Diagnosis and management of type 2 diabetes in adults: A review of the ICSI guideline

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Diabetes is a complex chronic disease that affects approximately 25% of people above the age of 60 in the United States. This poses a significant challenge to primary care physicians to provide optimal treatment plans to improve metabolic control and to minimize debilitating complications. This article provides a summary of the recent guideline published by the Institute for Clinical Systems Improvement (ICSI) for the Diagnosis and Management of Type 2 Diabetes Mellitus in Adults. The purpose of this guideline is to provide a comprehensive approach to the diagnosis and management of prediabetes and type 2 diabetes in adults. Management strategies from the evidence-based guideline will include recommendations for nutrition therapy, physical activity, self-management approaches, and pharmacologic agents.


Key words: diabetes, glucose, hyperglycemia, insulin, prediabetes

Drugs discussed: acarbose, aspirin, exenatide injection, glimepiride, glipizide, glyburide, human amylin analog, hydrochlorothiazide, lisinopril, metformin, miglitol, nateglinide, pioglitazone, pramlintide acetate injection, repaglinide, rosiglitazone, simvastatin, sitagliptin.

C ase scenario: Mrs. M. is a 70-year-old woman with a history of hypertension, dyslipidemia, and type 2 diabetes treated with diet control for the past year. She monitors her blood glucose levels 1 to 2 times a week and says that lately the readings have been between 180 and 200 mg/dL. A recent dilated eye exam by her ophthalmologist did not show any evidence of diabetic retinopathy. Over the past month, Mrs. M. has complained of increasing fatigue and nocturia and has suffered two falls. She states that she never misses a dose of her medications, which include hydrochlorothiazide, lisinopril, simvastatin, and aspirin. Physical examination reveals a mildly obese woman with blood pressure of 142/86 mm Hg, a pulse of 78, and trace pedal edema. Laboratory studies demonstrate normal renal function (blood urea nitrogen, 11 mg/dL; creatinine 0.9 mg/dL); and glycosylated hemoglobin (HbA1c) of 7.9%. What advice could Mrs. M.'s doctor offer her? Should her doctor start her on any diabetic medication?

To determine the best course of action, her primary care physician should turn to an up-to-date clinical practice guideline found through the National Guideline Clearinghouse: The Institute for Clinical Systems Improvement (ICSI) Diagnosis and Management of Type 2 Diabetes Mellitus in Adults (2008). ICSI is a nonprofit organization that supports and promotes the use of evidence-based health care in all of its scientific documents in order to advance improvements in patient safety and efficiency. The objective of this guideline is to provide a comprehensive approach to the diagnosis and management of type 2 diabetes in adults 18 to 75 years old. The recommendations cover screening, nutrition, physical activity, monitoring, medications, and the prevention and diagnosis of diabetes-related complications. The ICSI guideline, intended for primary health care professionals, was created after an extensive literature review. The quality and strength of the literature to support the recommendations were evaluated using an acceptable grading scale. Each individual study was evaluated by a work group for its ability to address issues of inclusion and exclusion bias, generalizability, quality of data collection, and analysis. The work-group members included representatives from endocrinology, primary care medicine, nursing, pharmacy, and health.
education. Potential conflicts of interest were disclosed by all members of the work group.

Type 2 diabetes accounts for 90% to 95% of all diabetes cases. The pathophysiology includes a combination of metabolic disorders that lead to insulin resistance, uncontrolled hepatic glucose production, insulin resistance in muscle and adipose tissue, progressive decline in pancreatic insulin secretion, and other hormonal imbalances. Hyperglycemia is usually present years before the diagnosis of diabetes, often leading to pathologic and functional changes in target organs. Age is an independent risk factor for the development of hyperglycemia. It is estimated that 20% of men and more than 15% of women 65 to 74 years of age have diabetes.

Management of prediabetes
Prediabetes is the term recommended for patients with impaired glucose tolerance or impaired fasting glucose (Table 1). Evaluation of patients with elevated glucose levels involves an appropriate history, physical examination, and laboratory evaluation. If a diagnosis of prediabetes is made, patients should be referred for education and lifestyle interventions. Primary care physicians should monitor patient progress and review treatment goals on an annual basis. Treatment entails intensive lifestyle behavioral changes that include a nutrition and physical activity plan by a registered dietitian, health educator, or other qualified health professional. Ongoing support should be provided for the behavioral changes to be successful. In addition, patients should undergo appropriate cardiovascular risk reduction.

Recent randomized clinical trials have demonstrated efficacy in preventing diabetes by pharmacotherapy with biguanides, glitazones, and alpha-glucosidase inhibitors. However, lifestyle changes are most efficacious. In a Diabetes Prevention Program Research Group study, efficacy of lifestyle modification was most pronounced in participants more than 60 years of age. Moderate activity of 150 minutes per week reduced the development of diabetes by 71% in this age group.

