Chapter **30**

Diabetes: The Pandemic and Potential Solutions

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NATURE AND DISTRIBUTION OF DIABETES

Diabetes is a metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both (American Diabetes Association 2004).

Classification of Diabetes

Diabetes takes three major forms. Type 1 diabetes results from destruction of the beta cells in the pancreas, leading to absolute insulin deficiency. It usually occurs in children and young adults and requires insulin treatment. Type 2 diabetes, which accounts for approximately 85 to 95 percent of all diagnosed cases, is usually characterized by insulin resistance in which target tissues do not use insulin properly. A third type of diabetes, gestational diabetes, is first recognized during pregnancy. Other rare types of diabetes include those caused by genetic conditions (for example, maturity-onset diabetes of youths), surgery, drug use, malnutrition, infections, and other illnesses.

The Burden of Diabetes

Diabetes affects persons of all ages and races. The disease reduces both a person's quality of life and life expectancy and imposes a large economic burden on the health care system and on families.

Secular Trend and Projections. In 2003, the worldwide prevalence of diabetes was estimated at 5.1 percent among people age 20 to 79 (table 30.1). The prevalence of diabetes was higher in developed countries than in developing countries. In the developing world, the prevalence was highest in Europe and Central Asia and lowest in Sub-Saharan Africa. Some of these variations may reflect differences in the age structures and level of urbanization of the various populations. By 2025, the worldwide prevalence is projected to be 6.3 percent, a 24 percent increase compared with 2003. The largest increase in prevalence by 2025 is expected to be in East Asia and the Pacific, and the smallest in Sub-Saharan Africa. In terms of those affected, the biggest increase in the developing countries is projected to take place among adults of working age.

In 2003, 194 million people worldwide ages 20 to 79 had diabetes, and by 2025, this number is projected to increase to 333 million, a 72 percent increase (table 30.1). The developing world accounted for 141 million people with diabetes (72.5 percent of the world total) in 2003. During the same period, the number of people with diabetes is projected to double in three of the six developing regions: the Middle East and North Africa, South Asia, and Sub-Saharan Africa.

Diabetes-Related Mortality and Disability. The death rate of men with diabetes is 1.9 times the rate for men without diabetes, and the rate for women with diabetes is 2.6 times that for women without diabetes (W. L. Lee and others 2000). Premature mortality caused by diabetes results in an estimated 12 to 14 years of life lost (Manuel and Schultz 2004; Narayan and others 2003). Cardiovascular disease

Table 30.1 Estimated Numbers of People Age 20 to 79 with Diabetes, Mortality, DALYs, and Direct Medical Costs Attributable to Diabetes, by Regions

Region	Number of people (thousands)		Prevalence (percent)		Direct medical costs, 2003 (US$ million)		Deaths, 2001 (thousands)	Disability-adjusted life years, 2001 (thousands)
	2003	2025	2003	2025	Low estimate	High estimate		
Developing countries	140,849	264,405	4.5	5.9	12,304	23,127	757	15,804
East Asia and the Pacific	31,363	60,762	2.6	3.9	1,368	2,656	234	4,930
Europe and Central Asia	25,764	33,141	7.6	9.0	2,884	5,336	51	1,375
Latin America and the Caribbean	19,026	36,064	6.0	7.8	4,592	8,676	163	2,775
Middle East and North Africa	10,792	23,391	6.4	7.9	2,347	4,340	31	843
South Asia	46,309	94,848	5.9	7.7	840	1,589	196	4,433
Sub-Saharan Africa	7,595	16,199	2.4	2.8	273	530	82	1,448
Developed countries	53,337	68,345	7.8	9.2	116,365	217,760	202	4,192
World	194,186	332,750	5.1	6.3	128,669	240,887	959	19,996

Source: Number of persons with diabetes, prevalence of diabetes, and direct medical costs of diabetes, International Diabetes Federation 2003b; all other information, WHO 2004.

(CVD) causes up to 65 percent of all deaths in developed countries of people with diabetes (Geiss, Herman, and Smith 1995).

The World Health Organization (WHO) estimates that, in 2001, 959,000 deaths worldwide were caused by diabetes, accounting for 1.6 percent of all deaths, and approximately 3 percent of all deaths caused by noncommunicable diseases. More recent estimates by WHO suggest that the actual number may be triple this estimate and that about two-thirds of these deaths occur in developing countries (WHO 2004). Within the developing regions, most deaths caused by diabetes occurred in East Asia and the Pacific and the fewest in Sub-Saharan Africa (table 30.1).

Diabetes-related complications include microvascular diseases (for example, retinopathy, blindness, nephropathy, and kidney failure) and macrovascular diseases (coronary heart disease, stroke, peripheral vascular disease, and lower-extremity amputation). Those complications result in disability. In the United States, a much higher proportion of people with diabetes than of people without diabetes have physical limitations: 66 percent compared with 29 percent (Ryerson and others 2003). Disabilities are even more pronounced among older people (Gregg and others 2000).

The World Health Organization estimated that, in 2001, diabetes resulted in 19,996,000 disability-adjusted life years (DALYs) worldwide. More than 80 percent of the DALYs resulting from diabetes were in developing countries (table 30.1). East Asia and the Pacific had the largest burden, and the Middle East and North Africa had the smallest burden. DALYs resulting from diabetes increased by 250 percent worldwide from 1990 to 2001 and by 266 percent for low- and middle-income countries (Mathers and others 2000).

