METABOLIC SURGERY

Epidemiology of Diabetes—Status of a Pandemic and Issues Around Metabolic Surgery

Paul Z. Zimmet[1] and K. George M.M. Alberti[2]

Diabetes Care 2016;39:878–883 | DOI: 10.2337/dc16-0273

The number of people with diabetes worldwide has more than doubled during the past 20 years. One of the most worrying features of this rapid increase is the emergence of type 2 diabetes in children, adolescents, and young adults. Although the role of traditional risk factors for type 2 diabetes, such as genetic, lifestyle, and behavioral risk factors, has been given attention, recent research has focused on identifying the contributions of epigenetic mechanisms and the effect of the intrauterine environment. Epidemiological data predict an inexorable and unsustainable increase in global health expenditure attributable to diabetes, so disease prevention should be given high priority. An integrated approach is needed to prevent type 2 diabetes and must recognize its heterogeneity. Future research needs to be directed at improved understanding of the potential role of determinants, such as the maternal environment and other early life factors, as well as changing trends in global demography, to help shape disease prevention programs. Equally important is a better understanding of the role of metabolic surgery in helping to address the management both of persons with type 2 diabetes and of those persons in the community who are at higher risk for type 2 diabetes, particularly in emerging nations where the diabetes epidemic is in full flight.

BACKGROUND—DIABETES EPIDEMIOLOGY AND BARIATRIC SURGERY

In the 1990s, a conference addressing bariatric (metabolic) surgery and diabetes, particularly type 2 diabetes, would have seemed unusual. However, today, there are very good reasons justifying such a conference. Type 2 diabetes is a progressive disorder with an unknown number of metabolic causes (1,2). The epidemiology of type 2 diabetes globally is reasonably well defined (3), but its management poses real challenges despite years of research, and this is why today bariatric surgery may have an important role in both the treatment and prevention of type 2 diabetes. Although this article will address the epidemiology of type 2 diabetes, it is important to address and contextualize other issues that influence the place and role of metabolic surgery in the management and prevention of type 2 diabetes. This includes the degree of obesity and ethnic variation that may determine the use of such surgery, the availability and accessibility of the surgery, and the resources and expertise required as well as the means of follow-up in many parts of the world.

Even with an increasing number of new drug therapies that address as yet not fully understood metabolic targets, the treatment of type 2 diabetes remains unsatisfactory (4).The preferred first line of treatment is lifestyle intervention with diet and exercise (5). Although this approach can be quite effective, it is successful in a minority of people with type 2 diabetes (4). Pharmacological intervention is almost inevitable, and, because of the potential number of metabolic defects, not a single

[1]Baker IDI Heart & Diabetes Institute and Monash University, Melbourne, Australia
[2]Kings College Hospital, Denmark Hill, London, U.K.

Corresponding author: Paul Z. Zimmet, paul.zimmet@bakeridi.edu.au.

Received 8 February 2016 and accepted 13 March 2016.

See accompanying articles, pp. 857, 861, 884, 893, 902, 912, 924, 934, 941, 949, and 954.

therapeutic agent, let alone a combination of agents, provides the answer to metabolic control. There is often a need to intensify therapy with the addition of more antidiabetic medications, including insulin, and often in increasing amounts (4). Almost invariably, this has the effect of weight gain, an outcome that is clearly undesirable in the management of a person with type 2 diabetes (6).

Against this setting, it is no surprise that metabolic (bariatric) surgery (7) has appeal for improving type 2 diabetes management, given that it can have a dramatic effect on glycemic control (8,9). This modality of treatment has not yet found an established place in algorithms for the management of type 2 diabetes. Thus, for the purpose of raising this concept for discussion and debate as an option in future treatment algorithms, we provide below an example of a possible scenario where metabolic surgery could be included and considered (Fig. 1).

