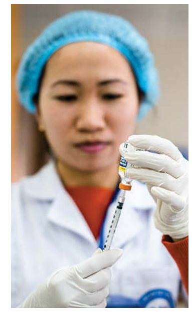

Chapter 12

Diabetes: An Update on the Pandemic and Potential Solutions

Mohammed K. Ali, Karen R. Siegel, Eeshwar Chandrasekar, Nikhil Tandon, Pablo Aschner Montoya, Jean-Claude Mbanya, Juliana Chan, Ping Zhang, and K. M. Venkat Narayan

INTRODUCTION

Diabetes mellitus is a chronic metabolic disease with deadly, disabling, and costly consequences for individuals, families, communities, and countries. Although they are phenotypically distinct, diabetes subtypes (type 1, type 2, gestational, and other forms) are all defined by elevated blood glucose levels. Approximately 95 percent of diabetes cases worldwide are type 2 diabetes (previously known as *adult-onset* or *non-insulin-dependent* diabetes), which is the focus of this chapter. Type 1 diabetes (previously known as *insulin-dependent* diabetes) most commonly begins in childhood and adolescence. Gestational diabetes refers to elevated blood glucose levels during pregnancy among women without previous diabetes and is associated with fetal, birthing, and early childhood complications as well as higher risk of the mother developing postgestation diabetes.

The growth of diabetes and its impacts have accelerated worldwide since the end of the twentieth century (NCD-RisC 2016), likely correlated with expansion of diabetes risk factors, especially population aging and obesity. Diabetes is a multifactorial condition. Because genetic, epigenetic, lifestyle, economic, and psychosocial factors all contribute to the development of diabetes (McCarthy 2010; Stumvoll, Goldstein, and van Haeften 2005), preventing and managing the condition require action at policy, program, clinical practice, and individual levels (Hill and others 2013).

Reliable and meaningful estimates of burdens, risk factors, and effectiveness and cost-effectiveness of interventions as well as evaluations of existing policies, are limited; data are especially scarce in low- and middle-income countries (LMICs). This chapter focuses on what can and should be done to address diabetes. We present the available data regarding global burdens and trends in diabetes; review available evidence and assess the effectiveness and cost-effectiveness of interventions to prevent, detect, and control diabetes; and report summary expert opinions regarding the priority and feasibility of implementing these interventions. Assimilating evidence from countries at different income levels, we provide global perspectives on the diabetes pandemic, recommend priority interventions, and identify remaining data gaps.

GLOBAL BURDEN

Distribution and Prevalence

An estimated 415 million people—8.8 percent of the world's adult population—have diabetes (IDF 2015), and 75 percent of people with diabetes live in LMICs. Worldwide, specific populations and geographies

Corresponding author: Mohammed K. Ali, Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, United States; mkali@emory.edu.

experience very high prevalence of diabetes, notably the Western Pacific (for example, the Federated States of Micronesia) and Indian Ocean islands (for example, Mauritius), the Middle East (for example, Kuwait), North Africa (for example, the Arab Republic of Egypt), Native Americans, and urban South Asia (Ali, Bhaskarapillai, and others 2016; IDF 2015; Knowler and others 1978; Zabetian and others 2013). In addition, the world's most populous countries, such as China (Yang and others 2010), India (Anjana and others 2011), and the United States (CDC 2016), have very high absolute numbers of people with diabetes: 92.4 million, 65.1 million, and 29 million, respectively.

Worldwide, an estimated 46.5 percent of people with blood glucose levels in the diabetes range are undiagnosed (IDF 2015). It is estimated that, on average, one-quarter of people with diabetes in HICs are undiagnosed; in LMICs, in contrast, two-thirds to three-quarters are undiagnosed.

Globally, an equally high number of people are at high risk for developing diabetes because they have higher-than-normal fasting (impaired fasting glucose [IFG]) or postprandial (impaired glucose tolerance [IGT]) blood glucose levels, or both, or high glycated hemoglobin levels. Having any of these high-risk conditions is called prediabetes and puts individuals at 5–12 times higher annual risk of developing diabetes than the general population (Gerstein and others 2007). Although IFG and IGT may be phenotypically different and represent different pathophysiologies, accurate global estimates regarding the distribution of these subtypes of prediabetes are not available because the blood tests required to diagnose prediabetes are relatively expensive and logistically inconvenient to administer. Furthermore, standardizing and verifying whether individuals are fasting can be challenging. Estimates from the International Diabetes Federation (IDF) do not include individuals with isolated IFG (iIFG) or fully capture those with combined IFG-IGT; the IDF estimates that 318 million people (6.7 percent of the adult population) worldwide have some form of IGT (IDF 2015). This lack of data has major implications for understanding the natural history of different types of diabetes and implementing appropriate interventions.

Complications

Diabetes is associated with acute and chronic complications. Acutely, people with diabetes can experience fluctuations in blood glucose levels that require medical attention. Because people with type 1 diabetes require insulin treatment, acute complications occur more commonly in that population and can be fatal if untreated.

Long-standing and poorly controlled diabetes—both types 1 and 2—is associated with increased risks of neurological, renal, ophthalmic, cardiovascular, cognitive, and psychiatric illnesses, and even cancers and infections. Despite our understanding of how diabetes progresses and increases the risk of complications, the understanding of the global distribution of diabetes complications is limited. In most LMICs, testing instruments (for example, retinal cameras) and technical capacity to operate and interpret the tests are too costly or scarce.

Diabetes leads to loss of sensory and motor function as well as poor circulation of the hands and feet, increasing the risks of infection, poor wound healing, and eventual amputation. Diabetes is a leading cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD), requiring dialysis or transplantation. Retinopathy, cataracts, and glaucoma related to diabetes are very common and lead to visual disturbance and blindness. Coronary heart disease, heart failure, and stroke are two to four times more common among persons with diabetes than among similar persons without diabetes. Persons with diabetes often have comorbid depression and a higher risk of developing dementia. The coexistence of depression and diabetes markedly increases the risk of mortality as well as loss of productivity in persons who are gainfully employed; the increasingly early onset of diabetes and depression is a major concern in this context. There is also growing appreciation of a link between diabetes and cancers, particularly because people with diabetes are living longer and are less likely to die from cardiovascular disease (CVD) or CKD (Gregg, Cheng, and others 2012; Gregg and others 2014; Gregg, Sattar, and Ali 2016). In addition, diabetes and cancers share some risk factors such as older age; tobacco use; and oxidant rich, low-fiber diets (Giovannucci and others 2010).

Diabetes and infections increasingly occur together. This is particularly relevant for LMICs, which face a substantial residual burden of infectious diseases. It is not clear whether people with diabetes have more infections, but the coexistence of diabetes and tuberculosis and group B streptococci (Dooley and Chaisson 2009; Magee, Blumberg, and Narayan 2011) is of policy importance because of the added health system burden when these interactions occur. In particular, the coexistence of tuberculosis and diabetes may be associated with poorer recovery and higher risk of tuberculosis relapse, resistance, and death, although the data are inconclusive, as discussed in greater detail in chapter 16 of this volume (Magee and others 2016). Diabetes reportedly occurs increasingly among people infected with human immunodeficiency virus (HIV); this metabolic dysfunction may be related to the HIV infection itself, higher life expectancy with HIV treatments, the treatments themselves, or some combination of these factors (Ali, Magee, and others 2014). The long-term implications of these interactions are actively evolving.

Whether acute, chronic, or infectious, complications increase the use and cost of health care, decrease productivity and quality of life, and increase the risk of mortality for people with diabetes. Though type 1 diabetes is not a focus of this chapter, it is important to note that the disease occurs earlier in life than type 2 diabetes; therefore, if it is poorly controlled, people with type 1 diabetes have more years lived with disability and are at risk for more years of life lost. This is an important policy consideration.