Economic Burden of Diabetes

Diabetes imposes large economic burdens on national health care systems and affects both national economies and individuals and their families. Direct medical costs include resources used to treat the disease. Indirect costs include lost productivity caused by morbidity, disability, and premature mortality. Intangible costs refer to the reduced quality of life for people with diabetes brought about by stress, pain, and anxiety.

Direct Medical Costs. Good data on the direct medical costs of diabetes are not available for most developing countries. Extrapolation from developed countries suggests that, in 2003, the direct costs of diabetes worldwide for people age 20 to 79 totaled at least US$129 billion and may have been as high as US$241 billion (table 30.1). In the developing world, the costs were highest in Latin America and the Caribbean and lowest in Sub-Saharan Africa. The direct health care costs of diabetes range from 2.5 to 15.0 percent of annual health care budgets, depending on local prevalence and sophistication of the treatments available (International Diabetes Federation 2003b).

Indirect and Intangible Costs. In developing countries, the indirect costs of diabetes are at least as high, or even higher, than the direct medical costs (Barcelo and others 2003). Because the largest predicted rise in the number of people with diabetes in the next three decades will be among those in the economically productive ages of 20 to 64 (King, Aubert, and Herman 1998), the future indirect costs of diabetes will be even larger than they are now.

Diabetes lowers people's quality of life in many ways, including their physical and social functioning and their perceived physical and mental well-being. With a value of

1 representing the health-related quality of life without illness and 0 representing death, people with type 2 diabetes had a value of 0.77 in the population of the United Kingdom prospective diabetes study (Clarke, Gray, and Holman 2002).

Risk Factors for Diabetes

Risk factors for diabetes vary by disease type.

Type 1 Diabetes. Type 1 diabetes is most likely a polygenic disease, and a number of potential environmental risk factors have been implicated—including dietary factors; breastfeeding; initiation of bovine milk; infectious agents (for example, enterovirus, rotavirus, and rubella); chemicals; and toxins—but the results have been inconclusive (Akerblom and Knip 1998).

Type 2 Diabetes. The risk for type 2 diabetes is higher in monozygotic twins and people with a family history of diabetes (Rich 1990). This finding strongly suggests that genetic determinants play a role, but so far few genes have been associated with type 2 diabetes.

Environmental factors include prenatal factors, obesity, physical inactivity, and dietary and socioeconomic factors (Qiao and others 2004). Exposure to diabetes in utero increases the risk of developing type 2 diabetes in early adulthood (Dabelea and others 2000). Disproportionate growth and low birthweight increase the risk of developing diabetes and insulin resistance. In the postnatal environment, breastfeeding protects against the development of obesity, insulin resistance, and diabetes (Pettitt and others 1997; Young and others 2002).

The strongest and most consistent risk factors for diabetes and insulin resistance among different populations are obesity and weight gain (Haffner 1998): for each unit increase in body mass index, the risk of diabetes increases by 12 percent (Ford, Williamson, and Liu 1997). The distribution of fat around the trunk region, or central obesity, is also a strong risk factor for diabetes (Yajnik 2001). Diabetes risk may be reduced by increasing physical activity. Conversely, a sedentary lifestyle and physical inactivity are associated with increased risks of developing diabetes (Hu and others 2003). Some studies report a positive relationship between dietary fat and diabetes, but specific types of fats and carbohydrates may be more important than total fat or carbohydrate intake. Polyunsaturated fats and long-chain omega-3 fatty acids found in fish oils (Adler and others 1994) may reduce the risk of diabetes, and saturated fats and trans fatty acids may increase the risk of diabetes (Hu, van Dam, and Liu 2001). Sugar-sweetened beverages are associated with an increased risk of diabetes (Schulze and others 2004). High intakes of dietary fiber and of vegetables may reduce the risk of diabetes (Fung and others 2002; Stevens and others 2002).

Increased affluence and Westernization have been associated with an increase in the prevalence of diabetes in many indigenous populations and in developing economies (Rowley and others 1997; Williams and others 2001). Conversely, in developed countries, those in lower socioeconomic groups have a higher risk of obesity and consequently of type 2 diabetes (Everson and others 2002). Surrogates for socioeconomic status, such as level of education attained and income (Paeratakul and others 2002; Robbins and others 2001) are inversely associated with diabetes in high-income countries.

INTERVENTIONS AND DELIVERY MODES

Interventions against diabetes include those for preventing the disease, those for detecting the disease in its asymptomatic stage, and those for managing the disease to reduce its complications.

Preventing Type 1 Diabetes

Not enough scientific evidence is available to indicate that type 1 diabetes can be prevented, although various interventions have been explored. Examples of tested interventions include eliminating or delaying exposure to bovine protein and using insulin or nicotinamide for people at high risk of developing the disease.

Preventing Type 2 Diabetes

Four major trials—in China, Finland, Sweden, and the United States—have demonstrated that intensive lifestyle interventions involving a combination of diet and physical activity can delay or prevent diabetes among people at high risk (Eriksson and Lindgarde 1991; Knowler and others 2002; Pan and others 1997; Tuomilehto and others 2001). In the largest randomized, controlled trial to date, the Diabetes Prevention Program (Knowler and others 2002), the goals of the intensive lifestyle intervention were weight loss of 7 percent of baseline bodyweight through a low-calorie diet and moderate physical activity for at least 150 minutes per week. After 2.8 years of follow-up, the average weight loss was 4.5 kilograms for those in the lifestyle intervention group and less than 0.3 kilograms for those in the placebo group. The lifestyle intervention reduced the incidence of diabetes by 58 percent.

