.1	NA	7.8–11.1	5.6–6.9
2006 (WHO)	7.0	11.1	NA	7.8–11.1	6.1–6.9
2009 (ADA)	7.0	11.1	≥6.5	7.8–11.1	5.6–6.9
2011 (WHO)	7.0	11.1	≥6.5	7.8–11.1	6.1–6.9

*This value is for whole blood glucose concentration[10]. ADA, American Diabetes Association; FPG, fasting plasma glucose; 2 h PG, 2 h post-load plasma glucose: IFG, impaired fasting glycaemia; IGT, impaired glucose tolerance; NA, not applicable; NDDG, National Diabetes Data Group.

measurement of glycaemia (for example, haemoglobinopathies). In 2010, an ADA position statement indicated that people with HbA_{1c} levels of 5.7–6.4% were also at increased risk of developing diabetes mellitus and should be considered to have 'prediabetes' (REF. 22). However, due to lack of clear evidence, no such recommendation has been made by the WHO.

Consequently, a range of methods and criteria are now used to diagnose diabetes mellitus: FPG ≥7.0 mmol/l; or a 75 g OGTT 2 h PG ≥11.1 mmol/l; or HbA_{1c} ≥6.5%[23]. Not surprisingly these different criteria do not identify all the same individuals as having diabetes mellitus and the different criteria result in large variations in the estimated prevalence of undiagnosed diabetes mellitus (FIG. 2). In a US population, the prevalence of previously undiagnosed diabetes mellitus was 2.5% by FPG, 4.9% by 2 h PG and 1.6% by HbA_{1c}, with only 1.2% meeting all three of the criteria[23]. Furthermore, the relative frequencies and extent of overlap of individuals who meet these criteria vary considerably from one population to another[24].

The controversy about prediabetes

Although the criteria for diabetes mellitus are problematic, those for people at high risk of developing T2DM who are designated as having 'intermediate hyperglycaemia' by the WHO[19] or 'prediabetes' by the ADA[25] are even more confusing. The WHO criteria for intermediate hyperglycaemia are 2 h post 75 g OGTT plasma glucose levels of 7.8–11.0 mmol/l (IGT) or FPG of 6.1–6.9 mmol/l with 2 h PG <7.8 mmol/l (IFG). These levels are in accord with the 1997 ADA criteria[17], but in 2003 the ADA lowered the threshold of FPG for IFG to 5.6 mmol/l, increasing the prevalence of IFG twofold to threefold[26,27] (FIG. 3). The incidence of diabetes mellitus in people with FPG levels of 5.6–6.0 mmol/l is much lower than in people with FPG levels of 6.1–7.0 mmol/l, who have an incidence of diabetes mellitus that is similar to that seen in people with IGT[28].

After HbA_{1c} was accepted as a basis for diagnosing diabetes mellitus, the ADA then indicated that people with levels of HbA_{1c} ≥5.7–6.5% should also be considered as a high risk category (prediabetes)[25]. The WHO guidelines committee, despite accepting HbA_{1c} for the diagnosis of diabetes mellitus, rejected this proposal and retained the FPG and 2 h PG as the only criteria for intermediate hyperglycaemia.

By the ADA definition, if one or more of HbA_{1c}, FPG or 2 h PG are measured, there are 18 possible combinations of criteria that can designate people as having prediabetes! These criteria identify much larger numbers of people as having prediabetes than the WHO criteria for intermediate hyperglycaemia, where there are only three possible combinations: IFG; IGT; or IGT and IFG[19]. The extent to which these many combinations overlap is unclear, but emerging evidence now suggests that the aetiology of hyperglycaemia in people with only IFG (that is, isolated IFG) differs from that in people with IGT[29,30]. These findings might have profound implications on the optimal ways to prevent progression to diabetes mellitus in people with isolated IFG. Up to the present time, prevention of diabetes mellitus by lifestyle intervention has only been shown to be effective in people with IGT with or without IFG, and to be ineffective in those with isolated IFG[30]. Such disparities in the interpretation of the condition of prediabetes clearly causes difficulty in comparing the prevalence of the condition in different countries and also in defining who might best benefit from intervention[26,31,32].

Correct measuring of plasma glucose

A further major consideration in this debate is the actual practical measurement of FPG and indeed the 2 h PG. A considerable number of individuals will not actually fast, and for the 2 h glucose test it is critical that people have an adequate carbohydrate intake on the day before the OGTT[16]. In addition, globally, variable attention is paid to both quality assurance and to sample handling. It is very unlikely that appropriate quality assurance measures have been applied to all the field studies of diabetes mellitus prevalence or that samples have been rapidly assayed or the blood separated quickly enough to prevent some loss of glucose in the sample[16]. These factors should be taken into account when estimating the prevalence of dysglycaemia in any population.