Mortality

Worldwide, life expectancy has been rising. Even mortality rates attributable to other leading noncommunicable diseases, such as CVD, stroke, some cancers, and chronic respiratory disease, have been declining (Ali and others 2015). However, both the age-standardized mortality rate and absolute number of deaths from diabetes have been rising.

Some regional variation is evident in deaths attributable to diabetes, as shown in table 12.1. North Africa and the Middle East, Latin America and the Caribbean, and the Western Pacific regions have the highest proportions of and increases in deaths attributable to diabetes (IDF 2015). South Asia has the highest absolute number, with almost 25 percent of all diabetes deaths globally.

However, the magnitude of deaths attributable to diabetes is probably underestimated because death certifications and mortality approximations list only one cause of death. At least half of all deaths in people with diabetes are related to CVD (Geiss, Herman, and Smith 1995; IDF 2015; Moss, Klein, and Klein 1991), and CKD contributes significantly to deaths among people with diabetes (Levitt 2008; Zimmet 2009); however, these deaths are assigned to CVD or CKD, not diabetes. The World Health Organization (WHO) estimates that deaths attributable to diabetes amounted to 2.8 percent of all deaths globally in 2010, not including deaths attributable to CVD and CKD (32.0 percent and 1.5 percent, respectively). However, diabetes contributes to at least 21 percent of coronary heart disease and 13 percent of stroke mortality worldwide (Danaei and others 2006). Incorporating these aspects, the IDF estimates that diabetes is responsible for 5 million adult deaths annually, or 8.4 percent of all deaths globally (IDF 2015; Roglic and others 2005).

Morbidity and Disability

In addition to shortening life expectancy by 7–15 years (Franco and others 2007; Morgan, Currie, and Peters 2000), diabetes is associated with considerable morbidity and disability. Disability-adjusted life years (DALYs) reflect the combined burdens of disability and premature mortality associated with different diseases. Earlier age of onset of diabetes increases the duration of exposure to diabetes, the associated disability (Bardenheier and others 2016), and the risk

Table 12.1 Percentage of All Deaths and DALYs Lost Attributable to Diabetes, Globally and by Region

WHO Estimates[a]			IDF Estimates	
Region	**DALYs lost**	**Deaths**	**Region**	**Deaths**
Global	2.1	2.9	Global	8.4
Latin America	3.4	5.9	South and Central America	~12.0
Eastern and South-East Asia	3.2	3.9	South-East Asia	~14.0
South Asia	1.6	2.6	Western Pacific	~16.0
Middle East and North Africa	3.1	4.1	Middle East and North Africa	~13.0
Sub-Saharan Africa	0.8	1.8	Africa	~8.5
Eastern and Central Europe	2.3	1.1	Europe	~10.5
High-income countries	2.8	2.7	North America	~13.5

Sources: IDF 2013; WHO 2014.
Note: DALYs = disability-adjusted life years; IDF = International Diabetes Federation; WHO = World Health Organization. Estimates are approximations where IDF- and WHO-defined regions are different.
a. Does not include deaths or DALYs lost attributable to chronic kidney disease or cardiovascular diseases attributable to diabetes.

of an early death. Globally, diabetes accounted for 2.1 percent of DALYs lost from all diseases in 2010, with Latin America experiencing the highest (3.4 percent) and Sub-Saharan Africa experiencing the lowest (0.8 percent) DALYs from diabetes.

Diabetes-related disability can be temporary or permanent and can have physical (Lavigne and others 2003; Tunceli and others 2007), psychological (Degmecic and others 2014; McKellar, Humphreys, and Piette 2004; Nicolucci and others 2013; Piette, Richardson, and Valenstein 2004), and social impacts on functioning (Lavigne and others 2003). With regard to physical manifestations, diabetic neuropathy and foot disease accounted for more than half of all diabetes-related years lived with disability, while amputation, vision loss, and CKD attributable to diabetes accounted for 5 percent each (Vos and others 2012). Even in the absence of physical complications or disability, self-care of diabetes itself requires structure and diligence: persons requiring insulin have to monitor their glucose meticulously and time their dietary intake; may experience episodes of hypoglycemia or hyperglycemia; and are advised to undertake routine preventive medical visits, such as annual eye exams (Brod and others 2014; Fu and others 2009; Nicolucci and others 2013). Some studies report that 20 percent of persons with diabetes and their families experience some form of social stigma and discrimination (Kovacs Burns and others 2013; Nicolucci and others 2013), although these incidents are context-dependent. Adults with diabetes experience more depression, anxiety, and cognitive dysfunction than their nondiabetic counterparts. These psychosocial issues negatively affect their social integration, quality of relationships (Aalto, Uutela, and Kangas 1996; Hempler, Ekholm, and Willaing 2013), and self management, creating a vicious cycle.

Economic Burdens

Diabetes is associated with high and long-standing direct medical and nonmedical costs for patients and their caregivers. Worldwide, an estimated 12 percent of all annual direct medical expenditures (an estimated US$673 billion), including outpatient consultations, diagnostic testing, medications, emergency visits, and inpatient procedures and care, are for diabetes (IDF 2015).

Diabetes is also associated with substantial indirect costs (lost productivity attributable to absenteeism, suboptimal work performance, and premature deaths) as well as intangible costs (related to psychosocial harm). Both of these costs are difficult to quantify empirically.

CONSIDERATIONS IN LMICS

Worldwide, the patterns of morbidity and mortality associated with diabetes vary because of differences in populations (differences in maternal and childhood nutrition, exposure to infectious diseases, and level of awareness and health literacy), behavior (likelihood of seeking health care), health financing (health care coverage through public payer or insurance schemes), physical access to care, health facility resources and infrastructure (ability to support high-quality and effective lifestyle interventions and self-management), provider clinical practices, mechanisms for monitoring and delivering quality care, and policies to support diabetes prevention and management. In LMICs, it is especially hard to quantify these factors given the general lack of robust population-based longitudinal data. However, significant and lofty barriers in LMICs clearly have to be overcome to manage diabetes more effectively.

Most LMICs face two significant challenges: (1) lack of coverage of routine tests and inability of patients to pay for them, leading to a high proportion of undiagnosed cases; and (2) limited access to routine care and medications such as insulin that can be life-saving, as well as a general lack of human and infrastructural resources (refrigeration for insulin, for example), leading to poor health outcomes (Beran and Yudkin 2006; Beran, Yudkin, and de Courten 2005; Sobngwi and others 2012). The issue of affordable access to insulin is especially acute for type 1 diabetes because this lifelong medicine is essential for keeping these patients alive.

There are very few, if any, data from LMICs regarding coverage or access to health services and treatments. A WHO study in four LMIC regions showed generally low availability of insulin in both the public and private health sectors, and the cost of a one-month supply of insulin was equivalent to several days of a person's wages (Mendis and others 2007). A 47-country survey conducted by IDF Europe (n.d.) is also illustrative of major disparities in availability, accessibility, and affordability of medications to control diabetes across country-income groups. The data reflect varying levels of annual spending per capita on diabetes (from less than US$100 in the Kyrgyz Republic to US$9,000 in Switzerland) and public financing of diabetes care (from 22 percent in Georgia to 85 percent in the Netherlands). Financial or geographic barriers to accessing medications and preventive services result in suboptimal care (Beran and Yudkin 2006; Beran, Yudkin, and de Courten 2005; Zhang and others 2012) and delayed presentation, giving rise to disabling and expensive-to-treat complications.