Pharmacological studies of diabetes prevention have been reviewed in detail elsewhere (Kanaya and Narayan 2003). In summary, a variety of specific medications have been tested (for example, metformin, acarbose, orlistat, troglitazone, angiotensin-converting enzyme [ACE] inhibitors, statins, estrogens, and progestins) and have been found to lower diabetes incidence, but the expense, side effects, and cumulative years of drug intervention are practical concerns. Except for the Diabetes Prevention Program (Knowler and others 2002), no trial of medication intervention has directly compared the effectiveness of a drug to that of lifestyle modification.

Screening for People with Diabetes or Prediabetes

The benefits of early detection of type 2 diabetes through screening are not clearly documented, nor is the choice of the appropriate screening test established. Questionnaires used alone tend to work poorly; biochemical tests alone or in combination with assessment of risk factors are a better alternative (Engelgau, Narayan, and Herman 2000).

Managing Diabetes

High-quality evidence exists for the efficacy of several current treatments in reducing morbidity and mortality in people with diabetes. These interventions are summarized in table 30.2.

In addition, a review of previous studies (Norris, Engelgau, and Narayan 2001) found positive effects for short follow-up (less than six months) of self-management training

Table 30.2 Effectiveness and Cost-Effectiveness of Interventions for Preventing and Treating Diabetes in Developed Countries

Strategy	Benefit	Quality of evidence[a]	Cost-effectiveness ratio (US$/QALY)[b]
Preventing diabetes			
• Lifestyle interventions for preventing type 2 diabetes	Reduction of 35–58 percent in incidence among people at high risk	I	1,100 (Diabetes Prevention Program Research Group forthcoming)
• Metformin for preventing type 2 diabetes	Reduction of 25–31 percent in incidence among people at high risk	I	31,200 (Diabetes Prevention Program Research Group forthcoming)
Screening for diabetes			
• Screening for type 2 diabetes in general population	Reduction of 25 percent in microvascular disease	III	73,500 (CDC Diabetes Cost-Effectiveness Study Group 1998)
Treating diabetes and its complications			
• Glycemic control in people with HbA1c greater than 9 percent	Reduction of 30 percent in microvascular disease per 1 percent drop in HbA1c	I	Cost saving (CDC Diabetes Cost-Effectiveness Study Group 1998)
• Glycemic control in people with HbA1c greater than 8 percent	Reduction of 30 percent in microvascular disease per 1 percent drop in HbA1c	I	34,400 (CDC Diabetes Cost-Effectiveness Study Group 1998; Klonoff and Schwartz 2000)
• Blood pressure control in people whose pressure is higher than 160/95 mmHg	Reduction of 35 percent in macrovascular and microvascular disease per 10 mmHg drop in blood pressure	I	Cost saving (CDC Diabetes Cost-Effectiveness Study Group 1998)
• Cholesterol control in people with total cholesterol greater than 200 milligrams/deciliter	Reduction of 25–55 percent in coronary heart diseases events; 43 percent fall in death rate	II-1	63,200 (CDC Diabetes Cost-Effectiveness Study Group 1998)
• Smoking cessation with recommended guidelines	16 percent quitting rate	I	12,500 (CDC Diabetes Cost-Effectiveness Study Group 1998)
• Annual screening for microalbuminuria	Reduction of 50 percent in nephropathy using ACE inhibitors for identified cases	III	47,400 (Klonoff and Schwartz 2000)
• Annual eye examinations	Reduction of 60 to 70 percent in serious vision loss	I	6,000 (Klonoff and Schwartz 2000; Vijan, Hofer, and Hayward 2000)
• Foot care in people with high risk of ulcers	Reduction of 50 to 60 percent in serious foot disease	I	Cost saving (Ragnarson and Apelqvist 2001)
• Aspirin use	Reduction of 28 percent in myocardial infarctions, reduction of 18 percent in cardiovascular disease	I	Not available
• ACE inhibitor use in all people with diabetes	Reduction of 42 percent in nephropathy; 22 percent drop in cardiovascular disease	I	8,800 (Golan, Birkmeyer, and Welch 1999)
• Influenza vaccinations among the elderly for type 2 diabetes	Reduction of 32 percent in hospitalizations; 64 percent drop in respiratory conditions and death	II-2	3,100 (Sorensen and others 2004)
• Preconception care for women of reproductive age	Reduction of 30 percent in hospital charges and 25 percent in hospital days	II-2	Cost saving (Klonoff and Schwartz 2000)

Source: Authors.

Note: mmHg = millimeters of mercury; QALY = quality-adjusted life year.

a. I indicates evidence from at least one randomized, controlled trial; II-1 indicates evidence from a well-designed, controlled trial without randomization; II-2 indicates evidence from cohort or case control studies; and III indicates opinions of respected authorities (U.S. Preventive Services Task Force 1996).

b. We adjusted cost-effectiveness ratios to 2002 U.S. dollars using the consumer price index for medical care. In cases in which multiple studies evaluated the cost-effectiveness of an intervention, we report the median cost-effectiveness ratio.

on knowledge, frequency, and accuracy of self-monitoring of blood glucose; self-reported dietary habits; and glycemic control. Effects on lipids, physical activity, weight, and blood pressure varied.

COST-EFFECTIVENESS OF INTERVENTIONS AND PRIORITIES

Most of the interventions to prevent and treat diabetes and its complications significantly affect the use of health services. The limitations of clinical trials include their failure in most cases to capture the entire intervention effect over a lifetime and to include all segments of a population to whom the intervention may apply. Evaluating the cost-effectiveness of interventions often requires the use of computer simulation models, but data availability, technical complexity, and resource needs present a significant barrier to constructing such models for developing countries. Furthermore, data on interventions are often available only from developed countries, and these data are often extrapolated to developing countries.