<table>
<thead>
<tr>
<th>Table 1. Diabetes terminology</th>
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<tbody>
<tr>
<td><strong>Prediabetes</strong></td>
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<td>Hyperglycemia not sufficient to meet the diagnostic criteria for diabetes.</td>
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<td>Diagnosis based on:</td>
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Data derived from the American Diabetes Association.

Patients who meet the goals should be evaluated yearly.

Patients who meet treatment goals should continue to be evaluated yearly. Patients who fail to meet treatment goals should undergo further intensive education and counseling on lifestyle interventions.

Management of diabetes
The major goal for the management of diabetes is to provide a comprehensive approach that focuses on self-management strategies such as proper nutrition, increased physical activity (150 minutes per week), and pharmacologic therapy to prevent diabetes-associated complications. In managing the patient with diabetes, it is important to obtain a detailed history of past and current treatment programs, including nutrition, physical activity, and medications. Additionally, records of recent glucose monitoring should be reviewed, and the frequency of complications such as hypoglycemia and severe hyperglycemia should be obtained.

Medical nutrition
The goal of medical nutrition therapy is to assist patients in making lifestyle and behavioral changes that will improve metabolic outcomes. The ICSI recommendations are based on promoting optimal nutrition through healthy food choices and active lifestyle to maintain normal blood glucose, blood pressure, and lipid levels. Achieving these goals can help to reduce the risk for chronic complications of diabetes and macrovascular and microvascular diseases. Instruction on medical nutrition may be offered by a provider with medical expertise in this topic and is covered by Medicare Part B.

Aging is associated with many
changes that may predispose older adults to nutritional deficiencies. Such changes include alterations in taste, smell, mastication, and hepatic and renal function. In addition, common problems such as difficulty in preparing food and polypharmacy can interfere with adequate nutrition. Because of these concerns, nutrition prescription should be individualized and must start with a thorough assessment of clinical, nutritional, psychosocial, and environmental factors. Limited research exists on the changes in nutritional needs with aging; therefore, the recommendations for older patients must be extrapolated from the general population.

**Weight control** Moderate weight loss of 5% can improve metabolic goals in overweight or obese patients. Combining lower fat and caloric consumption with 30 minutes of regular physical activity most days provides the greatest benefit. The effectiveness of pharmacologic interventions for weight loss has not been convincingly demonstrated.

**Carbohydrates** Carbohydrates should be distributed evenly throughout the day to smaller meals and snacks. Monitoring carbohydrates remains a key strategy in achieving glycemic control, and it is more important to monitor carbohydrate totals rather than the type of carbohydrate. Sucrose and sucrose-containing foods do not need to be restricted but should be substituted with other carbohydrate sources. If additional sucrose is added during a meal, this additional glucose load should be covered by insulin or glucose-lowering medication. Added fructose as a sweetening agent is not recommended because it may adversely affect plasma lipids. However, healthful food choices such as fructose-containing fruits, vegetables, and other foods do not need to be avoided. Use of sugar alcohols such as sorbitol or mannitol in small amounts is safe but may cause diarrhea. Artificial sweeteners are safe when consumed within approved daily intake.

**Protein** Protein intake should be 15% to 20% of total daily calories. This may need to be reduced in patients with diabetes and earlier stages of chronic kidney disease. Protein does not increase plasma glucose concentrations but does increase serum insulin responses, thus protein should not be used to treat acute hypoglycemia or to prevent nighttime hypoglycemia.

**Protein should not be used to treat acute hypoglycemia.**

**Fat** Healthy patients should maintain a daily diet with no more than 30% of their total calories coming from fat, with an intake of saturated fats less than 7% and cholesterol less than 200 mg. Intake of trans fatty acids should be minimized. In patients with elevated cholesterol and low-density lipoprotein (LDL) cholesterol, the National Cholesterol Education Program therapeutic lifestyle recommendations should be implemented. This includes the same diet recommended for healthy people but increases the soluble fiber intake to 10 g to 25 g per day and plant stanols/sterols to 2 g per day. Incorporating 2 to 3 servings of plant stanols and sterols, which naturally occur in some fruits, vegetables, nuts, and cereals, into the daily diet will decrease total and LDL cholesterol. Two or more servings of fish per week provide n-3 polyunsaturated fatty acids and are recommended.

**Sodium** Sodium intake should be limited to 2,000 mg per day for patients with diabetes and symptomatic heart failure. Intake should be less than 2,300 mg per day for patients with diabetes whether they are normotensive or hypertensive.

**Physical activity** Exercise in the elderly can significantly slow the decline in maximal aerobic capacity, improve risk factors for atherosclerosis, slow the decline in age-related lean body mass, decrease central adiposity, and improve insulin sensitivity. However, positive effects of increased physical activity diminish within days of cessation. As such, regular exercise of 30 minutes most days of the week is necessary to gain its benefits. Strategies of initiation of physical activity include incorporating 10 minutes of increased activity into each day. Such activities include using stairs instead of elevators, parking away from building entrances, and walking to do errands. Self-monitoring by using time records, journals, or pedometers and participating in enjoyable activities may improve compliance. There is no evidence that stress testing is necessary in asymptomatic persons before initiating a moderate intensity program such as walking. However, cardiac stress testing should be considered for persons with moderate to high risk for cardiovascular disease who are initiating a vigorous aerobic exercise program that exceeds daily routine activities. Cardiac testing is especially recommended in persons with a 10-year Framingham risk score of 10% or greater.