EFFECTIVENESS OF INTERVENTIONS

In the past half century, well-conducted studies from across the world have created a strong base of evidence about interventions that can help prevent diabetes among high-risk individuals (Gillies and others 2007; Knowler and others 2002; Tuomilehto and others 2001). In addition, robust data from trials and epidemiological studies—conducted largely in high-income settings—have shown that proactively and intensively managing diabetes lowers the risk of cardiovascular, kidney, eye, and limb diseases and of death (Holman and others 2008; Nathan and others 2005). Interventions to address diabetes, their efficacy, the level of evidence to support these interventions, and the few studies of this nature from LMICs are cataloged in annex 12A.

Fewer data are available from LMICs themselves to aid decision makers in these contexts. Ongoing studies are evaluating the implementation of diabetes prevention in South Africa (Pengpid, Peltzer, and Skaal 2014) and Brazil (Pimentel and others 2010); other studies are piloting novel approaches to preventing diabetes (Hegde and others 2013; McDermott 2012; McDermott and others 2014), but data are as yet unavailable or the sample sizes are too small to support generalizations. However, as annex 12A shows, the estimated effects in LMICs are comparable to those in HICs. The major considerations regarding the use of HIC data for LMIC settings are possible differences in the patterns of disease and comorbidities, as well as possible differences in accessibility, availability, affordability, and implementation capacity in lower-resource settings (Basu and others 2015).

Screening for Prediabetes and Diabetes

Diabetes meets many of the criteria for screening (Wilson and Jungner 1968), with (1) reliable tests to identify elevated glucose, (2) a precursor phase (prediabetes), and (3) interventions to delay onset and manage the disease (DCCT Research Group 1993; UKPDS Group 1998b). However, screening for diabetes and prediabetes continues to be a fiercely debated topic (Echouffo-Tcheugui and others 2011; Engelgau and Gregg 2012; Engelgau, Narayan, and Herman 2000). Lack of consensus surrounds two issues: the long-term benefits of screening for hard outcomes like CVD or mortality (Norris and others 2008; Rahman and others 2012) and the possible harm it could cause, such as increased anxiety or discrimination (Paddison and others 2011; Park and others 2008); and the cost-effectiveness of screening.

Not understanding the condition or knowing that one is affected causes two types of difficulties. First, high blood glucose can progressively damage tissues and lead to complications; according to studies in both the United States and India, up to 30 percent of people with newly diagnosed diabetes already were experiencing retinopathy, nephropathy, and CVD at the time of diagnosis (Casagrande, Cowie, and Fradkin 2013; Unnikrishnan and others 2007). Second, not knowing or understanding one's condition precludes adopting healthful behaviors or seeking care, both of which are needed to manage diabetes.

For these reasons, early detection is thought to confer opportunities to intervene earlier, slow disease progression, address comorbidities like hypertension that commonly coexist with prediabetes and diabetes, and possibly even lower the growing costs of managing diabetes and its complications. Furthermore, studies have shown that screening has minimal psychological impacts (Eborall, Davies, and others 2007; Eborall, Griffin, and others 2007; Echouffo-Tcheugui and others 2011) and causes no significant harm, especially if testing is targeted to high-risk individuals (those with established diabetes risk factors like age over 40 years, minority ethnicity, family history of diabetes, obesity, physical inactivity, other cardiometabolic risk factors like dyslipidemia, or history of gestational diabetes) rather than universal (Selph and others 2015).

The cost-effectiveness of screening depends on both the yield in the population offered testing and the cost-effectiveness of the intervention (Glumer and others 2006; Waugh and others 2007). Given that interventions to prevent diabetes among persons with prediabetes is so cost-effective (DPP Research Group 2012), screening for both prediabetes and diabetes is more cost-effective than screening for diabetes alone (Echouffo-Tcheugui and others 2011; Gillies and others 2008; Hoerger and others 2004; Khunti and others 2012). Ultimately, clinical guidelines play a role in whether and how clinicians offer testing for different conditions, and guidelines will depend on yield, availability of tools for testing, and resources and interventions to address the condition in the given locality. This last issue should not be taken lightly—there are few or no data for many countries around the world regarding the adequacy and readiness of health systems to cope with increased numbers of people with prediabetes and diabetes needing intervention if a widespread screening policy or program were adopted.

Preventing Diabetes

Large randomized controlled trials (RCTs) in China (Pan and others 1997), Finland (Tuomilehto and others 2001), India (Ramachandran and others 2006), Japan (Kosaka, Noda, and Kuzuya 2005), and the United States

(Knowler and others 2002) have shown that, among individuals with established IGT, structured approaches to modifying behavior (exercising more, consuming fewer high-energy calories, increasing fiber intake, and modest weight loss) lowered the incidence of diabetes by approximately 30 percent to 60 percent compared with simple advice regarding diet and exercise. These structured interventions included regular counseling or coaching sessions delivered by health (or allied health) professionals and weight monitoring, as well as extended support in some cases. The applicability of evidence from trials in people with IGT to those with iIFG—the most prevalent form of prediabetes in many parts of the world—remains open for investigation.

These lifestyle interventions are also associated with long-term benefits, including greater likelihood of regression to normal blood glucose levels (Perreault and others 2009), sustained reductions in diabetes incidence, better cardiometabolic control, and fewer long-term eye complications and cardiovascular deaths (Gong and others 2011; Li and others 2014).

Data also show that pharmaceutical agents to lower glucose, lose weight, or both (for example, biguanides) in people with prediabetes can lower diabetes incidence (Gillies and others 2007).

Managing Diabetes

To manage diabetes and prevent diabetes-related complications, large RCTs—again, largely from HICs—have assessed the benefits of lifestyle interventions; surgical procedures; and pharmaceutical approaches to lowering blood glucose, blood pressure, and lipid levels; as well as avoiding tobacco.

A trial to assess whether intensive lifestyle interventions could lower CVD found no effect at 9.6 years of follow-up (Look AHEAD Research Group 2006, 2013). However, intensive lifestyle modification and weight loss have been associated with a four to six times higher (partial or complete) remission from diabetes (7 percent to 12 percent for intervention vs. 2 percent for control arm participants) (Gregg, Chen, and others 2012); less need for medication and health care (Redmon and others 2010); less loss of mobility (Rejeski and others 2012); less new sleep apnea and higher remission from obstructive sleep apnea (Foy and others 2011); 34 percent lower incidence of depression (Wing 2010); 31 percent lower incidence of ESKD (Otto and others 2007); 14 percent lower incidence of retinopathy (O'Riordan 2013); delayed bone loss (Lipkin and others 2014); and improved patient-reported quality of life, particularly physical function (Look AHEAD Research Group 2014). Given the high personal and monetary costs of these morbidities, lifestyle intervention in people with diabetes is effective and cost-effective (Li and others 2010; Redmon and others 2010).

Surgical procedures are often used to address obesity and diabetes. Extensive evidence shows that gastric bypass surgery and other approaches to compress the stomach (laparoscopic banding) have benefits, including sustained weight loss, improved cardiometabolic profiles, remission (Gloy and others 2013; Li, Lai, and others 2013; Ricci and others 2015), and possibly even prevention (Merlotti and others 2014) of diabetes. Because of the cost and risk of complications, surgical approaches are reserved for individuals who are morbidly obese or for whom other approaches have not been effective (ADA 2016; IDF 2013; NICE 2013).