Estimating the Cost-Effectiveness of Interventions in Developing Countries

To assess the cost-effectiveness of interventions in developing countries, we updated the results from Klonoff and Schwartz's (2000) comprehensive review by including studies that were published up to 2003. Table 30.2 summarizes the cost-effectiveness of interventions for the developed countries, mainly in the United States. The results show that the cost-effectiveness of interventions varies greatly—from cost saving (an intervention is both more effective and less expensive than the comparator) to US$73,500 per quality-adjusted life year (QALY) gained.

We estimated the cost-effectiveness ratio of diabetes interventions for the six developing regions shown in table 30.3. We assumed that the effectiveness of these interventions, as measured in QALYs, was the same as in developed countries but that the cost of interventions and other diabetes care differed between developed and developing countries and also among the six developing regions. Using this assumption, we estimated the cost-effectiveness ratio for a developing region as the cost-effectiveness ratio in the developed country, mainly represented by the United States**,** multiplied by the ratio of costs in the developing region to the cost in the developed countries, which we calculated as follows. These cost-effectiveness ratios are based on costs and benefits over a lifetime, except for preconception care for women of reproductive age**.**

We estimated that the cost of intervention and other diabetes care in the United States was 8.6 times the cost in Latin America and the Caribbean. This cost ratio was an average of four cost ratios—each weighted by its share (Barcelo and others 2003)—for outpatient care, inpatient care, drugs and laboratory tests, and treatment for diabetic complications. The cost ratio for each cost component was calculated as the cost of medical services or drugs in the United States divided by the cost of the same services or drugs in Latin America and the Caribbean. U.S. data for medical services and drugs for routine diabetes care, plus treatment cost for diabetes complications, were obtained from a 1998 cost-effectiveness Markov model of the U.S. Centers for Disease Control and Prevention (CDC). Data for laboratory service were obtained from the 2001 Clinical Diagnostic Laboratory Fee Schedule from the U.S. Centers for Medicare Services (available from http://www.cms.gov). Data for Latin America and the Caribbean were obtained from three countries—Argentina (Gagliardino and others 1993), Brazil (Health Policy Division of the Brazilian Ministry of Health), and Mexico (Villarreal-Rios and others 2000).

We applied Mulligan and others' framework (2003) to estimate the costs of intervention and diabetes care in each developing region. Assuming that cost estimates are available for one of the regions, this framework allows the development of a relative cost index for health care services that can then be used to obtain cost estimates for the other five regions. Using costs estimated by Mulligan and others (2003), we first estimated three health service indexes, including hospital bed days, outpatient and inpatient services, and laboratory tests and procedures. We then combined the three indexes into one overall index for diabetes care in accordance with the share of each component in developing countries (Barcelo and others 2003). Finally, we estimated the costs of intervention and diabetes care in the other five developing regions by multiplying the cost of care in the Latin America region by the overall regional relative cost index.

Ranking Implementation Priorities

We assessed the implementation priority and feasibility of interventions, as explained in table 30.3.

Level 1 Interventions. All three interventions in this category are cost saving and are also feasible in terms of all four aspects considered. The barrier to implementing these interventions may be a short-term hike in intervention costs.

Glycemic control in a population with poor control (hemoglobin A1c greater than 9 percent or another measure of glucose control in situations where HbA1c tests may be unaffordable) is cost saving because the reduction in medical care costs associated with both short-term and long-term complications is greater than is the cost of intervention. Glycemic control for people with type 1 diabetes involves insulin use and, for people with type 2 diabetes, depending on the stage and severity of the disease, consists of diet and physical activity, oral

Table 30.3 Cost-Effectiveness of Interventions for Preventing and Treating Diabetes and Its Complications in Developing Regions

	Cost/QALY (2001 US$)							
Intervention	**East Asia and the Pacific**	**Europe and Central Asia**	**Latin America and the Caribbean**	**Middle East and North Africa**	**South Asia**	**Sub-Saharan Africa**	**Feasibility[a]**	**Implementing priority[b]**
Level 1								
Glycemic control in people with HbA1c higher than 9 percent	Cost saving	Cost saving	Cost saving	Cost saving	Cost saving	Cost saving	++++	1
Blood pressure control in people with pressure higher than 160/95 mmHg	Cost saving	Cost saving	Cost saving	Cost saving	Cost saving	Cost saving	++++	1
Foot care in people with a high risk of ulcers	Cost saving	Cost saving	Cost saving	Cost saving	Cost saving	Cost saving	++++	1
Level 2								
Preconception care for women of reproductive age	Cost saving	Cost saving	Cost saving	Cost saving	Cost saving	Cost saving	++	2
Lifestyle interventions for preventing type 2 diabetes	80	100	130	110	60	60	++	2
Influenza vaccinations among the elderly for type 2 diabetes	220	290	360	310	180	160	++++	2
Annual eye examination	420	560	700	590	350	320	++	2
Smoking cessation	870	1,170	1,450	1,230	730	660	++	2
ACE inhibitor use for people with diabetes	620	830	1,020	870	510	460	+++	2
Level 3								
Metformin intervention for preventing type 2 diabetes	2,180	2,930	3,630	3,080	1,820	1,640	++	3
Cholesterol control for people with total cholesterol higher than 200 milligrams/deciliter	4,420	5,940	7,350	6,240	3,680	3,330	+++	3
Intensive glycemic control for people with HbA1c higher than 8 percent	2,410	3,230	4,000	3,400	2,000	1,810	++	3
Screening for undiagnosed diabetes	5,140	6,910	8,550	7,260	4,280	3,870	++	3
Annual screening for microalbuminuria	3,310	4,450	5,510	4,680	2,760	2,500	++	3