Our proposal could be considered in situations where there is poor metabolic control with medical treatment or in high-risk situations. In addition, it must be recognized that adequate resources must be available to provide this option. For any proposed increase in metabolic surgeries, the resources, finances, and workforce need to be in place, and, as a result, surgery may be an option only in the more developed countries. It is clearly not a realistic option in resource-poor areas or nations. Thus, any algorithm including metabolic surgery needs to be considered in the context described above.

Today, given the recognized importance of metabolic control for persons with diabetes to prevent or delay complications (10), it is essential for future health care planning to have epidemiological data to understand not only the drivers of the diabetes epidemic, but also the economic impact (11). This extends to the resources, finances, and workforce needed for managing the increasing number of people with or at risk for type 2 diabetes.

THE EPIDEMIOLOGY OF TYPE 2 DIABETES

Two landmark epidemiological studies reported in the 1970s heralded the diabetes epidemic that we recognize today. In 1971, Bennett et al. (12) reported the extremely high diabetes prevalence among American Pima Indians. Fifty percent of Pima adults ≥35 years of age had diabetes. However, few believed that this result was the forerunner of the contemporary worldwide diabetes epidemic. The magnitude of the Pima Indian findings was supported by our report in 1975 describing the highest ever national diabetes prevalence of >34% in persons ≥15 years of age in the Micronesian community of the Central Pacific island of Nauru (13). This remains today as the highest national diabetes prevalence yet described. Further studies (14–16) in other Pacific nations by our group and others have confirmed the high prevalence rates.

Today, type 2 diabetes, long considered a relatively uncommon and low-profile disease, is now a major international public health problem (1,3) and one of the major health challenges of the 21st century. It may yet be, along with obesity, the greatest chronic disease epidemic in the history of human existence. The meteoric rise of the global estimate, a greater than twofold increase, from 151 million people with diabetes in 2000 (17) to the current estimate of 415 million (18), provides a firm basis for this claim.

Ascertaining a Global Perspective of the Diabetes Epidemic

The International Diabetes Federation (IDF) *Diabetes Atlas* (18) provides predictions for the top 10 countries with the highest number of people with diabetes in 2015 and the expected numbers in 2040 (Table 1). The two countries with the highest number are China and