More intensive control of blood glucose has been shown to reduce complications such as retinopathy, CKD, and neuropathy in the short term (DCCT Research Group 1993; UKPDS Group 1998a, 1998b) and complications such as coronary heart disease, strokes, and related deaths in the long term (Hayward and others 2015; Holman and others 2008; Nathan and others 2005; UKPDS Group 1998a); these findings related to intensive glycemic control are applicable to both type 1 and type 2 diabetes patients. Meta-analyses and reviews of glucose-lowering trials all show some long-term macrovascular benefit, more so for reducing coronary disease than for reducing cerebrovascular disease (Tandon, Ali, and Narayan 2012). The optimal blood glucose level associated with the greatest benefit remains controversial after major trials have shown no short-term benefit from very aggressive glycemic targets of glycated hemoglobin less than 6 percent (Duckworth and others 2009; Gerstein and others 2008; Patel and others 2008). Still, studies that target less aggressive, but still very good, levels of glycated hemoglobin (7 percent) reduced long-term myocardial infarction and all-cause mortality between 15 percent and 40 percent (Ali, Narayan, and Tandon 2010; Hayward and others 2015; Holman and others 2008). For this reason, experts recommend individualizing glucose targets to the patient's comorbid, psychosocial, and clinical circumstances (Inzucchi and others 2012; Ismail-Beigi and others 2011). In addition, activities that support better glycemic control (like self-management education) may promote patient adherence, encourage better metabolic control, and prevent hypoglycemia (Norris, Engelgau, and Narayan 2001). Culturally appropriate health education has net benefits, especially for glycemic control and possibly for improved lifestyles (Attridge and others 2014). Similarly, self-monitoring of blood glucose, even in patients not using insulin, may improve glycemic control (Farmer and others 2012; Sarol and others 2005), although debates still surround the cost, episodes of hypoglycemia, and quality of life experienced by those adopting self-monitoring (Malanda, Bot, and Nijpels 2013; Polonsky and Fisher 2013).

Lowering blood pressure and lipids also has been shown to reduce microvascular and macrovascular complications, both in RCTs and in large meta-analyses (Kearney and others 2008; Turnbull and others 2005). Still, there is no consensus on the most optimal blood pressure and cholesterol targets, but age- and comorbidity-appropriate treatment goals are advocated. Intensive approaches (behavioral therapies, medications) to decrease or cease tobacco use are unequivocally associated with higher likelihood of sustaining tobacco avoidance and reducing macrovascular events (Critchley and Capewell 2003; Mohiuddin and others 2007).

Strong data support comprehensive control of all risk factors along with provision of protective medications, such as angiotensin-converting enzyme inhibitors (ACEi) and angiotensin-receptor blockers (ARBs). Compared with standard care, comprehensive care implemented among people with diabetes and microalbuminuria (urine albumin greater than or equal to 30 milligrams per 24 hours) was associated with 60 percent fewer complications after eight years of follow-up and 60 percent to 80 percent lower mortality after 13 years in an RCT in Denmark (Gaede and others 2003; Gaede, Lund-Andersen, and others 2008).

Screening for and Preventing Complications

Care guidelines recommend regular screening to detect and treat diabetes complications in their early stages, before irreversible clinical manifestations and disability set in (ADA 2016; IDF 2013; NICE 2013). Because there is a preclinical latent phase before each complication sets in, it is recommended that individuals with diabetes undergo regular eye, foot, and urine checks.

Eye disease, particularly diabetic retinopathy, occurs in all people with diabetes, given sufficient duration of disease (Klein and others 1989a, 1989b). Annual or even biennial retinal screening is recommended—depending on the availability of resources and feasibility—to detect changes early and institute therapy (Echouffo-Tcheugui and others 2013). Once detected, evidence from trials shows conclusively that photocoagulation therapy significantly preserves vision (DRS 1981, 1991).

No treatments exist to reverse diabetic nerve damage. However, because people with diabetes have a 25 percent lifetime risk of experiencing foot ulceration, regular assessments and foot care are considered invaluable for detecting sensorimotor, autonomic, and vascular abnormalities (Boulton and others 2008). Assessments can be coupled with managing symptoms, educating patients regarding appropriate foot care, and preventing deterioration (ADA 2016). Simple foot care education with periodic assessment and care can reduce the risk of amputation, and efforts are increasing to disseminate resources in LMICs for training health care workers in foot care (McGill 2005; Tulley and others 2009).

To prevent deterioration of kidney function, annual urine screening and use of ACEi and ARB medications are recommended once microalbuminuria sets in (ADA 2016). Early kidney disease increases the risk of CVD and ESRD (Fox and others 2012). Blood glucose and blood pressure management in general, and ACEi/ARB use in particular, have been shown to reduce these major adverse outcomes (Lewis and others 1993) in people with modestly elevated excretion of urinary albumin, as discussed in greater detail in chapter 13 of this volume (Anand and others 2017).

Finally, guidelines encourage annual influenza vaccination and a lifetime pneumococcal vaccination for people with diabetes older than age 60 years. Although there are no RCTs of vaccination among people with diabetes, observational studies show fewer influenza-like illnesses, fewer pneumonia-like illnesses, and fewer hospitalizations among persons with diabetes who were vaccinated compared with those who were not (Colquhoun and others 1997; Heymann and others 2004; Lau and others 2013; Pozzilli and others 1986; Rodriguez-Blanco and others 2012).

TRANSLATING EVIDENCE INTO ACTION

Clinical and epidemiological data have been assimilated into expert preventive and clinical guidelines that are widely accessible (ADA 2016; IDF 2013; NICE 2013), but achieving real health gains requires more than just an accessible compendium of interventions. Complex conditions like diabetes require stakeholders and resources to coalesce at policy, program, clinic, and individual levels. However, because of barriers among policy makers (competing priorities), providers (low accountability, time constraints, lack of incentive schemes), and patients (low motivation), implementation of recommended preventive and care services for diabetes is falling far short of desired goals.

Gaps in Diagnosis and Care

Huge gaps are evident, even in HICs—for example, almost 90 percent of the 86 million people with prediabetes who would be eligible for preventive services

(Li, Geiss, and others 2013) and up to 30 percent of the 29 million people with diabetes in the United States alone (Ali, Bullard, and others 2014) are not aware of their condition, are not engaged in diabetes prevention programs, or are not caring for their diabetes. Because glycated hemoglobin tests are costly and oral glucose tolerance tests are time consuming and disliked by patients, data are lacking to show what proportions of people are at high risk for or have diabetes in LMICs and are aware of their prediabetes or diabetes status; almost no data are representative of entire populations (Narayan and others 2012).

Similar gaps exist with regard to managing diabetes and controlling risk factors. Data from Africa, Asia, Europe, Latin America, and the United States all show that more than half of people with diabetes are not meeting recommended targets to prevent complications (Ali and others 2013; Gakidou and others 2011; Mudaliar and others 2013; Sobngwi and others 2012; Stone and others 2013). Data from eight countries in Europe show that, although 80 percent to 98 percent of people with diabetes had recorded values for glycated hemoglobin, blood pressure, and lipid values in the past 12 months, few had achieved the recommended values (54 percent, 19 percent, and 55 percent, respectively) (Stone and others 2013). For the United States, similar findings were reported using nationally representative surveillance data: only half of all people with diabetes were meeting individual targets, and only 14 percent were controlling all three factors and avoiding tobacco (Ali and others 2013). In Africa, the gaps in care are even larger. In six African countries, fewer than half (47 percent) of all respondents with diabetes had glycated hemoglobin levels recorded in the past year, 29 percent had glycated hemoglobin less than 6.5 percent, and only 13 percent and 65 percent were treated with lipid-lowering or antihypertensive medications, respectively (Sobngwi and others 2012). Systematic reviews of diabetes care in Latin America and Asia show wide variations in risk factor goals, but the findings are similar (Mudaliar and others 2013; Shivashankar and others 2015), suggesting that patient, provider, and system barriers perpetuate gaps in care.

To address these gaps and improve the reach, adoption, effectiveness, and sustainability of diabetes prevention and care interventions, more implementation science (also known as translation research) is needed (Glasgow and others 2001; Jilcott and others 2007). Wider implementation and sustainability of health care and prevention interventions require consistent and strong evidence, adapting the interventions to the context, mobilizing stakeholders and resources, and identifying the processes that permit effective engagement among stakeholders (Brownson, Fielding, and Maylahn 2009).