Source: Authors.

a. Feasibility was assessed based on difficulty of reaching the intervention population (the capacity of the health care system to deliver an intervention to the targeted population), technical complexity (the level of medical technologies or expertise needed for implementing an intervention), capital intensity (the amount of capital required for an intervention), and cultural acceptability (appropriateness of an intervention in terms of social norms and/or religious beliefs). ++++ indicates feasible for all four aspects, +++ indicates feasible for three of the four, ++ indicates feasible for two of the four, and + indicates feasible for one of the four.

b. Implementing priority was assessed by combining the cost-effectiveness of an intervention and its implementation feasibility; 1 represents the highest priority and 3 represents the lowest priority.

glucose-lowering agents, and insulin. Patient education is an essential component of these interventions to encourage patients to comply with medication regimes and to change to and maintain healthy lifestyles.

Glucose is generally poorly controlled in people with both type 1 and type 2 diabetes, mostly because of lack of access to insulin and other diabetes supplies in developing countries. For example, the mean HbA1c level for people with diabetes in India was 8.9 percent in 1998 (Raheja and others 2001). A survey conducted by the International Diabetes Federation in 1997 (2003b) showed that no country in Africa had 100 percent accessibility to insulin. Ensuring adequate access to insulin should be an important priority for developing countries.

Blood pressure control for people with diabetes and hypertension reduces the incidence of both microvascular and macrovascular diseases. Major medication interventions include an ACE inhibitor, thiazide diuretics, or a beta blocker. Blood pressure control is cost saving mainly because of its large health benefits and relatively low intervention costs. Even in the United States, moderate blood pressure control costs less than US$250 per patient per year. Because many blood pressure medications are generic drugs, the costs are much lower in developing countries. In addition, the prevalence of people with poor control of blood pressure may be high in developing countries. For example, in Latin America and the Caribbean, 60 percent of people with type 2 diabetes in 2000 had blood pressure higher than 140/90 mmHg (Gagliardino, de la Hera and Siri 2001).

Complications related to foot problems are common among diabetics in developing countries. For example, in India, 43 percent of diabetes patients had foot-related complications (Raheja and others 2001). Interventions for foot care are low tech and require little capital. Interventions for foot care in developing countries should include educational programs for patients and professionals (for example, on foot hygiene, treatment of calluses, awareness of functional infections, and care for skin injuries); access to appropriate footwear; and multidisciplinary clinics. All three interventions could be cost saving, mainly because the cost of the interventions is low and the interventions can reduce the risk of foot ulceration and amputation, which are costly. Applying these interventions for high-risk patients, such as those with at least one previous foot ulcer or amputation, would yield even larger savings (Klonoff and Schwartz 2000).

Level 2 Interventions. The six interventions in this category are either cost saving and not feasible in one or more aspects or cost less than US$1,500 per QALY and are at least moderately feasible. Thus, interventions in this category represent good value for money but may present some difficulties in terms of feasibility.

Preconception care among women of reproductive age includes patient education and intensive glucose management. This intervention reduces short-term hospital costs for both mothers and infants and improves birth outcomes. However, the intervention may not be feasible in some developing countries because of the resources needed for the intervention and the difficulty of reaching the target population.

The lifestyle intervention for preventing type 2 diabetes costs US$60 to US$130 per QALY over a lifetime, depending on the region. The potential population eligible for a lifestyle intervention (those with impaired glucose tolerance or impaired fasting glucose) is large in developing countries. The International Diabetes Federation (2003b) estimates that the prevalence of impaired glucose tolerance was at least as high as the prevalence of diabetes in all regions. The expertise required for the intervention, such as dietitians and exercise physiologists, and the capacity of health care systems to handle the large populations eligible for the intervention may present a barrier to implementing the intervention in many developing countries.

People with diabetes are at higher risk of complications from influenza and pneumococcal infections than those without diabetes. Influenza vaccinations are a relatively cost-effective intervention, mainly because of the low intervention cost. However, the level of adoption for the intervention would depend on a country's ability to deliver the intervention to the targeted population.

The detection of proliferative diabetic retinopathy and macular edema by dilated eye examination followed by appropriate laser photocoagulation therapy prevents blindness. Annual screening and treatment programs for diabetic retinopathy cost US$700 or less per QALY gained in developing countries. The intervention is more cost-effective among older people, those who require insulin (Klonoff and Schwartz 2000), or those with poor glucose control (Vijan, Hofer, and Hayward 2000). In addition, screening less frequently, such as every two years, may be more cost-effective than screening every year (Vijan, Hofer, and Hayward 2000). Eye complications among people with diabetes are common in developing countries; for example, 39 percent of people with diabetes in India had eye-related complications (Rajala and others 1998). Although laser treatment is an effective intervention, such treatment may not be available in many developing countries or may be extremely costly.

ACE inhibitors can lower the blood pressure of those with hypertension and delay the onset or prevent further progression of renal disease for those with diabetes. Compared with screening for microalbuminuria and treating only those who have the condition, offering ACE inhibitors to all people with diabetes was more cost-effective at less than US$1,020 per QALY gained. This intervention was more cost-effective among younger people and was sensitive to the cost of drug. Thus, lowering the cost of the medication is a key factor for the success of this intervention in developing countries.