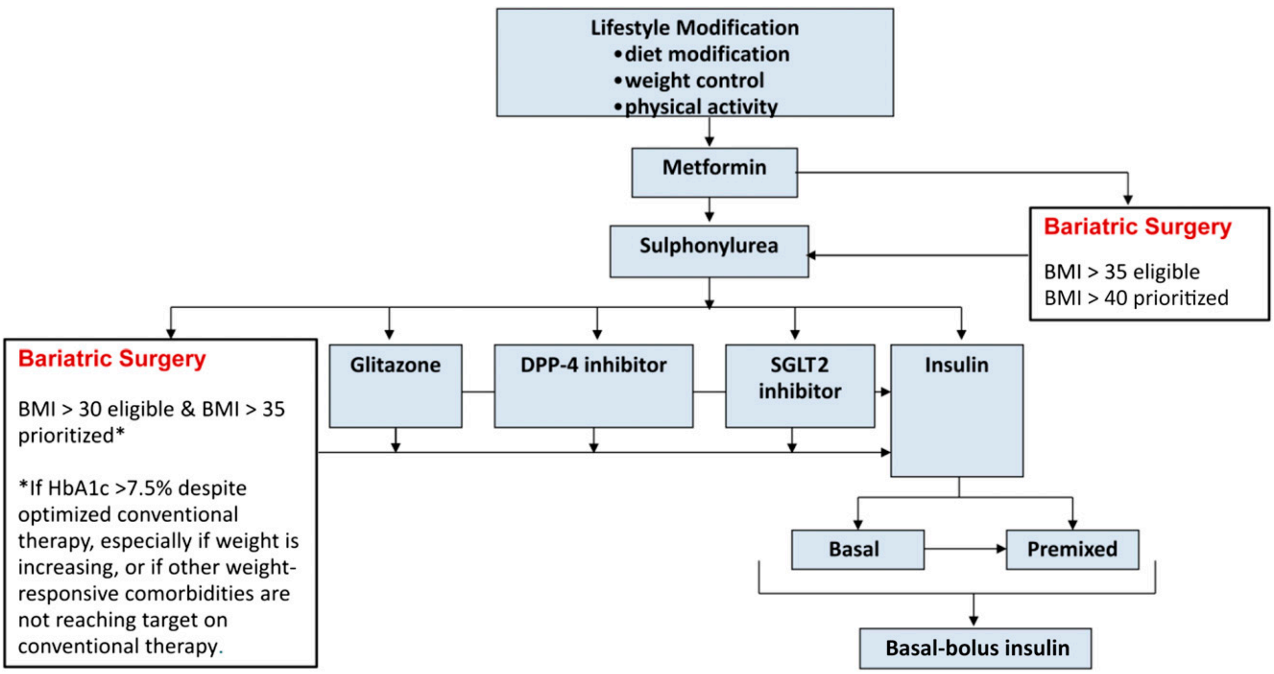

Figure 1—A proposed management algorithm for metabolic control in type 2 diabetes. DPP-4, dipeptidyl peptidase-4; SGLT2, sodium–glucose cotransporter 2.

Table 1—Top 10 countries/territories for number of people with diabetes (20–79 years of age), 2015–2040 (18)

2015			2040		
Rank	Country/territory	Number of people with diabetes	Rank	Country/territory	Number of people with diabetes
1	China	109.6 million (99.6–133.4)	1	China	150.7 million (138.0–179.4)
2	India	69.2 million (56.2–84.8)	2	India	123.5 million (99.1–150.3)
3	U.S.	29.3 million (27.6–30.9)	3	U.S.	35.1 million (33.0–37.2)
4	Brazil	14.3 million (12.9–15.8)	4	Brazil	23.3 million (21.0–25.9)
5	Russian Federation	12.1 million (6.2–17.0)	5	Mexico	20.6 million (11.4–24.7)
6	Mexico	11.5 million (6.2–13.7)	6	Indonesia	16.2 million (14.3–17.7)
7	Indonesia	10.0 million (8.7–10.9)	7	Egypt	15.1 million (7.3–17.3)
8	Egypt	7.8 million (3.8–9.0)	8	Pakistan	14.4 million (10.6–20.4)
9	Japan	7.2 million (6.1–9.6)	9	Bangladesh	13.6 million (10.7–24.6)
10	Bangladesh	7.1 million (5.3–12.0)	10	Russian Federation	12.4 million (6.4–17.1)

India. However, given recent national data from China (19) and India (20), the IDF predictions are likely to be underestimates. The Gulf region in the Middle East is another area where there is a notable increase in numbers of people with diabetes. This region and Asia have become "hot spots" for the diabetes epidemic, largely as a result of rapid economic development, urbanization, and lifestyle changes (11,18).

As a result, and given the growing prosperity now evident in Asia and the Gulf regions, they may be considered target locations for where metabolic surgery could become an important measure for treating and preventing diabetes in selected subjects. On the other hand, the major burden of diabetes, some 80%, now lies in developing countries rather than developed countries (18). This is an issue of concern when considering where metabolic surgery fits into the picture, especially as some of these nations have the highest prevalence of obesity as well as of type 2 diabetes globally.

Both the IDF and World Health Organization have been providing estimates on the growth of diabetes worldwide since 1997. In 1998, King et al. (21) estimated that there were 135 million people with diabetes in 1995, and predicted 300 million people by 2025. A later report (22) suggested that there were 171 million people with diabetes in 2000, and predicted 366 million people by 2030. It appears that these reports have consistently underestimated the global burden given that a 2011 IDF report (23) estimated there were already 366 million people with diabetes, a number previously forecast for 2030. The most recent prediction is that in 2040 there will be 642 million people with diabetes worldwide (18).

