Diabetes is an epidemic that is expected to continue, leading to increased morbidity and mortality and greater expenditure of healthcare dollars. According to the Centers for Disease Control and Prevention data, 11% of individuals aged 20 years or older in the United States have diabetes. Approxi-
mately 23% of individuals aged 60 years or older have diabetes, a percentage that is expected to increase as the baby boomer population ages.\(^1\) Furthermore, based on 2002-2003 data, 25% of children newly diagnosed as having diabetes have type 2 diabetes mellitus (T2DM). Individuals diagnosed with early-onset T2DM (diagnosed before 30 years of age) have been shown to develop complications such as diabetic nephropathy, renal failure, blindness, and atherosclerotic vascular disease in their 30s.\(^2\)

Diabetes also represents a substantial economic burden, with both direct and indirect costs. Approximately $1 of every $5 in healthcare spending is used for someone with diagnosed diabetes. The total estimated cost of diabetes in 2007 was $174 billion.\(^3\)

Prevalence of Diabetes
The prevalence of diabetes is increasing. In 1995, the prevalence of diabetes in adults worldwide was approximately 135 million.\(^4\) The global prevalence of diabetes in adults aged 20 years and older in 2000 was estimated to be 171 million. India, followed by China and then the United States, has the highest number of individuals with diabetes (Table 1).\(^5\) Globally, diabetes prevalence is similar in men and women. However, there are differences in prevalence by age and developing countries. Diabetes prevalence is slightly higher in men younger than 60 years and in women at older ages.\(^5\) In developing countries, the majority of individuals with diabetes are aged between 45 and 64 years, while in developed countries, the majority are older than 64 years.\(^5\)

Based on demographic changes, by 2030, the number of people older than 64 years with diabetes will be more than 82 million in developing countries and...
more than 48 million in developed countries. The total number of people with diabetes is projected to rise to 366 million in 2030. The greatest relative increases are expected to occur in the Middle Eastern crescent, sub-Saharan Africa, and India. The most striking demographic change in global terms will be the increase in the proportion of the population that is older than 65 years. If the prevalence of obesity also increases by 2030, the number of cases of diabetes may be even higher than estimated.

United States

The prevalence of diabetes and obesity in the United States increased by epidemic proportions between 1994 and 2007, with nearly 24 million people diagnosed as having diabetes. In 2007 alone, 1.6 million new cases were diagnosed among adults aged 20 years or older. Of the nearly 24 million people with diabetes (nearly 8% of the US population), 5.7 million were unaware of their disease. In addition, 57 million people in the United States, or one-sixth of the population, were classified in 2007 as having impaired fasting glucose, or “prediabetes” or “at risk for diabetes,” as a possible eventual risk for diabetes. Based on these data, the diabetes epidemic and all of the comorbidities associated with the disease will continue.

Diabetes is a disease that afflicts people from all ethnicities. The prevalence of diabetes varies among several ethnicities in the United States (Table 2). Within the Hispanic population, the incidence rate is 8.2% among Cuban Americans, 11.9% among Mexican Americans, and 12.6% among Puerto Ricans. Among all ethnicities, one in three people from the year 2000 are predicted to develop diabetes while one in two people of black or Hispanic origin are predicted to acquire this disease. These populations therefore warrant special consideration for diabetes in the primary care setting.

Role of Primary Care Providers

Most individuals with diabetes are cared for by their primary care provider rather than the endocrinologist. Therefore, it is critical to identify diabetes early and to treat intensively with treatment guidelines in mind. It is of equal importance to identify individuals with “at risk for diabetes” and provide sufficient lifestyle modifications for these individuals. The role of identifying and managing T2DM is particularly relevant among osteopathic physicians, 40% of whom are in family or general practice.

Diagnosis: The HbA1c Assay

In light of the worldwide interest to develop a standardized assay for measuring glycated hemoglobin (HbA1c) levels and the evidence of the prognostic significance of HbA1c, the HbA1c assay has been recommended by a subcommittee of the American Diabetes Association (ADA) to be adapted as a diagnostic tool for diabetes. Earlier this year, the ADA added the HbA1c assay to their criteria for the diagnosis of diabetes.