Smoking cessation includes both counseling and using medication such as a nicotine patch. Smoking cessation appears to be the least cost-effective among the level 2 interventions. However, the benefits of smoking cessation may be underestimated because our calculations only took the reduced risk of CVD into account (Earnshaw and others 2002). Adding the health benefits derived from preventing cancer and pulmonary diseases would improve the cost-effectiveness of smoking cessation. Considering the high prevalence of smoking in developing countries, smoking cessation should be a high-priority intervention, but the availability of the nicotine patch may be a barrier to implementing this intervention in developing countries.

Level 3 Interventions. The five interventions included in this category cost at least US$1,640 per QALY but could cost as much as US$8,550 per QALY. Compared with the level 1 and 2 interventions, those in this category are also less feasible. In general, depending on cost-effectiveness and feasibility, these interventions may not always be justifiable for all people in developing countries, given the limited health care resources. However, these interventions may be reasonable for selected subpopulation groups, such as those who can afford them.

Metformin therapy for preventing type 2 diabetes among people at high risk, such as those with prediabetes, is feasible because the drug is affordable in many developing countries; however, the intervention may not be good value for money. Cholesterol control intervention for people with diabetes falls into the same category. The cost-effectiveness of both these interventions would improve if the costs of the drug could be lowered.

The aim of intensive glucose control is to lower the glucose level of a person with diabetes to a level close to that of a person without diabetes. Implementing this intervention is a lower priority, mainly because of its relatively low cost-effectiveness in the context of the limited health care resources in developing countries. Although the U.K. Prospective Diabetes Study clearly demonstrates that lowering glucose levels can prevent or delay long-term diabetes complications (UKPDS Group 1998), the marginal return on very intensive glucose control in developing countries was relatively small.

Screening for undiagnosed diabetes is a low-priority intervention mainly because of its relatively high cost per QALY. However, screening for undiagnosed diabetes can be a worthwhile intervention for subpopulation groups, such as those that have a high prevalence of undiagnosed diabetes. In the United States, for example, screening for undiagnosed diabetes among African Americans was estimated to be 10 times more cost-effective than screening among other population groups (CDC Diabetes Cost-Effectiveness Study Group 1998). In addition, screening for undiagnosed diabetes may be a worthwhile intervention for patients with risk factors for other chronic diseases, such as hypertension, high lipid profiles, and prediabetes.

Annual screening for microalbuminuria was a low-priority intervention because screening added costs with no significant benefits. Treating all persons with diabetes with ACE inhibitors was a better treatment option than screening for microalbuminuria and treating only those who have the condition.

Cost-Effectiveness of a Polypill to Prevent CVD

A meta-analysis estimated that a hypothetical polypill could reduce the risk of CVD by 80 percent among all people over 55 or people with diabetes of any age (Wald and Law 2003). This hypothetical pill is a combination of three half-dose antihypertensive medications—aspirin, statin, and folic acid (see also chapter 33). Currently, neither is it available for use, nor have estimates of its benefits and adverse effects been confirmed in a formal, randomized, controlled trial. The idea is thus still theoretical. The cost-effectiveness of this hypothetical pill was, however, simulated using a computer model of people with newly diagnosed diabetes in the United States (Sorensen and others 2004), and the assessment found that a polypill intervention would cost US$11,000 per QALY gained. The intervention would be cost saving if such a pill cost US$1.28 or less per day. We estimated that the cost-effectiveness ratio of the polypill ranged from US$560 to US$1,280 per QALY gained for the six developing regions. This result was sensitive to changes in the cost of the intervention, but the intervention remained cost-effective within the most likely ranges of its cost (Sorensen and others 2004). A barrier to this intervention, in addition to the feasibility of producing such pill, is that its benefits and side effects would still have to be established in a randomized clinical trial.

Cost-Effectiveness of Diabetes Education

People with diabetes play a central role in managing their disease. Thus, diabetes education is an integral part of diabetes care. The goal of diabetes education is to support the efforts of people with diabetes to understand the nature of their illness and its treatment; to identify emergency health problems at early, reversible stages; to adhere to self-care practices; and to make necessary changes to their health habits (International Diabetes Federation 2003b). Health providers can deliver diabetes education programs in various settings. Evaluating the effectiveness of health education is challenging because of the difficulty of separating out its effect from that of other interventions. Nevertheless, a review of literature published in the United States suggests that self-management diabetes education may be cost-effective (Klonoff and Schwartz 2000).

Training in diabetes self-management reduces medical costs for diabetes care in developing countries in the short term. A multicenter intervention study in 10 Latin American countries demonstrated that an education program could reduce the cost of drugs by 62 percent (International Diabetes Federation 2003b), and another program in Argentina found a reduction in diabetes-related costs of 38 percent (Gagliardino and Etchegoyen 2001). Because the costs of education programs are generally low, the intervention may be cost-effective. Training patients to better manage their diabetes is also feasible because of its low technical complexity, low capital requirements, and cultural acceptability. Thus, diabetes education should be a high-priority intervention for all developing regions.

LESSONS AND EXPERIENCE

A number of lessons can be learned from the experiences in countries where the interventions described have been implemented.

Prevention

Data are sparse on community- or population-based strategies for preventing diabetes along with other chronic diseases such as CVD. Available studies on preventing type 2 diabetes have used clinic-based approaches targeted at high-risk groups, and researchers generally agree that type 2 diabetes can be prevented or its onset delayed. Putting these results into practice, however, is fraught with difficulties and unanswered questions, such as the following:

- Who would benefit from diabetes prevention?
- How can those who may benefit be identified?
- What are the costs and cost-effectiveness of diabetes prevention at a population level?
- How should results be extrapolated from developed countries to developing countries, whose priorities and approaches may be different?