The need for reliable estimates

Reliable data on the burden posed by major types of diabetes mellitus are needed for many reasons beyond just raising and maintaining awareness of diabetes mellitus[33]. These include meeting national and local needs for planning purposes to identify current and future health-care priorities, to estimate direct and indirect economic and societal costs of the disease and to allocate appropriate health-care resources and expenditures for health-care delivery. These

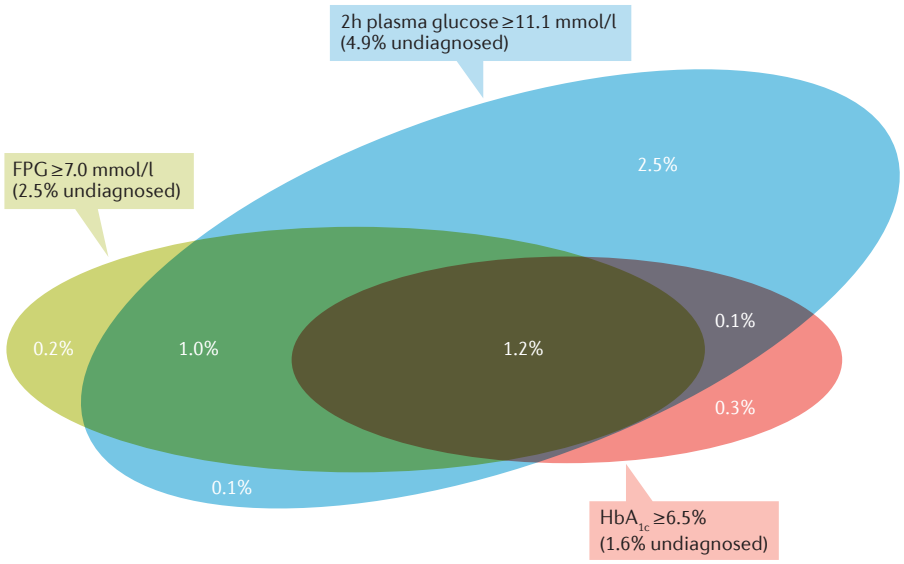

Figure 2 | **The percentage of the US population aged 20–74 years (NHANES 2005–2006, *n* = 2,017) with undiagnosed diabetes mellitus by three diagnostic criteria[23].** The thresholds for diagnosis are HbA_{1c} ≥6.5%, fasting plasma glucose (FPG) ≥7.0 mmol/l and 2 h post-load plasma glucose ≥11.1 mmol/l. Republished with permission of American Diabetes Association, from *Diabetes Care* **33**, 562–568 (2010); permission conveyed through Copyright Clearance Center, Inc.

data are also very important for identifying groups or populations that might have unique or special needs related to diabetes mellitus, and to help define and set research priorities. Ongoing reliable data are also needed not only to project future trends, but to monitor the effects of treatment and to determine the needs, plans, design and effectiveness of prevention activities.

Incidence and prevalence

Traditionally, the incidence of T1DM in children and adolescents has been determined on the basis of registries of newly diagnosed patients with insulin-treated diabetes mellitus within defined populations, which assumes that almost all cases represent T1DM and that few cases escape early detection[34,35]. However, during the past 30 years, it has become apparent that the majority of patients with diabetes mellitus have the T2DM form[1,16]. Furthermore, monogenic forms of diabetes mellitus such as maturity-onset diabetes in the young, although fairly uncommon, are also increasingly being recognized[1,19]. In addition to the emergence of T2DM in this age group, an unexplained but increasing incidence of T1DM has also been observed during the past 25 years[34–36]. This changing landscape now requires new and improved approaches to documenting the occurrence and types of diabetes mellitus in childhood and adolescence, such as that developed in the USA for the SEARCH study. This study requires ongoing ascertainment and careful characterization of cases in sentinel communities to determine incidence[37,38].

In adults, the frequency of diabetes mellitus is usually quantified from prevalence studies as the disease is common enough to justify contacting and testing all members, or a representative sample, of the target population. Although previously diagnosed diabetes mellitus can be ascertained by interview or questionnaire, previously undiagnosed diabetes mellitus, which usually constitutes a sizeable proportion of those affected, is identified by performing diagnostic testing on those not already known to have the disorder. A diagnosis is made by measuring plasma levels of glucose either while fasting and/or 2 h after a 75 g oral glucose load, with levels of HbA_{1c} being used in some of the latest studies[20,21]. Generally, the majority of newly recognized cases are assumed to have T2DM.