Implementing Diabetes Prevention

Numerous studies have evaluated the short-term impacts of implementing structured lifestyle interventions to prevent diabetes in different settings. Only a few of these have been in LMICs, largely in South Asia (Iqbal Hydrie and others 2012; Karalliedde and others 2014; Ramachandran and others 2013; Sathish and others 2013; Weber and others 2012). Data from a trial that tested the delivery of lifestyle interventions using mobile phones in India showed a 36 percent reduction in diabetes incidence compared with advice delivered at baseline (Ramachandran and others 2013). Results from a study at clinics in India also showed a 30 percent to 35 percent reduction in diabetes incidence (Weber and others 2016). In the United States, individuals at high risk for diabetes who enrolled in and completed adapted lifestyle intervention programs in clinics, workplaces, places of worship, or community settings achieved an average 4 percent weight loss (Ali, Echouffo-Tcheugui, and Williamson 2012); this amount is considered clinically meaningful, although somewhat lower than the 7 percent weight loss observed in the large Diabetes Prevention Program (DPP) study (Knowler and others 2002). Based on early successes, diabetes prevention programs are being scaled up in countries such as Finland (Saaristo and others 2010), the United States (Albright and Gregg 2013), and parts of Australia (Dunbar and others 2014; Janus and others 2012). These real-world diabetes prevention programs were also associated with meaningful (and quite similar to the DPP study) reductions in other metabolic parameters such as blood pressure and lipids, which lowers the need for medications and lowers overall vascular risk (Mudaliar and others 2016).

Implementing Better Diabetes Care

To improve diabetes management and lower the risk of complications, patient-level, provider-level, and system-level barriers that block achievement of care goals need to be addressed. Several interventions have been tested to address these barriers, either individually or together. The data show that targeted patient-level (reminders, education, motivation by care coordinators), provider-level (reminders, audit and feedback), and system-level (structured team-based care or electronic decision support systems) intervention strategies are promising (Renders and others 2001; Stellefson, Dipnarine, and Stopka 2013; Tricco and others 2012). Empowerment, case management, and task delegation are associated with the greatest effects on risk factors. Although scarce, data in settings outside Europe and the United States—for example, using structured care or peer educators in Cambodia (MoPoTsyo Patient Information Centre 2015); team-based care in Hong Kong SAR, China (Chan and others 2009); or multicomponent interventions (for example, care coordinators and decision-support software) like the chronic care model in India (Ali, Singh, and others 2016)—have shown promise, improving detection, controlling risk factors, lowering ESRD incidence and death, and demonstrating cost-effectiveness (Ko and others 2011). These models may also be of particular relevance as the population of people with comorbidities, such as diabetes and depression or diabetes and HIV/AIDS, grows.

Despite the efforts to adapt interventions to local contexts, two aspects of sustainable implementation warrant further discussion: (1) resources and capacity to implement and (2) context-specific stakeholder perspectives. Our efforts to compile data regarding the value of diabetes interventions and stakeholder perspectives are described in the following sections.

ECONOMIC EVALUATIONS OF DIABETES INTERVENTIONS

To identify and compare the value of different diabetes-focused interventions—that is, the resource inputs required to achieve benefit—we reviewed and synthesized the available literature regarding cost-effectiveness of interventions to detect, prevent, and manage diabetes and its complications. The methodology is described in annex 12B; median and individual study incremental cost-effectiveness ratios (ICER) are provided in annex 12B (table 12B.1) and annex 12C (tables 12C.1–12C.4), respectively.

Cost-Effectiveness

To synthesize the broad findings, we placed all diabetes interventions into four categories:

- Screening for diabetes, prediabetes, or gestational diabetes
- Preventing type 2 diabetes in high-risk individuals
- Managing diabetes (lifestyle interventions; self-management education; self-monitoring of blood glucose; intensive glycemic, blood pressure, and lipid control; case management)
- Screening for and prevention of diabetes-related complications (retinopathy, neuropathy, nephropathy).

Screening for Undiagnosed Diabetes, Prediabetes, or Gestational Diabetes

Cost-effectiveness estimates regarding screening for undiagnosed diabetes, prediabetes, or gestational diabetes were based largely on simulation models because RCTs of screening are neither feasible nor ethical. The modeled estimates are subject to the assumptions defined by each group of investigators. From studies that modeled different scenarios of which patients to screen, when to initiate, and how often to repeat screening, the following themes emerged:

- Screening for undiagnosed diabetes alone is not cost-effective, but screening for both prediabetes and undiagnosed diabetes is.
- Opportunistic screening of entire populations is extremely resource-intensive (CDC 1998; Hoerger and others 2004; Kahn and others 2010), while more targeted screening of individuals at a certain age (45 years) or at any age if risk factors for diabetes already exist is far more cost-effective (Hoerger and others 2004; Kahn and others 2010; Mortaz and others 2012). This finding has led the American Diabetes Association and the National Institute for Health and Care Excellence, among others, to recommend two-stage screening for asymptomatic adults—in other words, asking about risk factors, followed by blood testing.
- Screening is more cost-effective if followed by an intervention than is screening alone, and is both ethically and economically beneficial (Gillies and others 2008; Hoerger and others 2007; Nicholson and others 2005; Schaufler and Wolff 2010).
- Cost-effectiveness of screening also varies depending on the measure used to estimate blood glucose. Although data are limited, oral glucose tolerance and glycated hemoglobin tests are far more expensive than capillary glucose tests. However, cheaper tests need to be assessed for their accuracy and performance (false negative or positive rates).
- Screening all pregnant women can be costly (Nicholson and others 2005; Werner and others 2012), but it may be more cost-effective if followed by postpartum lifestyle management (Lohse, Marseille, and Kahn 2011; Marseille and others 2013) or if the prevalence of gestational diabetes continues to rise. Some HICs advocate screening all pregnant women at 24–28 weeks gestation because of the rising prevalence of gestational diabetes (U.S. Preventive Services Task Force 2014).

Preventing Diabetes among High-Risk Individuals

With respect to diabetes prevention, the findings for high-risk individuals with prediabetes were confirmed by a comprehensive review conducted by the Community

Preventive Services Task Force (Li and others 2015; Pronk and Remington 2015):

- The efficacy, effectiveness, and cost-effectiveness data on diabetes prevention are limited to people with isolated IGT, combined IFG-IGT, or both; there are only extrapolations, but no real data, for people with iIFG.
- Within-trial economic evaluations generally find higher cost per quality-adjusted life year (QALY) gained (DPP Research Group 2003; Irvine and others 2011; van Wier and others 2013) for individual one-on-one lifestyle modification programs than modeled estimates.
- Modeling studies demonstrate that to lower costs, variations of the following could be offered: intervention intensity, number of sessions, type of provider (lay persons vs. medically trained personnel), and delivery format (group vs. one-on-one).
- In pragmatic studies, group-based lifestyle counseling is more feasible and less costly to implement (Absetz and others 2007; Herman and others 2005; Katula and others 2013; Li and others 2015; Segal, Dalton, and Richardson 1998) than interventions delivered to individuals (Eddy, Schlessinger, and Kahn 2005; Lindgren and others 2007; Palmer, Roze, and others 2004).
- Over a longer time horizon, costs per QALY gained for primary prevention drops (DPP Research Group 2012).
- Metformin is not cost-effective in the short term but can be cost saving in the long term (DPP Research Group 2003, 2012). Generic metformin substantially lowers costs (Palmer and Tucker 2012) compared with models based on costs from trials (Herman and others 2005).
- Innovations that lower the costs of delivering primary prevention interventions and that optimize identification, adoption and engagement, adherence, and maintenance will likely be even more cost-effective. This is especially possible in LMICs, as demonstrated in India (Ramachandran and others 2007), but such innovations have not been quantified widely or for different contextual permutations.