In fact, it is really not feasible to obtain an exact picture of the global burden because many developing nations do not even have national data, so it should be made clear to all that the estimates of diabetes are just estimates. Researchers can draw only broad inferences from the IDF estimates and cannot take them as absolute factual data. So, it is important to ask whether the exercise is worthwhile from either an epidemiological or a public health perspective.

Secular Trends in the Type 2 Diabetes Epidemic

As discussed earlier, there are clearly limitations to the current approaches discussed above for defining a true global picture of the global burden, the status of the epidemic, and progress in addressing it. In our view, the best way to define the picture currently is to observe the secular increases in a number of key nations that confirm the dramatic rise in numbers and the trends, and to provide useful information on the determinants of type 2 diabetes.

A number of very useful examples of secular trends exist, and possibly the most dramatic example of a national rise in diabetes is in the People's Republic of China. An earlier study in 1980 in Shanghai (24) showed a prevalence of $<$1%, whereas a more recent national survey (19) revealed a prevalence of 11%. Yet another study (25) in the Qingdao region showed a dramatic increase in urban diabetes prevalence of 11.3% (both men and women) in 2001–2002, and 19.2% (in men) and 16.1% (in women) in 2006. A 2008 report (20) from India noted a secular increase in diabetes prevalence in urban communities (from 13.9% in 2000 to 18.2% in 2006) and rural communities (from 6.4% in 2000 to 9.2% in 2006). A recent study (26) from India, the Chennai Urban Rural Epidemiology Study (CURES), has shown one of the highest incidences of diabetes yet reported. In that study, there was an incidence of 22.2 per 1,000 person-years. After a median follow-up period of 9.1 years, diabetes had developed in 59% of those persons with prediabetes.

The Indian Ocean island nation of Mauritius has provided a "natural" barometer for the evolving global diabetes epidemic (27,28). Its population of $\sim$1.3 million people is composed of Asian Indians (68%), Africans (27%), and Chinese (3%), and this ethnic distribution reflects approximately two-thirds of the world population. Our studies there have covered almost 25 years, and they have shown a 64% secular increase in the prevalence of diabetes from 12.8% in 1987 to 23.4% in 2009 (27). We predicted the rising epidemic for China and India from this study (28), and the subsequent dramatic increase in diabetes in mainland China and India in recent decades is confirmation of that phenomenon.

Yet another example of a substantial secular increase in diabetes is in Turkey over the 12 years from 1997 to 2010. There was a 90% increase in diabetes over the 12 years (29). Notable secular increases have been seen even in populations with a mainly European background. For example, in Canada in the province of Ontario, there was a 69% increase in diabetes prevalence over

10 years (5.2–8.8%) between 1995 and 2005 (30). Also, a very recent report (31) from the U.S. from 1988 to 2012 estimated secular prevalence trends in total diabetes, diagnosed diabetes, and undiagnosed diabetes using National Health and Nutrition Examination Survey data. Between 1988–1994 and 2011–2012, the prevalence of diabetes increased in the overall population and in all subgroups evaluated, with a higher prevalence found among participants who were non-Hispanic black, non-Hispanic Asian, and Hispanic.

Although reports of increase in secular trends in diabetes are quite common, the reverse is unusual. Nevertheless, there are notable examples of secular decreases, particularly in relation to reduced economic circumstances. The Pacific island Nauruans (Micronesians) were once the wealthiest nation per capita in the world from their rich phosphate deposits. In 1975, they had the highest national prevalence of diabetes (13). With the exhaustion of the phosphate deposits through mining, there was a disastrous fall in their economy, accompanied by a 100% fall in diabetes prevalence over the next 30 years (11,32). Similarly, an economic crisis in Cuba lasting from 1991 to 1995 saw a marked and rapid reduction in mortality from diabetes and coronary heart disease accompanied by an average population-wide loss of 5.5 kg in weight (33). When things improved, the weight regain in the Cuban population was associated with an increase in diabetes prevalence, incidence, and mortality. Nauru and Cuba demonstrate how the patterns of diabetes, and indeed related disorders, are dependent on the economic circumstances of a nation.

