

The Chronic Burden of Diabetes

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Abstract

Unmanaged diabetes mellitus is a major problem for patients, healthcare providers, and health insurers alike. The incidence of diabetes is growing rapidly and at present approximately 8% of the population is afflicted with this disease. When diabetes goes undiagnosed or untreated, the repercussions can be disastrous physically, as well as economically. In order to improve quality of life and healthcare economics, it is time for managed care systems to identify the barriers to improving the care of diabetes.

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For author information and disclosures, see end of text.

Defining the Problem of Type 2 Diabetes

Unmanaged diabetes mellitus (DM) is a major problem not only for patients, but healthcare providers and health insurers as well. DM is a chronic, mostly silent disease whose incidence is growing and negatively impacts every body tissue when blood glucose levels are not normalized. DM is among those few diseases that are identified by a lab value, although the disease should be defined by its chronic complications as well. When blood glucose levels are elevated a person is diagnosed with 1 of the 2 major types of diabetes. Type 1 diabetes results when the beta cells in the pancreas are destroyed and thus do not produce insulin. Type 2 diabetes results from a progressive insulin secretory defect on the background of insulin resistance (insulin insensitivity).¹ The healthcare system faces several major problems due to diabetes: (1) type 2 diabetes is growing in prevalence as people's lives become more sedentary and the general population becomes more obese; (2) it is an expensive disease that consumes an inappropriate proportion of the healthcare dollar; and (3) our acute healthcare-based system does not adequately diagnose nor treat chronic diseases like diabetes. There is good news, however, since we know that if patients get diagnosed, educated, and follow a treatment protocol, outcomes of care can be greatly improved. This article will provide information about the impact of diabetes, the barriers to treating it, and then summarize the consequences of sustained hyperglycemia on a patient with diabetes.

The prevalence of diabetes and prediabetes is very high. At present, approximately 24 million children and adults in the United States have diabetes (8% of the population).² Up to 24% have not been diagnosed yet and another 57 million people are estimated to have prediabetes. Type 1 diabetes has been diagnosed in 1 in every 400 to 600 children and adolescents. Approximately 23.1% of people over age 60 have DM and the prevalence increases with each additional decade of life. Prevalence of DM is at least 2 to 4 times higher among non-Hispanic black, Hispanic/Latin American, American Indian, and Asian/Pacific Islander women than among non-Hispanic white women.¹ Diabetes is quickly growing in incidence and by the year 2030, nearly 400 million people worldwide will be trying to find a way to normalize their blood glucose levels.^{2,3}

Other alarming statistics include¹:

- In the past 20 years, the prevalence of diabetes has doubled and will do so again in the next 16 years;

- Every 20 minutes 60 Americans will be diagnosed with DM;
- 1 in every 3 children born today will develop diabetes during his/her lifetime;
- 9 Americans die every 20 minutes from diabetes-related complications;
- 2 of every 3 diabetes patients die from heart disease or stroke;
- Type 2 diabetes accounts for up to 95% of diabetes cases and is often comorbid with hypertension, dyslipidemia, and hypercoagulation factors;
- 1 in every 3 children in the United States is obese or overweight and this value has tripled in the past 25 years;
- Treatment inertia is a major concern since diabetes patients remain on monotherapy for more than 1 year after their first glycosylated hemoglobin (A1C) level was more than 8%;
- It is estimated that more than 85% of patients are given medical care by general practitioners who cannot afford more than 8 to 12 minutes per patient and are concerned with acute healthcare problems not chronic conditions; and
- Even with all of the medications we now have and proven methods to improve care of patients with diabetes, a little over 50% of type 2 patients are not at target levels.⁴

Costs of Diabetes

The yearly cost for treating a person with diabetes is over 5 times more than a person without diabetes (\$13,243 vs \$2560). Many healthcare experts believe that if healthcare organizations would identify patients earlier, educate them, and initiate an effective treatment protocol, significant money could be saved. In 2002, \$132 billion was spent on diabetes and by 2007 the value grew to \$174 billion.⁵ It is estimated that the value will be more than \$350 billion by 2025 and \$2.6 trillion in the next 30 years. Note that of the \$174 billion, \$116 billion was for medical expenditures and \$58 billion in reduced national productivity. The largest components of the medical costs for diabetes include hospital inpatient care (50%), medication and supplies (12%), retail prescriptions to treat complications (11%), and physician office visits (9%). The costs attributed to diabetes, however, omit the social cost of intangibles such as pain and suffering, care provided by nonpaid caregivers, excess medical costs associ-