According to this committee, whose members were appointed by the ADA, the European Association for the Study of Diabetes (EASD), and the International Diabetes Federation, a diagnosis of diabetes should be made when HbA1c levels are 6.5% or higher. The ADA recommends that the test be performed in a laboratory using a method that is certified by the National Glycohemoglobin Standardization Program and standardized to the Diabetes Control and Complications Trial assay. However, the HbA1c test may not be the single test, because of limited international standard, changes in glycation, certain ethnicities, age, abnormal hemoglobin, pregnancy, varying red blood cell turnovers, and renal disease.

According to the ADA, the criteria for diagnosing diabetes should be made when the patient has an HbA1c of 6.5% or higher, or a fasting plasma glucose (FPG) greater than 126 mg/dL, or a 2-hour plasma glucose (PG) greater than 200 mg/dL during an oral glucose tolerance test (OGTT), or, in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose level greater than 200 mg/dL. In the absence of unequivocal hyperglycemia, the first three criteria should be confirmed by repeat testing. The categories for increased risk of diabetes are an HbA1c level that is between 5.7% and 6.4%, an FPG level of 100 to 125 mg/dL, or a 2-hour PG level on the 75-g OGTT.

### Table 1

<table>
<thead>
<tr>
<th>Rank</th>
<th>Country</th>
<th>2000 Prevalence, No. in millions</th>
<th>2030 Country</th>
<th>Prevalence, No. in millions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>India</td>
<td>31.7</td>
<td>India</td>
<td>79.4</td>
</tr>
<tr>
<td>2</td>
<td>China</td>
<td>20.8</td>
<td>China</td>
<td>42.3</td>
</tr>
<tr>
<td>3</td>
<td>United States</td>
<td>17.7</td>
<td>United States</td>
<td>30.3</td>
</tr>
<tr>
<td>4</td>
<td>Indonesia</td>
<td>8.4</td>
<td>Indonesia</td>
<td>21.3</td>
</tr>
<tr>
<td>5</td>
<td>Japan</td>
<td>6.8</td>
<td>Pakistan</td>
<td>13.9</td>
</tr>
<tr>
<td>6</td>
<td>Pakistan</td>
<td>5.2</td>
<td>Brazil</td>
<td>11.3</td>
</tr>
<tr>
<td>7</td>
<td>Russian Federation</td>
<td>4.6</td>
<td>Bangladesh</td>
<td>11.1</td>
</tr>
<tr>
<td>8</td>
<td>Brazil</td>
<td>4.6</td>
<td>Japan</td>
<td>8.9</td>
</tr>
<tr>
<td>9</td>
<td>Italy</td>
<td>4.3</td>
<td>Philippines</td>
<td>7.8</td>
</tr>
<tr>
<td>10</td>
<td>Bangladesh</td>
<td>3.2</td>
<td>Egypt</td>
<td>6.7</td>
</tr>
</tbody>
</table>


### Table 2

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Prevalence, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic whites</td>
<td>6.6</td>
</tr>
<tr>
<td>Asian Americans</td>
<td>7.5</td>
</tr>
<tr>
<td>Hispanics</td>
<td>10.4</td>
</tr>
<tr>
<td>Non-Hispanic blacks</td>
<td>11.8</td>
</tr>
</tbody>
</table>

that is 140 to 199 mg/dL. For all of these tests, the risk is continuous, becoming disproportionately greater at the higher ends of the ranges.

**Treatment Algorithm and Guidelines**

In 2009, the ADA/EASD released a consensus statement for the management of T2DM. According to this consensus statement, HbA1c levels should be lower than 7.0%, but even lower levels should be sought if it is possible to do so without the risk of hypoglycemia. The recommendation is that all patients be treated with metformin and lifestyle modifications at diagnosis (Figure 1). Metformin should be initiated at 500 mg once or twice per day with meals (breakfast, dinner, or both) or 850 mg once per day. If gastrointestinal side effects have not occurred after 5 to 7 days, the dose can be advanced to 850 to 1000 mg twice per day (before breakfast and dinner). If gastrointestinal side effects subsequently occur, the dose should be decreased to 500 mg twice per day. Further attempts to advance the dose can be made at a later time.