The incidence of T2DM is rarely determined as this requires repeated tests in the same individuals over a defined period of time to ascertain the proportion of the population with newly developed diabetes mellitus. Such studies are usually conducted primarily for research to identify risk and causative factors. However, the incidence of clinically diagnosed T1DM or T2DM can be determined over time in communities or countries[39,40] with ongoing registries of diabetes mellitus linked to demographic data. Such studies are infrequent and are presently limited to a few affluent nations, but could become more widespread in future with the development of electronic medical record systems.

Integrity of the global estimates

As we are now faced with a global epidemic of T2DM and evidence of substantial secular increases in many nations[2], as well as the need for accurate monitoring and surveillance, the expectation might be that the majority of prevalence studies would follow a standardized protocol to ensure comparability. Given the variations in diagnostic methods and criteria that are currently used around the world, this expectation and requirement is clearly not being met[4].

In 1995, McCarty and Zimmet made the first attempt to estimate the global and regional burden of both T1DM and T2DM[41]. They estimated that in 1994, 110 million people had diabetes mellitus and that by 2010 the number would be almost 240 million. This was clearly an underestimate given the subsequent predictions[3,42,43]. Following this initiative, the WHO and the IDF have produced estimates on the growth of diabetes mellitus worldwide, starting in 1998. For example, in 1998, it was estimated that there were 135 million people with diabetes mellitus in 1995 and it was predicted that there would be 300 million by 2025 (REF. 42). A subsequent estimate proposed that there were 171 million people with diabetes mellitus in 2000 and predicted that this figure would rise to 366 million by 2030 (REF. 43), a number that had already been surpassed in 2013 (REF. 44).

Quite apart from the lack of standardization of many studies, another major problem in obtaining an accurate picture of the global burden of diabetes mellitus is that very few developing nations have national data. In fact, Makaroff and Cavan reported in 2015 that 'high quality' prevalence surveys of diabetes mellitus are available for only 57% of 221 countries and territories and only 19% of countries have OGTT-based prevalence data[45]. Many middle and low income nations lack the resources to undertake large surveys. As a result, the estimates of diabetes mellitus prevalence are obviously nothing more than rough guesses! Despite this limitation, global estimates are now provided in the IDF Diabetes Atlas every 2 years[3]. Some will agree that updating the Atlas so frequently serves a useful purpose and keeps diabetes mellitus 'on the radar' as an important health issue for governments, maintaining pressure

on them to address the epidemic. However, given the paucity of valid new data, whether the biannual IDF Diabetes Atlas updates serve the needs of epidemiology and public health in providing appropriate and timely information on the real burden for future planning is open to vigorous debate. In addition, an unfortunate outcome is that these global and national estimates are used without question by both the media and the scientific community.

To derive estimates for the many countries without national data, the IDF relies on extrapolating data from other nations with similar features (such as demography and ethnicity), which is a very fragile methodology[3]. Some examples of countries used in estimates from the past few years are shown in BOX 1 and some of these extrapolations can clearly be challenged as being inappropriate on ethnic and socio-economic grounds. For example, the use of South Africa as a comparator for Malawi, one of the poorest nations in Africa, is deemed to be inappropriate and Korea and Japan for Brunei Darussalam, equally so.

The WHO developed the STEPS programme in an attempt to address the problem of obtaining more accurate data[46]. This programme aims to provide rough estimates of the NCD load in a given nation. This strategy has its own notable limitations with lack of standardization of methodology and the diagnostic criterion for diabetes mellitus even within, and certainly between, countries. In addition, the STEPS programme has used FPG for the diagnosis of diabetes mellitus, which both grossly underestimates the prevalence of this disease and introduces methodological differences that make comparisons between national studies fraught with difficulty.

It is important to realise that the IDF[3], the WHO[5], the NCD Risk Factor Collaboration[4] and the Global Burden of Disease Collaboration (GBDC)[47] initiatives all have serious limitations from an epidemiological standpoint. These limitations mean that only very broad conclusions can be drawn from these attempts to estimate the prevalence of diabetes mellitus and its outcomes. The estimates should not be taken as 'gospel' truth and used without the relevant qualifications in citations in publications by other researchers. Certainly, definitive action is needed to develop improved processes for obtaining accurate data that reflect the true situation.