Managing Diabetes

Very few economic estimates of lifestyle interventions in individuals with diabetes are available. The prematurely discontinued Look AHEAD study resulted in no reduction in cardiovascular events (Look AHEAD Research Group 2013), but there were other benefits—specifically, reductions in morbidity and other health problems (Gregg, Chen, and others 2012; Redmon and others 2010; Rejeski and others 2012; Wing 2010). The cost-effectiveness of aerobic and resistance exercises and dietary changes for people with diabetes remains understudied (Coyle and others 2012; Eddy, Schlessinger, and Kahn 2005).

With respect to managing glucose levels through clinical interventions,

- Structured diabetes self-management education programs are cost-effective in studies from Mexico and Nigeria (Adibe, Aguwa, and Ukwe 2013; Diaz de Leon-Castaneda and others 2012) as well as in studies from Europe and the United States (Gillett and others 2010; Gozzoli and others 2001; Shearer and others 2004).
- Self-monitoring of blood glucose is recommended mainly for patients using insulin or oral glucose-lowering drugs who experience fluctuations in blood glucose. Home self-monitoring among non-insulin users is costly and offers low value (Pollock and others 2010; Tunis 2011; Tunis and Minshall 2008).
- The incremental costs to control glycemia intensively (aiming for near-normal glucose levels), compared with conventional treatment, tend to vary according to intensity, number, and costs of the medications used. In general, insulin therapies cost the most and metformin costs the least per QALY gained across all studies (Almbrand and others 2000; CDC Diabetes Cost-Effectiveness Group 2002; Clarke and others 2005; DCCT Research Group 1996; Eastman and others 1997; Palmer and others 2000; Wake and others 2000). The additional resources, patient burden, and risks of hypoglycemia and other potential harms need to be counterbalanced against the potential gains in reducing diabetes complications. This is especially important considering that glycemic control has large benefits in reducing disabling microvascular complications and modest benefits in reducing cardiovascular events over a long period of follow-up (Hayward and others 2015; Holman and others 2008; Nathan and others 2005; UKPDS Group 1998b); moreover, improvements in care, blood pressure control, lipid management, and tobacco cessation are producing the lowest average rates of macrovascular complications ever observed in some HICs (Gregg and others 2014).

With respect to clinical interventions to control CVD risk factors,

- Costs to control blood pressure depend on the target blood pressure. Median costs per QALY gained for blood pressure control are much lower than for glycemic control and likely attributable to a larger effect on CVD morbidity and mortality rather than on a lower cost to implement. Less aggressive targets cost much less per QALY gained than more aggressive targets (CDC Diabetes Cost-Effectiveness Group 2002; Clarke and others 2005; Elliott, Weir, and Black 2000).

- For lipid control, the economic data are largely limited to the use of statins; to our knowledge, there are no data for fibrates or niacin. The type and availability of generic statins as well as the risk level of individuals affect cost-effectiveness: (1) Models based on trial data (using patented medications) show that median costs per QALY gained from using statin therapy vary and can be very high. (2) Often, an intervention has the greatest effect on those at greatest risk. For them, the absolute reduction in incidence of events and mortality is greatest and the number needed to treat or prevent one disease event or death is smaller. As such, the ICER is more favorable. For example, the cost of using a statin per life year saved among people with diabetes and CVD is much lower than among people with diabetes alone (Annemans and others 2010; CDC Diabetes Cost-Effectiveness Group 2002; Grover and others 2000; Jonsson, Cook, and Pedersen 1999; Raikou and others 2007).
- Only one RCT of comprehensive risk factor management in diabetes patients has been conducted (the Steno-II study) (Gaede and others 2003; Gaede, Lund-Anderson, and others 2008). The within-trial ICER indicates a very favorable intervention. Case management in which nurses help patients focus on controlling combined risk factors also seems to provide good value (Gaede, Valentine, and others 2008; Mason and others 2005). More expansive training programs and focused clinics to manage diabetes risks can be much more resource intensive for the health gained (Brownson and others 2009; Gilmer and others 2007; Mason and others 2005).

Screening, Preventing, and Managing Complications

Cost-effectiveness of screening for retinopathy among people with diabetes depends on the equipment used (retinal camera, fundoscopy) and the regularity of screening (annual vs. every two years). Data for retinopathy screening are available for LMICs and HICs (Khan and others 2013; Maberley and others 2003; Tung and others 2008; Vijan, Hofer, and Hayward 2000). Innovations to lower costs, such as smartphone technology, may produce clear enough images, though further testing is needed before they become more mainstream (Blanckenberg, Worst, and Scheffer 2011; Haddock, Kim, and Mukai 2013; Kumar and others 2012; Suto and others 2014).

Of all the interventions to detect and prevent complications, neuropathy screening and foot ulcer prevention have the lowest median ICER and have been shown to be very cost-effective in both HIC and LMIC settings (Habib and others 2010; Ragnarson Tennvall and Apelqvist 2001).

Cost-effectiveness of screening for CKD also varies by the frequency of screening and risk level of persons getting tested:

- Shorter interval and frequent screening (biennial) is more costly than less frequent testing (every five years) (Kessler and others 2012)
- Screening individuals who are free of diabetes or hypertension tends to cost more per QALY gained than targeted screening of higher-risk individuals (Hoerger and others 2010).

The use of angiotensin-modifying agents (ACEi or ARB) to reduce the risk of ESRD among people with diabetes costs a median of US$36,000 per QALY gained in HIC settings (Palmer, Annemans, Roze, Lamotte, Lapuerta, and others 2004; Palmer, Annemans, Roze, Lamotte, Rodby, and Bilous 2004; Palmer and others 2007; Palmer, Valentine, and Ray 2007; Rosen and others 2005; Souchet and others 2003; Szucs, Sandoz, and Keusch 2004). There are no equivalent data in LMICs.

Valuing Interventions

Interpreting the value of investing in different health interventions in a specific context is challenging, especially when the data regarding cost-effectiveness were collected in different settings. The cost to implement interventions differs markedly across settings, as does the purchasing power of individuals and societies. In addition, the effectiveness of interventions may differ slightly in different settings, although there is no reason to believe that biological differences would be striking. Keeping these factors in mind, we compiled and calculated median ceiling ratios, that is, thresholds (of value) for decision makers to benchmark whether the median cost-effectiveness estimates reported fall into very cost-effective or cost saving, cost-effective, or not cost-effective ranges for their respective regions (annex 12D and annex table 12D.1) and even for country-income groups (low income, middle income, and high income) given the heterogeneity within regions. In addition, we used a regional cost index derived from health care input cost data compiled by the WHO to calibrate estimated cost-effectiveness for different LMIC regions (table 12.2). Although imperfect, this approach makes it possible to

Table 12.2 Converted Incremental Cost-Effectiveness Ratios for Interventions to Detect, Prevent, and Manage Diabetes by LMIC Region, 2012 U.S. Dollars