A 2015 report from the Framingham Heart Study cohort (34) found that the risk of new-onset diabetes was higher in the 2000s compared with the 1970s. However, the authors also found that diabetes incidence did not change significantly in the 2000s compared with the 1990s, despite an increase in mean BMI and despite there being more individuals with obesity in the 2000s. Among several potential factors that were suggested that may have contributed to the stable diabetes incidence observed was that the increased use of bariatric surgery in the 2000s may have affected diabetes incidence. Bariatric procedures increased 10-fold in the U.S. from ~16,200 in 1994 to 171,000 in 2005 (35). However, it was concluded that this would not explain the stable incidence rate between the 1990s and 2000s.

OBESITY AND DIABETES—ETHNIC DIFFERENCES IN RISK: RELEVANCE TO METABOLIC SURGERY

There are significant differences in the risk of type 2 diabetes due to obesity among ethnic groups (36,37). From a metabolic surgery perspective, this epidemiological reality is important for decision making. This applies not only in the countries of origin of ethnic peoples, but also to their diaspora communities where there has been large-scale migration of Chinese and Indian peoples to Western nations like the U.S. and U.K. (3,28). The diabetes epidemic in Asia has spurred an increasing interest in the relationship of obesity as a risk determinant of type 2 diabetes and other comorbidities in Asians (11). This has important implications for decisions on the criteria for bariatric surgery interventions. Type 2 diabetes develops in Asian people at a lower BMI compared with people of European origin (37). At any given level of BMI, type 2 diabetes is more likely to develop in an Asian person. This means that criteria based on obesity for a decision on metabolic surgery will be lower.

Are there determinants of the ethnic differences in diabetes or cardiovascular risk other than the suggested genetic contribution? Whincup et al. (38) have made the intriguing suggestion that factors operating in utero or at birth, including maternal nutrition and maternal glucose control, and body composition at birth, could be important contributors, and help to explain ethnic differences in type 2 diabetes and cardiovascular risk. Early-life events and the intrauterine environment can have an impact on the risk of many chronic diseases later in life, including obesity and type 2 diabetes (39).

Developed nations are failing badly in their attempts to control the obesity epidemic, a prime driver of type 2 diabetes (40). This also applies to developing nations with even more limited resources, so we can expect even less success as they tackle alarming increases in obesity and type 2 diabetes (40). We have suggested that this failure results in part from the focus on adult lifestyles, the traditional "scapegoat." However, this ignores the mounting evidence that biological and cultural factors operating early in life affect adult health status (39). To stem the rising obesity burden in both developing and developed countries, scientists and policy makers must address obesity-promoting factors from early childhood to adulthood (40).

DEVELOPMENTAL ORIGINS OF OBESITY AND TYPE 2 DIABETES: RELEVANCE TO PREVENTION

This concept of fetal origin of disease has now evolved into a conceptual framework of the developmental origins of health and disease (39). This draws on evidence from a number of epidemiological and population studies, including the Dutch Hunger Winter famine study (41) and the study of the Chinese famine of 1959–1961 (42). The risk of type 2 diabetes as a result of inadequate fetal nutrition is exacerbated in people who are exposed to more affluent nutritional environments in adult life, and who have excess and rapid weight gain in early adulthood. Indeed, mismatch between the intrauterine and adult-life environments might explain much of the contemporary diabetes epidemic in a number of developing countries, as has been suggested elsewhere (11).