Methodology for mortality data

Although prevalence data are important they provide only an immediate and limited view, or snapshot, of the magnitude and importance of diabetes mellitus as a global public health problem. The prevalence might rise and fall as a result of increasing incidence or decreasing mortality, and vice versa. Mortality data are important as they provide information not only on the number of deaths attributable to a disease, but for calculation of life expectancy, lifetime risk and numbers of years of life lost due to the disease. To address the call by the World Health Assembly[8] to reduce avoidable mortality from NCDs, and diabetes mellitus in particular, we need to measure mortality related to diabetes mellitus in an appropriate way.

Assessing mortality related to diabetes mellitus presents particular challenges. It cannot be accurately assessed from death certificates as deaths in patients with diabetes mellitus usually result from one of its complications (such as heart disease, stroke or renal failure), which are listed as the cause of death[48]. Furthermore, the cause of death often does not mention diabetes mellitus as either an underlying or contributory cause[48].

An optimal way to assess the number of deaths attributable to known diabetes mellitus is from ongoing registries of prevalent and new cases that can be linked to death registration data. However, such data are available in only a few developed countries, such as Denmark[39] and Sweden[49]. An alternative method is to apply the age and sex-specific relative risks of death in people with and without diabetes mellitus to diabetes mellitus prevalence data[50]. This method is used to calculate mortality related to diabetes mellitus in the IDF Diabetes Atlas[3]. The accuracy of this method depends on having sound diabetes mellitus prevalence data and reliable estimates of the relative risks of death in those with and without diabetes mellitus. The relative risks can be calculated from population-based longitudinal cohort studies such as DECODE[51], Da Qing[52] and AusDiab[53] or from death rates in representative cohorts of patients with diabetes mellitus compared with those in the general population, such as the South Tees study[54] and a Taiwanese national study[40]. However, most published studies of relative risk are from developed countries. Relative risks in developing countries might be different from those in developed countries, being higher because of poorer medical care, or lower because of high rates of competing causes of death[55–57]. Nevertheless, when appropriately applied, such calculations provide reasonable approximations of excess deaths attributable to diabetes mellitus, but with potentially large uncertainty intervals.

Excess mortality

On the basis of death certificates, the GBDC reported the number of deaths worldwide due to diabetes mellitus in 2013 as 1.3 million, with an additional 173,000 deaths from chronic kidney disease due to diabetes mellitus, giving a total of 1.47 million[47]. Similarly, the NCD Risk Factor Collaboration[4] and the WHO[5]

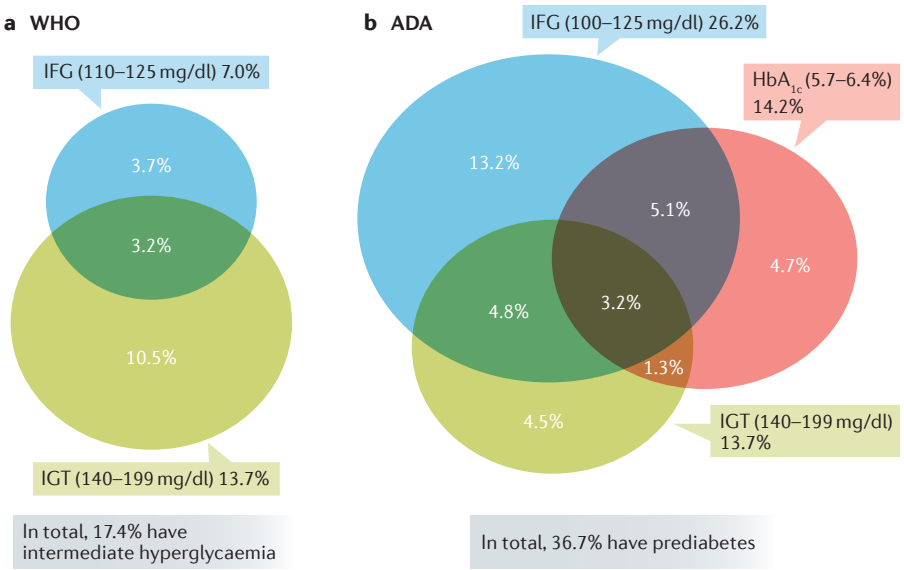

Figure 3 | **The percentage of US adults aged >18 years (NHANES 2005–2008) with a | intermediate hyperglycaemia (WHO) or b | prediabetes (ADA, 2003 criteria)[27].** IFG, impaired fasting glycaemia; IGT, impaired glucose tolerance.