ated with undiagnosed diabetes, and diabetes-attributed costs for healthcare expenditures (such as administrative costs, over-the-counter medications, clinician training programs, research, and infrastructure development). Expenses related to higher insurance premiums paid by employees and employers, reduced earnings through decreased productivity, and reduced overall quality of life for people with diabetes and their families and friends are also not included. In addition, the wasted money resulting from de-emphasis of prevention through improved nutrition and exercise is a managed care issue that has to be confronted soon.⁶ Lastly, most patients with diabetes are not educated about how to manage their diabetes and for those who are instructed, it occurs during the time following their diagnosis when it is least effective. It is telling that virtually all the money spent on diabetes is for treatment with less than 1% being allocated for prevention.⁷

Impact of Ineffective Treatment of Diabetes²

Another way to view diabetes is to look at the impact of diabetes complications on the healthcare system. Outcome studies prove that the present system is not adequate. Consider the following: heart disease accounts for 68% of the causes of death among diabetes patients age 65 or older (diabetes = cardiovascular disease); stroke was noted on 16% of diabetes-related death certificates among those age 65 years or older; the risk of stroke and heart disease is 2 to 4 times higher for diabetes patients; 75% of diabetes patients have hypertension, hyperlipidemia, and hypercoagulation problems; diabetes is the leading cause of new cases of blindness with up to 24,000 patients going blind each year; diabetes is the leading cause of kidney failure and accounts for 44% of new cases; up to 70% of diabetes patients have mild-to-severe forms of central nervous system damage; severe forms of diabetes nerve disease are a major contributing factor of lower-extremity amputations and more than 60% of nontraumatic limb amputations occur in diabetes patients; dental disease is rampant in diabetes patients; complications of pregnancy are common in women with poorly controlled diabetes; diabetes also causes many acute complications such as episodes of hypoglycemia, diabetic ketoacidosis, and hyperosmolar coma; and diabetes patients have

■ **Table 1.** Treatment Goals for Diabetes Patients¹

| Measure | Value |
|--|---|
| A1C, % | Generally <7% but individualized for patients at risk of hypoglycemia or cardiovascular disease |
| Preprandial capillary plasma glucose | 70-130 mg/dL |
| Postprandial capillary plasma glucose | ≤180 mg/dL |
| Low-density lipoprotein cholesterol | ≤100 mg/dL or <70 if a cardiovascular risk factor |
| High-density lipoprotein cholesterol | >50 mg/dL for females, >40 for males |
| Non-high-density lipoprotein | ≤130 mg/dL |
| Triglycerides | <150 mg/dL |
| Blood pressure | <130/80 mm Hg |
| A1C indicates glycosylated hemoglobin. | |

higher incidences of cancer, connective tissue disorders, infections, skin problems, etc.

Still another way to look at diabetes expenses is to ask, “How much could be saved if diabetes patients were treated to goal?” **Table 1** summarizes the treatment goals for diabetes patients related to blood glucose levels, A1C, lipids, and hypertension.¹ These are from the American Diabetes Association (ADA) and can be somewhat different from the American College of Endocrinologists (which can confuse and frustrate healthcare providers). **Table 2** summarizes the ADA’s Standards of Diabetes Care, which, if followed, have been shown to improve outcomes of diabetes care. It has been predicted that if 80% of diabetes patients met ADA goals, 11 million fewer complications would occur with a 30-year savings of \$50 billion. If patients with the help of the healthcare system controlled blood pressure, A1C, and low-density lipoprotein cholesterol, there would be a significant cost saving. Controlling high-density lipoprotein cholesterol, triglycerides, and using aspirin is probably cost neutral. It’s unfortunate that only a small percent of patients reach treatment objectives. Simply stated, treating diabetes costs far less than treating the resulting complications. If diabetes could be cured tomorrow, there would be a 45% reduction in serious complications with a predicted 30-year cost savings of \$700 billion. Also, for every successive 1% rise in A1C of more than 6%, there is an increase in medical costs of 4% to 30%, depend-

ing on the final A1C value. Another example is that when even a 1% reduction of A1C occurs, there is a significant reduction in healthcare costs. Thirty-year excess costs for a diabetes patient with an A1C value of more than 10% are \$60,000.⁸ Managing blood glucose, blood pressure, and blood lipids is cost-effective and improves the quality of life for patients.