For many years, the paradigm for risk determinants for obesity and type 2 diabetes has revolved around lifestyle and gene-environmental interaction producing the "diabesity" epidemic (1,3,11). Now epigenetic pathways and early-life events have received substantial attention in relation to type 2 diabetes (39), and give a new and welcome focus on the origins of obesity and why attempts to tackle obesity at a community level have been a failure (40). This concept of early-life events that can have an intergenerational effect has relevance to the issue of obesity and type 2 diabetes as it relates to efforts to prevent obesity, one of the major drivers of the diabetes epidemic.

PREVENTION OF DIABETES: IS THERE A ROLE FOR BARIATRIC SURGERY? IF SO, HOW?

There are now a number of studies (43–45) reporting the success of lifestyle and

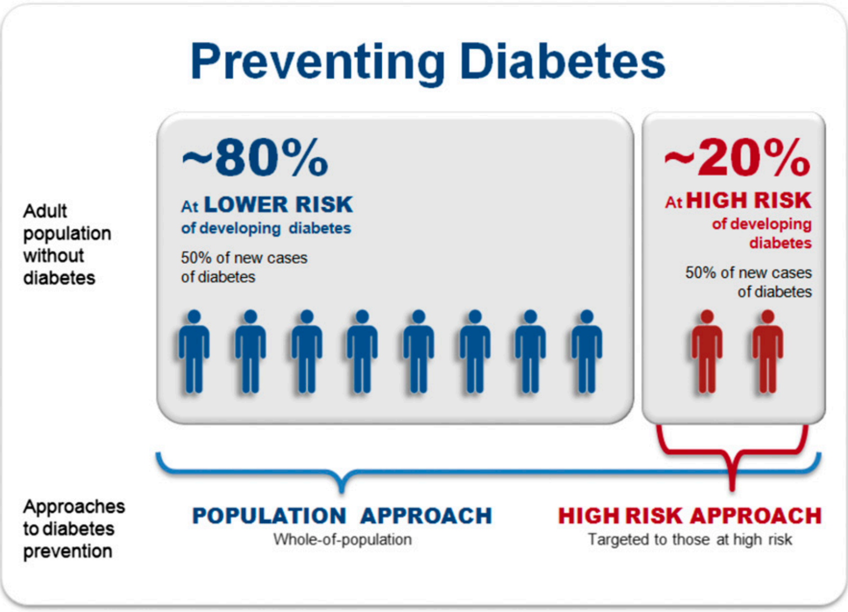

Figure 2—Approaches to type 2 diabetes prevention: population and high-risk interventions.

pharmacological approaches to the prevention of type 2 diabetes in high-risk subjects, particularly those with prediabetes. There are also reports (46) of the success of bariatric procedures in reducing progression to diabetes in persons with prediabetes. Nevertheless, many countries are not even able to muster appropriate lifestyle programs for type 2 diabetes treatment, let alone prevention. And, certainly, the costs and infrastructure required for metabolic surgery are far beyond their limited resources.

It needs to be stressed that bariatric surgery is not a magical solution to the global diabetes epidemic. Approximately 20% of the adult population in communities of European origin is considered to be at high risk for the development of diabetes (S. Colagiuri, unpublished observations). This group is expected to account for 50% of new diabetes diagnoses over the next decade, with the remainder of the population accounting for the remaining 50% (Fig. 2). It is in the high-risk category, particularly in people with other cardiovascular risk factors and/or comorbidities, such as severe or morbid obesity, where metabolic surgery may have a role in diabetes prevention. On the other hand, it is unlikely to have a place in programs focusing on lifestyle interventions for the whole community, most of whose members are at lower risk for the development of diabetes.