			Region					
Intervention	**Source of estimates**	**HIC estimates**	**EAP**	**ECA**	**LAC**	**MENA**	**SA**	**SSA**
Detection								
Screening for undiagnosed diabetes or prediabetes		11,250	820	1,102	1,364	1,158	683	618
Screening with or without intervention		10,908	796	1,069	1,323	1,123	662	599
Screening for gestational diabetes		20,362	1,485	1,995	2,470	2,097	1,236	1,119
Preventing type 2 diabetes among those at high risk								
Individual		17,750	1,295	1,739	2,153	1,828	1,077	975
Group		12,380	903	1,213	1,502	1,275	751	680
Individual	Models	7,582	553	743	920	781	460	417
Diabetes management								
Lifestyle change		48,793	3,559	4,782	5,918	5,025	2,961	2,681
Diabetes self-management education	Within trial	3,882	283	380	471	400	236	213
	Models	9,996	729	980	1,212	1,029	607	549
Self-monitoring of blood glucose		12,262	894	1,202	1,487	1,263	744	674
Intensive glycemic control	Within trial	20,720	1,511	2,030	2,513	2,134	1,257	1,138
	Models	30,304	2,210	2,970	3,676	3,121	1,839	1,665
Intensive blood pressure control	Within trial	1,164	85	114	141	120	71	64
	Models	2,974	217	291	361	306	180	163
Cholesterol control	Within trial	13,180	961	1,292	1,599	1,357	800	724
	Models	73,115	5,332	7,165	8,868	7,529	4,437	4,017
Case management	Within trial	12,944	944	1,268	1,570	1,333	785	711
	Models	23,035	1,680	2,257	2,794	2,372	1,398	1,266
Screening for and preventing diabetes complications								
Retinopathy screening		49,322	3,597	4,833	5,982	5,079	2,993	2,710
Foot care and assessments		25,859	1,886	2,534	3,136	2,663	1,569	1,421
Urine assessments		75,241	5,488	7,373	9,126	7,748	4,566	4,134
Preventing CKD and ESRD		35,817	2,612	3,510	4,344	3,688	2,173	1,968

Note: CKD = chronic kidney disease; EAP = East Asia and Pacific; ECA = Europe and Central Asia; ESRD = end-stage renal disease; HIC = high-income country; LAC = Latin America and the Caribbean; LMIC = low- and middle-income country; MENA = Middle East and North Africa; SA = South Asia; SSA = Sub-Saharan African.

categorize interventions based on their value for LMIC decision makers; however, an important caveat is that these calibrations are linear and would be more accurate if fixed and variable costs, marginal gains, and diminishing returns were accounted for.

Based on benchmarking of ICERs of different diabetes interventions against ceiling thresholds in low-income countries of different regions worldwide (table 12.2 and annex 12D, table 12D.1), blood pressure control and diabetes self-management education offered the greatest value, and together with screening for dysglycemia and primary prevention interventions, were considered cost-effective or very cost-effective across all regions. Interventions offering the least value were intensive glycemic control, lipid control, and screening for diabetic retinopathy and CKD.

PRIORITY INTERVENTIONS TO ADDRESS DIABETES

To collate stakeholder perspectives regarding appropriateness and priority ranking of interventions for diabetes prevention and management, we performed a systematic two-round Delphi process with a panel of leading experts representing diverse geographic regions characterized by varying levels of financial and human resource constraints. The methodology used is described in detail in annex 12E.

In round 1, respondents were asked to rank an adapted list of interventions identified by Narayan and others (2006) by priority and implementation feasibility in LMICs. They were also asked to rate four components of feasibility:

- *Reach.* Ability to reach the target population
- *Technical complexity.* Level of medical technologies or expertise needed to implement an intervention
- *Capital intensity*. Amount of capital resources required for an intervention
- *Cultural acceptability.* Appropriateness of an intervention based on social norms or religious beliefs in the respondent's geographic region.

Table 12.3 presents the average rankings across experts for both priority and feasibility, and for the four feasibility components.

With regard to average feasibility, the respondents ranked blood pressure control (3.67), preconception care among women with diabetes (3.42), screening for gestational diabetes (3.23), smoking cessation (3.21), and comprehensive foot care (3.19) as the most feasible interventions because they have the greatest reach, lowest technical complexity, and lowest resource needs and are likely to be the most culturally acceptable.

However, scores for feasibility diverged from scores for priority. Notably, only one of the six highest-priority interventions (preconception care among women with diabetes) was also considered highly feasible. Lifestyle interventions to prevent diabetes were considered the least feasible (2.29).

In round 2, respondents were asked to list up to 15 innovative or novel strategies that would facilitate diabetes prevention and control in LMICs and to rank them according to their priority and feasibility. The resulting list of 106 strategies was organized into 15 intervention categories; table 12.4 presents how many times each strategy was mentioned.

KNOWLEDGE GAPS

The effectiveness of interventions to prevent and control diabetes is undisputed. With two exceptions—screening for both prediabetes and diabetes and preventive interventions among persons with iIFGs—all of these interventions have been tested in well-designed, large RCTs. There is no reason to believe that effectiveness will be greatly different across different countries.

Table 12.3 Results of Delphi Surveys: Round 1 Expert Opinions Regarding Intervention Priority and Implementation Feasibility

Average ranking

			Feasibility Components			
Intervention	Priority	Implementation feasibility	Reach	Technical complexity	Capital intensity	Cultural acceptability
Glycemic control in people with glycated hemoglobin above 7 percent	3.75	2.75	2.42	2.67	2.33	3.58
Blood pressure control ACEi therapy for people with diabetes	3.89	3.67	3.42	4.00	3.33	3.92
Statin therapy for secondary prevention of cardiovascular disease in people with dyslipidemia	3.75	2.94	2.50	3.08	2.42	3.75
Smoking cessation	4.31	3.21	3.67	2.67	2.92	3.58
Annual (or biennial) screening for diabetic retinopathy	3.75	2.71	2.83	2.17	2.17	3.67
Comprehensive foot care for those at high risk	4.72	3.19	3.33	2.83	2.83	3.75

table continues next page

Table 12.3 Results of Delphi Surveys: Round 1 Expert Opinions Regarding Intervention Priority and Implementation Feasibility (continued)

Average ranking

Intervention	Priority	Implementation feasibility	Feasibility Components: Reach	Technical complexity	Capital intensity	Cultural acceptability
Screening for diabetic nephropathy and ensuring ACEi or ARB therapy in persons with diabetes	3.47	2.98	2.92	2.92	2.42	3.67
Intensive lifestyle intervention in persons with type 2 diabetes using a DPP-type intervention	3.61	2.65	2.58	2.58	2.25	3.17
Preconception care among women with diabetes	3.75	3.42	3.42	3.00	3.33	3.92
Screening for gestational diabetes in women at risk between 24 and 28 weeks gestation	3.75	3.23	3.25	3.08	2.75	3.83
Universal opportunistic screening for undiagnosed type 2 diabetes and multifactorial therapy for screen-detected people	3.47	2.67	2.92	2.67	1.67	3.42
Primary prevention through intensive lifestyle modification using the DPP intervention among those with prediabetes	3.89	2.29	2.08	2.17	1.92	3.00

Note: ACEi = angiotensin-converting enzyme inhibitors; ARB = angiotensin-receptor blocker; DPP = Diabetes Prevention Program. Priority and implementation feasibility are the *average* ranking across all respondents (N = 13). Priority ranking is scored on a scale of 1 to 5, where 1 indicates low priority and 5 indicates high priority. Feasibility is rated based on four criteria, each of which is scored on a scale of 1 to 5, where 1 indicates low feasibility and 5 indicates high feasibility. See text for description of each criterion.

Table 12.4 Number of Mentions for Priority or Feasibility of Innovative Intervention Strategies

Type of intervention	Number of mentions
Macro, environmental, and regulatory policies	
Access to essential medicines (for example, insulin)	9
Creation and implementation of fiscal and regulatory measures (taxing sugar-sweetened beverages)	8
Health promotion (diet and physical activity) in the general population (communities and workplaces)	6
Development of national guidelines and programs and policies	6
Health in all policies or creating environments to facilitate healthy living	5
Human resources development	
Training and sensitizing physicians in diabetes care and management	8
Training and sensitizing community health workers in diabetes education for prevention and control	7
Improve diabetes detection, prevention, and care	
Screening and addressing high-risk individuals	17
Quality-of-care improvement initiatives	7
Education and support programs for people with or at risk for diabetes	6

table continues next page

Table 12.4 Number of Mentions for Priority or Feasibility of Innovative Intervention Strategies (continued)

Type of intervention	Number of mentions
Secondary prevention of complications (foot, leg, and eye care)	4
Set-up and integration of diabetes care for other noncommunicable and infectious diseases	3
Consideration of polypill (and novel therapies) for cardiovascular disease	1
Research priorities	
Development of national surveillance surveys	5
Implementation research	1

Some variation in effectiveness is likely, perhaps because of supply-side differences in reach and implementation or because of demand-side differences in yield, adoption, adherence, and maintenance.