Treatment

The quality of diabetes care generally remains suboptimal worldwide, regardless of a particular country's level of development, health care system, or population (Engelgau and others 2003; Garfield and others 2003). The Costs of Diabetes in Europe—Type 2 study, conducted in eight European countries, found suboptimal diabetes care in each country (Liebl, Mata, and Eschwege 2002). In the United States, population-based surveys in the 1990s among adults age 18 to 75 with diabetes found that only 63 percent of them had had a dilated eye examination and only 55 percent had had a foot examination within the past year, 18 percent had poor glycemic control, 42 percent had good cholesterol control, and 66 percent had a blood pressure within the normal range (Saaddine and others 2002).

The Diabcare-Asia project was conducted in the late 1990s. Results from India, Singapore, and Taiwan (China) found that in 1998, 32 to 50 percent of the diabetic population had poor glycemic control (equivalent to HbA1c $>$ 8 percent), 43 to 67 percent had high cholesterol (greater than 5.2 millimoles per deciliter), and 47 to 54 percent had an abnormal level of triglyceride (greater than 1.7 millimoles per deciliter) (W. R. Lee and others 2001; Raheja and others 2001). Data from Latin America and the Caribbean showed that 41 percent of people with type 1 diabetes and 57 percent of those with type 2 diabetes had poor glucose control. Of those with type 2 diabetes, 56 percent had hypertension, 53 percent had high cholesterol, and 45 percent had abnormal triglycerides (Gagliardino, de la Hera, and Siri 2001).

Quality of Diabetes Care

Small, single-site studies indicate that several interventions to improve quality of care at the patient, provider, or system levels are promising (Narayan and others 2004). A systematic review (Renders and others 2001) found that multifaceted professional interventions may enhance providers' performance in managing diabetes care; that organizational interventions involving regularly contacting and tracking patients by means of computerized tracking systems or through nurses can also improve diabetes management; that patient-oriented interventions can improve patients' outcomes; and that nurses can play an important role in patient-oriented interventions by educating patients and facilitating patients' adherence to treatment regimes. (See also chapter 70.)

Interventions that could modify providers' behavior include education as part of more complex interventions that also focus on systems and on the organization of practices—for example, feedback on performance, reminder systems, consensus development, and clinical practice guidelines. Potential systemic interventions include the use of continuous quality improvement techniques; feedback on performance; physician incentives for quality; nurses to provide diabetes care (which is typically provided by physicians); computerized reminder systems for providers, alone or in combination with a performance feedback program; patient-tracking or other reminder systems to improve regular follow-up; dedicated blocks of time set aside for diabetes patients in primary care practices; team care; electronic medical record systems; and other methods, such as telephone and mailing reminders, chart stickers, and flow sheets to prompt both providers and patients.

Interventions that empower patients can be successful components of diabetes programs. A systems-oriented approach using manual or computerized systems that remind patients to make follow-up appointments and that prompt staff members to generate reminder cards for patients can improve compliance with follow-up and enhance efficiency of office practices. In addition, comprehensive implementation of multiple risk-factor interventions in real-life settings has been shown to reduce vascular events by more than 50 percent among people with diabetes (Gaede and others 2003).

The Institute of Medicine Committee on Quality of Health Care in America (2001) argues strongly that newer systems of care and newer ways of thinking are needed to tackle complex diseases such as diabetes. Furthermore, the model of the process of change in a simple mechanical system is woefully inadequate for dealing with the complex, interactive, and interconnected adaptive systems in which diabetes is prevented and treated. Applied research, designed to encompass the system as a whole and not simply its component parts, can enhance our understanding of complex health care dynamics for chronic diseases (Fraser and Greenhalgh 2001; Plsek and Greenhalgh 2001).

RESEARCH AND DEVELOPMENT AGENDA

The following subsections discuss the major issues for research and development.

Prevention

Well-designed community-based studies of primary prevention for type 2 diabetes are needed, especially as part of multifactorial interventions, in developing countries. Research is also needed into safer and cheaper drugs to prevent diabetes when lifestyle intervention either is not feasible or has failed. In addition, we need to know the long-term effects of diabetes prevention on CVD and other outcomes. More effective and cheaper ways to prevent the major complications of diabetes are also needed. Other areas also deserving of research include noninvasive methods for monitoring blood glucose and more effective and efficient ways of screening for prediabetes, diabetes, and early diabetes complications. Evidence of the benefits of diabetes education on outcomes is lacking, and organized research to assess effective components of diabetes education and their impact on control of risk factors and long-term outcomes should be a priority.

Epidemiological and Economics Research

Scant data are available on the future burden of diabetes and its complications in developing countries. Data on trends in and the effects of risk factors for diabetes in developing countries—obesity; birthweight; physical inactivity; television viewing; dietary factors; fast foods; socioeconomic factors; and effects of urbanization, industrialization, globalization, and stress—are also sparse. Low-cost ways to obtain such data in a standardized manner may be worth considering. More data are also needed on the costs of diabetes, the impact of the disease on quality of life, and the cost-effectiveness of various interventions in the context of developing countries (International Diabetes Federation 2003a).

Health Systems and Operational Research

Greater emphasis on translation research is needed. Well-designed and standardized studies of quality of care and outcomes will help (TRIAD Study Group 2002). Research aimed at understanding system-level complexity and finding ways to deliver chronic disease care that takes such complexity into account is also likely to yield profitable results (Institute of Medicine Committee on Quality of Health Care in America 2001). Computer models suitable for assessing cost-effectiveness and for forecasting the burden in developing countries are needed. Operational research aimed at understanding the tradeoffs and the best mix of resource allocation for diabetes and chronic disease care in developing countries is also needed.