The issue of prediabetes is gaining in awareness, as well as concern. The Centers for Disease Control and Prevention projects there are close to 60 million people with elevated fasting glucose levels or impaired glucose tolerance, a group defined as having “prediabetes.” It would be a major accomplishment if these patients could be identified and prevented from developing type 2 diabetes. The healthcare system and insurers could save billions of dollars. It is known that regular exercise for at least 30 minutes a day for 5 days a week along with a 5% to 7% weight loss will reduce development of type 2 diabetes by 58%. Many pharmaceutical manufacturers are trying to develop medications that will prevent weight gain or cause weight loss. It is also known that there is a direct correlation with increasing obesity and diagnosis of type 2 diabetes. A major campaign to decrease caloric intake and improve eating habits of the general population could save healthcare dollars. Weight management programs would appear to be a worthwhile investment by healthcare insurers and government agencies because of the negative impact of obesity on health.

Table 3 summarizes the diagnosis criteria for diabetes.¹ It is now recommended that those in the general population who are at high risk for diabetes get screened, so prediabetes patients and those who have diabetes and do not know it can be diagnosed and treated.

Barriers to Improving Care of Patients With Diabetes

There are many obstacles to getting patients with diabetes diagnosed early and then implementing an effective treatment protocol. Our US healthcare system focuses on acute healthcare; chronic conditions such as diabetes are typically not the priority of care. Family medicine and general practitioners receive little training in diabetes yet they provide the care to most patients. Reimbursement for

■ **Table 2.** Key Standards of Care for Patients With Type 2 Diabetes¹

| Area of Care | Recommendation |
|-------------------------------|---|
| A1C measurement | 2 times per year for patients meeting goals, up to 4 times per year for patients not meeting goals |
| Blood pressure management | <ul style="list-style-type: none"> • Blood pressure should be measured at every routine diabetes visit • Patients with diabetes should be treated to a systolic blood pressure <130 mm Hg and diastolic blood pressure <80 mm Hg |
| Exercise | <ul style="list-style-type: none"> • 150 min/wk of moderate intensity aerobic exercise; • Those without contraindications should perform resistance training 3 times per week |
| Foot care | <ul style="list-style-type: none"> • Perform an annual comprehensive foot examination to identify risk factors predictive of ulcers and amputations; • Provide general foot self-care education to all patients with diabetes |
| Immunizations | <ul style="list-style-type: none"> • Annually provide an influenza vaccine to all diabetic patients >6 mo of age • Administer pneumococcal polysaccharide vaccine to all diabetic patients >2 y of age |
| Dyslipidemia/lipid management | <ul style="list-style-type: none"> • In most adult patients, measure fasting lipid profile at least annually • In adults with low-risk lipid values (low-density lipoprotein cholesterol <100 mg/dL, high-density lipoprotein cholesterol <50 mg/dL, and triglycerides <150 mg/dL), lipid assessments may be repeated every 2 y |
| Medical nutrition therapy | Individuals with prediabetes or diabetes should receive individualized medical nutrition therapy |
| Nephropathy screening | <ul style="list-style-type: none"> • Perform an annual test to assess urine albumin excretion in all type 2 diabetes patients, starting at diagnosis • Measure serum creatinine at least annually in all adults with diabetes regardless of the degree of urine albumin excretion |
| Neuropathy screening | <ul style="list-style-type: none"> • All patients should be screened for distal symmetric polyneuropathy at diagnosis and at least annually thereafter using simple clinical tests • Electrophysiological testing is rarely needed, except in situations where the clinical features are atypical • Screening for signs and symptoms of cardiovascular autonomic neuropathy should be instituted at diagnosis of type 2 diabetes |
| Retinopathy screening | <ul style="list-style-type: none"> • Patients with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist shortly after the diagnosis of diabetes • Subsequent examinations should be repeated annually by an ophthalmologist or optometrist. Less frequent exams (every 2-3 y) may be considered following ≥1 normal eye exams |
| Self-monitored blood glucose | >3 times daily for patients using insulin; can be used less frequently by other patients |
| Smoking cessation | Advise to all patients |