Although the above arguments justify the use of HIC data for LMIC contexts, there is no substitute for local, country-specific data because diabetes prevention and management interventions require sustained behavioral changes, and local social, environmental, cultural, political, and economic conditions affect successful implementation of and adherence to these interventions. Data from LMICs are far overshadowed by data from HICs. Most LMICs still do not have representative surveys that can identify the population-wide prevalence of diabetes, prediabetes, and subtypes of diabetes or the proportion of people with diabetes who are undiagnosed. There are almost no longitudinal data for understanding the natural history of diabetes and whether different ethnic, genotypic, or phenotypic variants of prediabetes and diabetes progress differently. There are also very few, if any, data regarding childhood- or adolescent-onset type 2 diabetes and interventions to address it, even though it appears to be a growing problem. More local observational and experimental data from LMICs are necessary.

In addition, there are key knowledge gaps regarding supply-side aspects of how to implement diabetes detection, prevention, and treatment in LMICs. The understanding of how well-tested diabetes prevention and treatment programs need to be adapted to optimize effectiveness in local LMIC circumstances, or indeed, to address comorbidities (such as diabetes and HIV/AIDS) is very cursory (see chapter 16 in this volume, Magee and others 2017). These aspects, as well as a better understanding of existing infrastructure, resources, and competencies, can help shape how diabetes prevention and treatment interventions will be delivered, by whom, and where. In addition, each country's health care financing varies considerably, and decision makers in payer institutions (ministries, insurance companies, employers) will want to know what up-front, fixed, and variable resource investments are required; what return on investment is possible; and over what time horizon. Indeed, trials of low-cost diagnostics and technologies for detection, prevention, and management hold much promise for lowering supply-side costs, but data are extremely scarce. These factors are important considerations and are relevant to integrating diabetes prevention and management services into routine systems.

There are also large gaps in the availability of qualitative data from LMICs (Hennink and others 2016). In particular, data that inform intervention adaptation, but also marketing, are crucial for generating demand for diabetes services. Intervention programs, tools, and facilities need to be coupled with efforts to optimize adoption, adherence to, and maintenance of the intervention. Generating demand requires effective messaging, communicating the opportunities through appropriate avenues, and using culturally sensitive wording and approaches. Communication needs to convince decision makers that these interventions fit within a context of supportive policies. Diabetes detection, prevention, and control could be facilitated or hindered at employer, insurance, or regulatory levels. For example, employers that support employee efforts to manage their disease risk may encourage better control and be rewarded through employee loyalty and performance.

In comparison with our understanding of individual-focused behavioral interventions, the evidence on societal-level nutrition, agricultural, physical activity, health financing, regulatory, and built-environment policies is weak in design and inconsistent across all countries (Roberto and others 2015). Any policy or program should be accompanied by robust evaluation with an appropriate control group and repeated assessments of exposures and outcomes (Soumerai, Starr, and Majumdar 2015). Evaluations of natural experiments (interventions not introduced or manipulated by researchers) using rigorous methods may provide efficient opportunities to guide future policy (Ackermann and others 2015). Indeed, we also do not know the comparative effectiveness and cost-effectiveness of individual versus population-level interventions.

RECOMMENDATIONS

To recommend priority interventions, we identified interventions for which the data about clinical effectiveness, topical importance, feasibility, and cost-effectiveness were most convergent. In other words, interventions that were, on aggregate, considered effective, important, feasible, and cost-effective were given highest priority. The following interventions to detect, prevent, and manage diabetes should be prioritized in LMICs:

- Blood pressure control among people with diabetes is considered a high priority, most feasible, and very cost-effective.
- Care management as well as aspects of care (self-management education) to support better risk factor control and preventive practices are considered effective and cost-effective and may be delivered by community health workers in practice.
- Lifestyle interventions to prevent diabetes among high-risk individuals are highly effective and cost-effective, but implementing them is challenging, which may reflect our limited understanding of the processes, personnel, financing, and infrastructure needed to deliver and sustain acceptable diabetes prevention services in various LMIC contexts. Yet lifestyle interventions may offer the greatest long-term possibility to slow the growth of diabetes worldwide and warrant further investigation regarding best practices.
- Good glycemic control has important microvascular benefits and may be achievable, but it comes at a fairly high cost. Lipid-lowering medications to prevent CVD events and mortality are also highly efficacious and quite achievable, but they are not universally cost-effective unless cheaper generic versions become widely available. Smoking cessation and foot care are considered important and feasible and have demonstrated value (Li and others 2010).

With respect to the priority actions and approaches to achieving these goals, we recommend pursuing the following supply- and demand-side interventions (in no specific order):

- Targeted (two-step) screening to identify people with prediabetes and diabetes (users of supply-side interventions) is cost-effective and should be a priority, and it should be espoused in guidelines and policy. This step should be complemented by efforts to ensure that the health system has adequate capacity to address the needs identified through screening.
- Purchasers of health care (governments, insurers, employers) should facilitate physical and financial access to essential medicines to treat diabetes and vascular risk factors in diabetes. These medicines should include at least insulin and two classes of oral glucose-lowering medications, at least two classes of blood-pressure-lowering medications, a statin, and possibly a selective serotonin reuptake inhibitor. Access to laboratory testing for periodic monitoring would complement the effectiveness of medications.
- Employers and providers should offer and deliver prevention (health promotion) and care (self-management support) services in clinical and nonclinical settings (workplaces and communities) through trained nonclinical staff (community health workers, lifestyle coaches). Although building capacity and creating infrastructure are expensive up-front costs, health payers, whether government or private, should consider the longer-term benefits and possibilities for financing operational costs sustainably through other means (user fees).
- Researchers should give high priority to addressing important knowledge gaps, especially regarding implementation and scalability.

CONCLUSIONS

The global burden of diabetes is colossal, especially among those least equipped to pay for treatment of end-stage disease. There is general consensus—combining evidence from published sources and expert opinions—that interventions to identify risk and to prevent and manage diabetes are effective, important, and provide value in most settings. There are large gaps in our understanding of how to facilitate implementation, engagement, and sustained success, especially in diverse settings. Governments could consider supporting research to address data gaps with regard to distribution and natural history of disease, implementation sciences, and cost-lowering technologies; building capacity; strengthening infrastructure; and covering up-front costs to catalyze socially valued programs.

Given the pluralistic and evolving needs and priorities in different countries and health care systems—many of which are experiencing changes in disease prevalence, capacity, and financing—ongoing research and evaluation of health system and societal interventions are essential to guide policy makers, donors, communities, and care providers.

ANNEXES

The annexes to this chapter are as follows. They are available at http://www.dcp-3.org/CVRD.

- Annex 12A. Effectiveness and Quality of Evidence Regarding Diabetes Screening, Prevention, and Treatment Interventions
- Annex 12B. Methodology for Cost-Effectiveness Analyses
- Annex 12C. Studies Reporting Cost-Effectiveness of Diabetes Screening, Prevention, and Treatment Interventions
- Annex 12D. Valuing Interventions—Regional Ceiling Ratios for Benchmarking
- Annex 12E. Gathering and Analyzing Stakeholder Perspectives to Prioritize Interventions

NOTE

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US$1,045 or less
- Middle-income countries (MICs) are subdivided:
  (a) lower-middle-income = US$1,046 to US$4,125
  (b) upper-middle-income (UMICs) = US$4,126 to US$12,745
- High-income countries (HICs) = US$12,746 or more.

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