Box 1 | **Examples of IDF national estimates based on extrapolations from other nations**

Brunei Darussalam (estimate)
- Japan
- Republic of Korea
- Singapore

Marshall Islands (estimate)
- Nauru
- Solomon Islands
- Tonga

Malawi (estimate)
- Botswana
- Mozambique
- South Africa

Eritrea (estimate)
- Kenya
- United Republic of Tanzania

IDF, International Diabetes Federation.

reported that 1.5 million deaths were caused by diabetes mellitus in 2012. However, their reports cite a further 2.2 million deaths attributable to excess risks from other causes related to high blood glucose levels, to give a total for 2012 of 3.7 million[4,5]. By contrast, the latest IDF Diabetes Atlas estimated that approximately 5.1 million deaths were attributable to diabetes mellitus among people aged 20–79 years in 2013 (REF. 3).

These major discrepancies largely stem from the futility of reporting mortality related to diabetes mellitus solely on the basis of death certificates, as used in the GBDC report[47] in 2013 and by the WHO[58] in 2014. The 2015 IDF estimate of 5 million deaths per year places diabetes mellitus, along with ischaemic heart disease and cerebrovascular disease (5.73 million and 4.58 million deaths per year, respectively), as one of the top three major worldwide causes of death from an NCD[3]. A similar figure is seen for accidental injuries (of all types), which are responsible for ~4.8 million deaths per year. A very disturbing feature is the extent that mortality related to diabetes mellitus has increased in recent years from about 2.0 million deaths in 2000 (REF. 50) to about 5.0 million in 2015 (REF. 3).

Increases in the global prevalence of diabetes mellitus in the past decade, especially in younger and middle aged adults[1,2] in developing countries, will lead to yet further increases in deaths attributable to diabetes mellitus in the future.

The consequences of high and increasing mortality from diabetes mellitus include rising numbers of life years lost, increases in disability adjusted life years and reduced life expectancy, all of which have important social and economic consequences. The one glimmer of hope is that in some developed countries, such as Sweden[49] and the USA[59], the individual risk of death in people with diabetes mellitus now seems to be falling as a result of improved management and treatment. However, the increases in diabetes mellitus prevalence in most nations over the past few years are likely to outweigh these improvements and lead to further future increases in mortality related to diabetes mellitus.

Assessing complications

Most of the global burden of diabetes mellitus is due to morbidity and mortality that arises from complications of the disease[2,47,60]. These complications commonly include excessive rates of coronary heart disease, heart failure, stroke, renal insufficiency and end-stage renal disease, retinopathy and blindness, peripheral sensory and motor neuropathy and lower extremity amputations[60]. The incidence of these and other complications increases with duration of diabetes mellitus and leads to disability and reduced life expectancy[60].

Unfortunately, no internationally recognized standardized classification, definitions or diagnostic criteria for the complications of diabetes mellitus are currently available. Consequently, the extent that they contribute to morbidity and mortality is unknown. If this issue were addressed, important advances in describing and understanding the burden they represent as well as help in defining eligibility and outcome measures for clinical trials would ensue.

The economic cost of diabetes mellitus is enormous. Some 12% of global expenditure on health is attributable to the care of patients with diabetes mellitus and related complications[3]. The continuing global diabetes mellitus epidemic is very likely to lead to a massive increase in health expenditure in both developed and developing countries.

Conclusions

A number of approaches could address the issues raised in this Perspectives article. Firstly, there is a compelling need for international consensus on uniform standards and criteria for reporting national data on the prevalence of diabetes mellitus. Secondly, better and up-to-date prevalence data from countries that lack such information are needed. Thirdly, information on relative risk of death is needed, especially in developing nations, to measure and monitor diabetes mellitus mortality. Fourthly, international standardized criteria for recognition, diagnosis and reporting for common complications of diabetes mellitus need to be developed. Finally, there must be a greater emphasis on the importance of monitoring secular changes to enable us to address the UN[7] and World Health Assembly[8] mandates.

Clearly, diabetes mellitus has become, and remains, perhaps the single most important public health challenge of the twenty-first century[2]. Major gaps still exist in our capacity to understand the burden it imposes both globally and nationally, and especially in low and middle income nations. For these reasons, international consensus and action is needed to ensure that the data needs are fulfilled by united global action. Only then will the real effect of diabetes mellitus on health, its socioeconomic burden and the range of interventions and resources needed to address and turn the epidemic around be understood.

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doi:10.1038/nrendo.2016.105
Published online 8 Jul 2016

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Author contributions

P.Z., K.G.A. and P.H.B. researched data for the article, contributed to discussion of the content, wrote the article and reviewed and/or edited the article before submission. D.J.M. contributed to discussion of the content and reviewed and/or edited the article before submission.

Competing interests statement

The authors declare no competing interests.