If the patient cannot tolerate the drug at any dose, other options should be considered, such as a sulfonylurea, basal insulin, glucagon-like peptide-1 (GLP-1) mimetic, or a dipeptidyl peptidase-4 (DPP-4) inhibitor, which can improve both postprandial blood glucose and fasting blood glucose. In a recent parallel-group, open-label trial, liraglutide, a GLP-1 agonist, was shown to be superior than sitagliptin, a DPP-4 inhibitor, for reduction of HbA1c.

Glucagon-like peptide-1 mimetics can also cause nausea, but patients who experience nausea with metformin will not necessarily experience nausea with GLP-1 mimetics. Dipeptidyl peptidase-4 inhibitors such as sitagliptin have been shown to be associated with an increased risk of gastrointestinal adverse events.

If HbA1c remains at 7% or higher after 3 months, the ADA recommends two alternate therapies (Figure 1). These therapy options are listed as Tier 1, the well-validated core therapies, and Tier 2, the less well-validated therapies.

Tier 1 treatment continues lifestyle adjustments and metformin and adds a sulfonylurea or basal insulin if not at goal. This step adds minimal cost but has some risk of adverse effects, including weight gain and hypoglycemia.

Tier 2 also continues lifestyle changes and metformin therapy, but it adds a GLP-1 agonist or a thiazolidinedione and insulin as add-on therapy (Figure 1). However, because a GLP-1 agonist is more expensive than other treatment options for add-on therapy and is administered by injection, GLP-1 agonists may represent potential barriers for patients. Another choice would be the addition of a DPP-4 inhibitor. Most patients will eventually need three or four medications to achieve glycemic goals. Potential side effects of Tier 2 therapies are nausea, edema, increased risk for fractures, and weight gain.

More recently, the American Association of Clinical Endocrinologists and the American College of Endocrinology have jointly established a treatment algorithm for glycemic control, with the HbA1c goal of 6.5% or lower. Lifestyle modification is recommended for all patients. In brief, the treatment algorithm (Figure 2) recommends the following based on HbA1c levels:

- 6.5% to 7.5%—Monotherapy is the first line of therapy. If the HbA1c goal is not achieved safely, dual therapy can be added after 2 to 3 months, and triple therapy in another 2 to 3 months if dual therapy is ineffective. Insulin therapy can then be added.

- 7.6% to 9%—Treatment begins with dual therapy and is followed by triple therapy and insulin during the following 4 to 6 months if HbA1c goals are not met.

- Higher than 9.0%—Treatment can include insulin in addition to other agents, depending on symptoms.

The algorithm is not driven by cost, but rather safety and efficacy of the agents. The basis for therapeutic choice was driven by a tier approach. Tier 1 included well-validated core therapies, such as metformin, sulfonylureas, and...
basal insulin, and Tier 2 included less well-validated core therapies, such as TZDs and GLP-1 agonists. At the time of publication, there was not enough exposure of DPP-4 inhibitors to place it in this algorithm.

The initiation of therapy with metformin is recommended unless the patient cannot tolerate the agent because of gastrointestinal problems. If that patient has a HbA1c of 8.5%, therapy may be initiated with two medications; however, HbA1c levels are unlikely to decrease by 2% without dual therapy unless the patient can make lifestyle changes. Glycated hemoglobin levels should be monitored in patients with diabetes every 3 to 4 months, and if not improved, therapy should be progressed, as specified in the algorithm.

**Conclusion**

Based on the growing national and global prevalence of diabetes, it is essential that physicians screen patients for diabetes and identify individuals at risk for diabetes. Strategies should be developed quickly to modify lifestyle and afford these individuals therapies to reduce blood glucose levels and hopefully reduce diabetes complications. Treatment algorithms and consensus statements as previously described can help physicians navigate treatment options based on patient profiles and ultimately slow the progression of T2DM.

**References**


Partnership to Fight Chronic Disease

The American Osteopathic Association has been an active member of the Partnership to Fight Chronic Disease (PFCD) since 2007. This supplement promotes the ideals of this partnership.

The PFCD is a national and state-based coalition of hundreds of provider, patient, community, business, and labor groups committed to raising awareness of the leading causes of death, disability, and rising healthcare costs in the United States—chronic diseases such as diabetes, asthma, cancer, and heart disease. In addition, the PFCD has worked to ensure that prevention and wellness measures were incorporated into healthcare reform legislation passed by Congress in 2010.

For additional information, visit www.fightchronicdisease.org.