As noted earlier, ~80% of people with diabetes live in low- and middle-income countries and communities (18). This presents an important challenge for the future because most people with diabetes live in countries with inadequate resources for anything but the most basic of treatments and for the capacity for prevention of obesity and diabetes. Also, in many developed nations, immigrants from less developed nations often have a much higher prevalence of diabetes than the host population, yet their access to metabolic surgery may be limited. This may also be the case for indigenous peoples in developed nations, such as Australia, the U.S., and Canada, along with not only economic but also social and cultural issues.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

References

1. Zimmet PZ, Magliano DJ, Herman WH, Shaw JE. Diabetes: a 21st century challenge. Lancet Diabetes Endocrinol 2014;2:56–64
2. Tuomi T, Santoro N, Caprio S, Cai M, Weng J, Groop L. The many faces of diabetes: a disease with increasing heterogeneity. Lancet 2014; 383:1084–1094
3. Chen L, Magliano DJ, Zimmet PZ. The worldwide epidemiology of type 2 diabetes mellitus—present and future perspectives. Nat Rev Endocrinol 2011;8:228–236
4. Zimmet P, Alberti KGMM. Surgery or medical therapy for obese patients with type 2 diabetes? N Engl J Med 2012;366:1635–1636
5. American Diabetes Association. Standards of medical care in diabetes—2015. Diabetes Care 2015;38(Suppl. 1):S1–S93
6. Zimmet P, Alberti KGMM, Rubino F, Dixon JB. IDF's view of bariatric surgery in type 2 diabetes. Lancet 2011;378:108–110
7. Dixon JB, Zimmet P, Alberti KG, Rubino F; International Diabetes Federation Taskforce on Epidemiology and Prevention. Bariatric surgery: an IDF statement for obese type 2 diabetes. Diabet Med 2011;28:628–642
8. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. N Engl J Med 2012;366:1577–1585
9. Schauer PR, Kashyap SR, Wolski K, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. N Engl J Med 2012;366:1567–1576
10. Inzucchi SE, Bergenstal RM, Buse JB et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2015; 38:140–149
11. Nanditha A, Ma RC, Ramachandran A, et al. Diabetes in Asia and the Pacific: implications for the global epidemic. Diabetes Care 2016;39:472–485
12. Bennett PH, Burch TA, Miller M. Diabetes mellitus in American (Pima) Indians. Lancet 1971;2:125–128
13. Zimmet P, Taft P, Guinea A, Guthrie W, Thoma K. The high prevalence of diabetes mellitus on a Central Pacific Island. Diabetologia 1977;13:111–115
14. Zimmet P, Dowse G, Finch C, Serjeantson S, King H. The epidemiology and natural history of NIDDM—lessons from the South Pacific. Diabetes Metab Rev 1990;6:91–124
15. Prior IA, Davidson F. The epidemiology of diabetes in Polynesians and Europeans in New Zealand and the Pacific. N Z Med J 1966;65:375–383
16. Colagiuri S, Colagiuri R, Na'ati S, Muimuiheata S, Hussain Z, Palu T. The prevalence of diabetes in the kingdom of Tonga. Diabetes Care 2002; 25:1378–1383
17. International Diabetes Federation. *Diabetes Atlas*. 1st ed. Brussels, Belgium, International Diabetes Federation. 2000
18. International Diabetes Federation. *Diabetes Atlas*. 7th ed. Brussels, Belgium, International Diabetes Federation, 2015
19. Xu Y, Wang L, He J, et al.; 2010 China Noncommunicable Disease Surveillance Group. Prevalence and control of diabetes in Chinese adults. JAMA 2013;310:948–959
20. Ramachandran A, Mary S, Yamuna A, Murugesan N, Snehalatha C. High prevalence of diabetes and cardiovascular risk factors associated with urbanization in India. Diabetes Care 2008;31:893–898
21. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care 1998;21:1414–1431
22. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047–1053