A1C indicates glycosylated hemoglobin.

assessing, educating, and treating diabetes patients does not cover costs, so the incentive to specialize in diabetes is low. Little effort or money is spent on programs to prevent diabetes. There is some controversy as to what the specific treatment targets should be. There is also controversy as to what treatment algorithm will be effective for most type 2 diabetes patients. Managed care/health main-

tenance organizations and government programs seem reluctant to aggressively confront the issue of diabetes. Many systems' barriers to fully effective management are created by discouraging monitoring or excessively restricting use of some medications. Problems are not only the fault of the system. For patients to be successfully treated, they need to make behavioral changes, stop smoking, lose

■ **Table 3. Criteria for the Diagnosis of Diabetes**^{1,9}

Fasting plasma glucose ≥ 126 mg/dL **OR**
 Symptoms of hyperglycemia and a casual (random) plasma glucose ≥ 200 mg/dL **OR**
 Two-hour plasma glucose ≥ 200 mg/dL during an oral glucose tolerance test using an equivalent of 75 g of anhydrous glucose dissolved in water

Overweight or obese patients should be tested for prediabetes and is positive if an impaired fasting glucose of 100 mg/dL or an impaired glucose tolerance of ≥ 140 mg/dL occurs

A1C $\geq 6.5\%$; use of A1C as a diagnostic tool is an evolving standard, though not currently supported in treatment guidelines

A1C indicates glycosylated hemoglobin.

weight, adhere to medication treatment regimens, exercise, visit healthcare providers often, eat less, count carbohydrates, give injections, test blood glucose, get laboratory tests, keep up with new developments, and find a supportive and knowledgeable physician and educator to encourage them to take charge of their diabetes. Education is a critical component for success, yet it is seldom encouraged, and reimbursement is insufficient. In addition, fear of hypoglycemia, social embarrassment, fear of failure, denial, and other factors create barriers.

Unfortunately, most managed care administrators anticipate that any given diabetes patient will remain in their coverage for only a few years and thus discourage costly treatments and programs. Over time, persistent hyperglycemia causes the development of many acute and chronic complications that are very costly to all of society. These patients eventually cost some insurer massive amounts of money to treat kidney, eye, heart, and other diseases. Barriers to diabetes care have to be overcome, and they can be—there is much hope. Keeping blood glucose and other parameters near normal reduces the complications and can save money.

Consequences of Sustained Hyperglycemia¹⁰

Patients who do not manage blood glucose, blood pressure, blood lipids, and coagulation factors die earlier and suffer numerous devastating complications that are very expensive to treat. It would seem logical and practical to get patients into a healthcare system that does everything possible to prevent heart, kidney, eye, nerve, skin, teeth/gum, and other costly problems. There are 2 major types of long-term complications of diabetes: macrovascular and microvascular disease. Macrovascular

disease, which affects the large vessels of the body, such as the coronary or lower extremity arteries (eg, femoral, popliteal), may result in myocardial infarction, stroke, and peripheral vascular occlusive disease, respectively. Up to 70% of deaths in people with type 2 diabetes are attributed to cardiovascular disease and stroke. The increased prevalence of macrovascular disease in people with diabetes is due to many factors, including, but not limited to, obesity, lipid abnormalities, hypertension, hyperglycemia, hypercoagulation factors, platelet dysfunction, inflammation, and endothelial dysfunction.

Microvascular disease in diabetes affects the small vessels, such as those supplying the retina, nerves, and kidneys. End-organ damage can lead to diabetic retinopathy and blindness; diabetic neuropathy, which may result in lower limb amputation; and diabetic nephropathy, often leading to end-stage renal disease requiring costly dialysis or transplantation. It is well established that chronic hyperglycemia results in these primary chronic microvascular complications of diabetes. Sustained hyperglycemia does not cause damage to other endocrine organs, but there is an increased incidence of thyroid, gonad, and other endocrine organ problems in diabetes patients. In addition to chronic hyperglycemia, diabetic microvascular complications arise from other metabolic alterations, which include, but are not limited to, insulin resistance, hypertension, and dyslipidemia. Under hyperglycemic conditions, blood flow and microvascular contractility changes are seen in the retina, microvessels of peripheral nerves, and kidney.