Basic Research

Further strategic unraveling of the genetic basis of type 2 diabetes and gene-environment interactions may help explain the diabetes epidemic and provide better understanding of the pathophysiology of the disease. It may also may lead to better prevention and treatment strategies. Understanding the role of prenatal influences, especially in developing countries, may offer productive opportunities for interventions. Because of the increasing occurrence of type 2 diabetes in children, as well as the role of obesity in accelerating the onset of type 1 diabetes, further research into the typology and classification of diabetes is vital. The rapid industrialization and economic development being experienced by several developing countries may make research into the role of socioeconomic factors, urban stress, and lifestyle factors on the causation of diabetes productive.

CONCLUSIONS

A growing diabetes pandemic is unfolding with rapid increases in the prevalence of type 2 diabetes. The direct health care costs of diabetes worldwide amount to 2003 US$129 billion per year. Estimates indicate that developing countries spend between 2.5 and 15.0 percent of their annual direct health budgets on diabetes care, and families with diabetic members spend 15 to 25 percent of their incomes on diabetes care.

A whole array of effective interventions to prevent diabetes and its complications is available, and we have attempted to assess their potential cost-effectiveness in developing regions. Using these estimations and a qualitative assessment of the feasibility of implementation, we have prioritized available interventions into the following three categories:

- level 1—cost saving and highly feasible
- level 2—cost saving or cost less than US$1,500 per QALY but pose some feasibility challenges
- level 3—cost between US$1,640 and US$8,550 per QALY and pose significant feasibility challenges.

Table 30.4 presents a summary of all major diabetes interventions, major health effects of the interventions, and level of implementation priority.

In addition, we propose diabetes education as an essential intervention. However, more organized research into the precise components of diabetes education and its effect on

Table 30.4 Key Cost-Effective Interventions for Preventing and Treating Diabetes and Its Complications

Intervention	Description	Applicable population	Major effect
Level 1[a]			
• Glycemic control in people with poor control	Insulin, oral glucose-lowering agents, diet and exercise	People with diabetes, all ages, HbA1c greater than 9 percent	Reduction in microvascular disease
• Blood pressure control	Blood pressure control medications	People with diabetes, hypertensive, all ages	Reduction in macrovascular disease, microvascular disease, and mortality
• Foot care	Patient and provider education, foot examination, foot hygiene, and appropriate footwear	People with diabetes, middle-aged or older	Reduction in serious foot diseases and amputations
Level 2[b]			
• Preconception care for women of reproductive age	Patient self-management	Women with diabetes who plan to become pregnant	Reduction in HbA1c level and hospital expenses of the mother and baby
• Lifestyle intervention to prevent diabetes	Behavioral change, including diet and physical activity, to reduce bodyweight	People who are at high risk (for example, prediabetes for type 2 diabetes)	Reduction in type 2 diabetes incidence by 58 percent
• Influenza vaccination	Vaccination	Elderly people with diabetes	Reduction in hospitalizations, respiratory conditions, and mortality
• Detection and treatment of eye diseases	Eye examination to screen for and treat eye diseases	People with diabetes, middle-aged or older	Reduction in serious vision loss
• ACE inhibitors	Angiotensin-converting enzyme medication	People with diabetes	Reduction in nephropathy, cardiovascular disease, and death
• Smoking cessation	Physician counseling and nicotine replacement therapy	People with diabetes, all ages, smokers	Increase in quitting rate and reduction in cardiovascular disease
Level 3[c]			
• Metformin therapy for preventing diabetes	Metformin medication	People who are at high risk (for example, prediabetes for type 2 diabetes)	Reduction in type 2 diabetes incidence by 33 percent
• Intensive glucose control	Insulin, oral glucose-lowering agents, or both	Diabetes, all ages, with HbA1c less than 9 percent	Reduction in microvascular disease
• Lipid control	Cholesterol-lowering medication	Diabetes, all ages, with high cholesterol	Reduction in cardiovascular disease events and mortality
• Screening for microalbuminuria	Screening for microalbuminuria and treating those who test positive	Diabetes, all ages	Reduction in kidney diseases
• Screening for undiagnosed diabetes	Screening for undiagnosed diabetes and treating those who test positive	People who are at high risk for type 2 diabetes	Reduction in microvascular disease
Essential background intervention[d]			
Diabetes education	Patient self-management	Diabetes, all ages	Reduction in HbA1c level and better compliance with lifestyle changes
Other promising intervention[e]			
Polypill	Hypothetical pill combining low doses of antihypertensive medication, aspirin, statin, and folate	Diabetes, all ages	Reduction in cardiovascular disease

Source: Authors.

a. Level 1 interventions are cost saving and highly feasible.

b. Level 2 interventions are cost saving or cost less than US$1,500 per quality-adjusted life year but pose feasibility challenges.

c. Level 3 interventions cost between US$1,640 and US$8,550 per quality-adjusted life year and pose significant feasibility challenges.

d. Diabetes education is the backbone on which many diabetes interventions depend, but empirical data on the effectiveness of diabetes education on outcomes and on the precise components of diabetes education are still lacking.

e. An intervention that appears promising but needs further research to document its effectiveness and/or safety. The polypill is only a theoretical concept at this time and is not available for implementation.

long-term outcomes is needed. We also propose that further research be launched in relation to the novel and potentially promising polypill.

Finally, this chapter suggests a number of interventions at the level of the patient, provider, and system that could help address the overall suboptimal quality of diabetes care; notes the possible benefits of making important drugs available at cheaper costs in developing countries; and suggests some research priorities for developing regions.

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