23. Whiting DR, Guariguata L, Weil C, Shaw J. IDF Diabetes Atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract 2011;94:311–321
24. Shanghai Diabetes Research Cooperative Group. Diabetes mellitus survey in Shanghai. Chin Med J (Engl) 1980;93:663–672
25. Ning F, Pang ZC, Dong YH, et al.; Qingdao Diabetes Survey Group. Risk factors associated with the dramatic increase in the prevalence of diabetes in the adult Chinese population in Qingdao, China. Diabet Med 2009;26:855–863
26. Anjana RM, Shanthi Rani CS, Deepa M, et al. Incidence of diabetes and prediabetes and predictors of progression among Asian Indians: 10-year follow-up of the Chennai Urban Rural Epidemiology Study (CURES). Diabetes Care 2015;38:1441–1448
27. Magliano DJ, Söderberg S, Zimmet PZ, et al. Explaining the increase of diabetes prevalence and plasma glucose in Mauritius. Diabetes Care 2012;35:87–91
28. Zimmet P, Alberti KGMM, Shaw J. Global and societal implications of the diabetes epidemic. Nature 2001;414:782–787
29. Satman I, Omer B, Tutuncu Y, et al.; TURDEP-II Study Group. Twelve-year trends in the prevalence and risk factors of diabetes and prediabetes in Turkish adults. Eur J Epidemiol 2013;28:169–180
30. Lipscombe LL, Hux JE. Trends in diabetes prevalence, incidence, and mortality in Ontario, Canada 1995-2005: a population-based study. Lancet 2007;369:750–756
31. Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and trends in diabetes among adults in the United States, 1988-2012. JAMA 2015;314:1021–1029
32. Khambalia A, Phongsavan P, Smith BJ, et al. Prevalence and risk factors of diabetes and impaired fasting glucose in Nauru. BMC Public Health 2011;11:719
33. Franco M, Bilal U, Orduñez P, et al. Population-wide weight loss and regain in relation to diabetes burden and cardiovascular mortality in Cuba 1980-2010: repeated cross sectional surveys and ecological comparison of secular trends. BMJ 2013;346:f1515
34. Abraham TM, Pencina KM, Pencina MJ, Fox CS. Trends in diabetes incidence: the Framingham Heart Study. Diabetes Care 2015;38:482–487
35. Robinson MK. Surgical treatment of obesity–weighing the facts. N Engl J Med 2009;361:520–521
36. Lear SA, Humphries KH, Kohli S, Chockalingam A, Frohlich JJ, Birmingham CL. Visceral adipose tissue accumulation differs according to ethnic background: results of the Multicultural Community Health Assessment Trial (M-CHAT). Am J Clin Nutr 2007;86:353–359
37. WHO Expert Consultation. Appropriate body mass index for Asian populations and its complications for policy and intervention strategies. Lancet 2004;363:157–163
38. Whincup PH, Nightingale CM, Owen CG, et al. Early emergence of ethnic differences in type 2 diabetes precursors in the UK: the Child Heart and Health Study in England (CHASE Study). PLoS Med 2010;7:e1000263
39. Gluckman PD, Hanson MA, Cooper C, Thornburg KL. Effect of in utero and early-life conditions on adult health and disease. N Engl J Med 2008;359:61–73
40. Gluckman PD, Hanson M, Zimmet P, Forrester T. Losing the war against obesity: the need for a developmental perspective. Sci Transl Med 2011;3:93cm19
41. Ravelli AC, van der Meulen JH, Michels RP, et al. Glucose tolerance in adults after prenatal exposure to famine. Lancet 1998;351:173–177
42. Li Y, He Y, Qi L, et al. Exposure to the Chinese famine in early life and the risk of hyperglycemia and type 2 diabetes in adulthood. Diabetes 2010;59:2400–2406
43. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. Diabetes Care 1997;20:537–544
44. Lindström J, Ilanne-Parikka P, Peltonen M, et al.; Finnish Diabetes Prevention Study Group. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. Lancet 2006;368:1673–1679
45. Knowler WC, Barrett-Connor E, Fowler SE, et al.; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393–403
46. Carlsson LMS, Peltonen M, Ahlin S, et al. Bariatric surgery and prevention of type 2 diabetes in Swedish obese subjects. N Engl J Med 2012;367:695–704