One of the principles and primary goals of diabetes management is to delay and/or prevent the

■ **Table 4. Clinical Causes and Consequences of Sustained Hyperglycemia**

| |
|---|
| Increased capillary basement membrane thickening, causing microvascular disease |
| Impairment of phagocytosis, resulting in impaired immunity and an inability to fight infections |
| Abnormally high levels of minor (glycosylated) proteins: advanced glycosylation end products that interfere with the protein's normal physiology |
| Glucose metabolized to sorbitol via the polyol pathway with deposition in cornea and in nerves |
| Increased aldose reductase that is a catalyst for producing excess sorbitol in cells |
| Faulty lipid metabolism yielding increased number of small low-density lipoprotein particles, low high-density lipoprotein, and hypertriglyceridemia |
| Hearing disorders, dental and gum problems |
| Increased blood pressure |
| Increased neonatal morbidity and mortality |
| Hemorrhagic factors affected adversely, including: |
| <ul style="list-style-type: none"> • Increased platelet adhesiveness • Increased serum fibrinogen levels • Increased blood viscosity • Decreased red blood cell flexibility |
| Numerous foot and lower limb problems including fungal infections |
| Increased coagulation factors like plasminogen activator inhibitor-1 |
| Increased apolipoprotein B |
| Increased C-reactive protein and other inflammatory factors; low levels of magnesium, vitamin D, and other micronutrients |
| Increased activation of some isoforms of protein kinase C causing reduced vascular contractility and increased vascular endothelial growth factor |
| Increased sialic acid levels in the blood |
| Increased weight |
| Increased incidence of cataracts, macular degeneration, glaucoma |
| Increased incidence of cancer |
| Genetic damage to sperm |
| Increased connective tissue problems; dermatopathy (skin problems are also common) |
| Oxidative stress throughout the body |

development of chronic complications. Numerous studies have proven that near-normalization of blood glucose will significantly decrease chronic diabetes complications. This has resulted in a renewed emphasis on empowering patients to tightly manage blood glucose, lipids, and blood pressure by using whatever available drugs or combination of drugs to achieve specific objectives and decrease the risk of chronic complications.

Two landmark studies, the Diabetes Control and Complications Trial (DCCT),¹¹ involving patients with type 1 diabetes, and the United Kingdom Prospective Diabetes Study (UKPDS),¹² involving patients with type 2 diabetes, conclusively demon-

strated that improved glycemic control contributes to significant microvascular risk reduction. The DCCT demonstrated a 63% relative risk reduction in retinopathy and 54% and 60% risk reductions in nephropathy and neuropathy, respectively. The UKPDS demonstrated up to a 21% risk reduction in retinopathy and a 33% risk reduction in nephropathy. A smaller study in patients with type 2 diabetes from Japan showed relative risk reductions of developing retinopathy (69%) and nephropathy (70%) in patients achieving tighter glycemic control compared with controls.

Theories on how hyperglycemia contributes to microvascular damage are emerging, with the

hope of providing additional pharmacotherapeutic interventions to prevent or slow the progression of chronic diabetes-related microvascular disease. The prominent contemporary biochemical pathway theories on how diabetes causes damage to the microvasculature include, but are not limited to¹⁰: (1) increased polyol (sorbitol/aldose reductase) pathway flux; (2) production of advanced glycosylation end products; (3) generation of reactive oxygen species (oxidative stress); and (4) activation of diacylglycerol and protein kinase C isoforms. A review that explores these biochemical pathways currently thought to contribute to the development of chronic diabetic microvascular complications can be found in the *ADA/PDR Medications for the Treatment of Diabetes*.¹⁰

Table 4 lists the numerous causes and consequences of sustained hyperglycemia that result in chronic diabetes complications often involving the microvasculature.¹⁰ Note that each condition resulting from poor management of diabetes listed is very costly to diagnose and treat. Other than a few of the factors that are genetically linked, the consequences could be reduced greatly or prevented with management of blood pressure, glucose, and lipids. It seems timely to better manage diabetes.

Conclusion

Diabetes is an increasingly prevalent, chronic disease that is costly to treat but even more costly not to treat. Patients with diabetes who manage their condition can usually reduce complications and have a better quality of life and not suffer from kidney, nerve, eye, and other expensive-to-treat conditions, as well. It is time for managed care systems to identify the barriers to improving the care of diabetes.

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