**Pharmacologic therapy** Research in the pathophysiology of insulin resistance, adipose tissue metabolism, and biotechnology has led to the development of a wide variety of classes of medications to treat diabetes (Table 2, page 15). Most of the trials demonstrating efficacy of these agents were in adult patients.

**Self-management** Patients with diabetes should be knowledgeable...
<table>
<thead>
<tr>
<th>Medication</th>
<th>Usual starting dose for the elderly</th>
<th>Usual maximum clinically effective dose per day</th>
<th>Contraindications</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metformin</strong></td>
<td>500 mg qd</td>
<td>1,000 mg bid</td>
<td>Renal insufficiency (use with caution in those over age 80) COPD Severe liver disease Alcoholism</td>
<td>Diarrhea Nausea Anorexia Metallic taste</td>
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<tr>
<td><strong>Sulfonylureas</strong></td>
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<td>glipizide</td>
<td>2.5 mg qd</td>
<td>10 mg bid</td>
<td>Diabetic ketoacidosis</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td>glyburide</td>
<td>1.25 mg qd</td>
<td>5 mg bid</td>
<td>Diabetic ketoacidosis</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td>glimepiride</td>
<td>1-2 mg qd</td>
<td>1-4 mg qd</td>
<td>Diabetic ketoacidosis</td>
<td>Hypoglycemia</td>
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<td><strong>Alpha-glucosidase inhibitors</strong></td>
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<tr>
<td>acarbose</td>
<td>25 mg qd</td>
<td>50 mg tid for patients weighing ≤60 kg or 100 mg tid for those &gt;60 kg</td>
<td>Renal impairment Abnormal LFTs Inflammatory bowel disease</td>
<td>Abdominal cramping Flatulence Diarrhea Elevated LFTs</td>
</tr>
<tr>
<td>miglitol</td>
<td>25 mg qd</td>
<td>100 mg tid</td>
<td>Renal impairment Abnormal LFTs Inflammatory bowel disease</td>
<td>Abdominal cramping Flatulence Diarrhea Elevated LFTs</td>
</tr>
<tr>
<td><strong>Dipeptidyl peptidase-4 inhibitor</strong></td>
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<tr>
<td>sitagliptin</td>
<td>100 mg qd</td>
<td>100 mg qd</td>
<td>Dose needs to be lowered in renal impairment</td>
<td>Nasopharyngitis URI Headache</td>
</tr>
<tr>
<td><strong>Meglitinides (short-acting secretagogues)</strong></td>
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<tr>
<td>repaglinide</td>
<td>0.5 mg/meal with HbA1c &lt;8% or no prior treatment 1-2 mg/meal with HbA1c &gt;8% or on other oral agent</td>
<td>4 mg/meal or 16 mg/day Needs to be taken 15 min before meals</td>
<td>Dose needs adjustment in hepatic impairment Avoid concomitant use of gemfibrozil and repaglinide</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td>nateglinide</td>
<td>60-120 mg tid before meals</td>
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<tr>
<td><strong>Glucagon-like peptide 1 agonist</strong></td>
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<tr>
<td>exenatide injection</td>
<td>5 mcg subcutaneously bid within 60 min before the morning and evening meal</td>
<td>10 mcg subcutaneously bid after 1 mo</td>
<td>ESRD (creatinine clearance &lt;30 mL/min) Diabetic ketoacidosis</td>
<td>Nausea Vomiling Diarrhea Weight loss</td>
</tr>
</tbody>
</table>

Table 2 is continued on pg 17
about the diabetes disease process and treatment options. An education plan should be identified based on the needs of the individual, and periodic reassessment of educational goals is recommended. Goals should be set to promote improved understanding of the disease and its treatment options; the side effects of medications; the prevention, detection, and treatment of complications; the monitoring of glucose levels; and psychosocial adjustment. Appropriate education may require the use of a diabetes educator or a multidisciplinary program that includes a dietician, a nurse, and a pharmacist. Accredited diabetes self-management programs by the American Diabetes Association are reimbursed by Medicare.

**Glycemic control** Assessment of glycemic control can be based on HbA\(_1c\) or glucose levels. HbA\(_1c\) yields an accurate measure of glucose control during the prior 6 to 8 weeks and is not influenced by food intake, physical activity, or acute metabolic stress. Clinicians should monitor HbA\(_1c\) every 3 to 6 months (quarterly in those with poor control). Treatment goals should be individualized. Physicians should discuss and document treatment goals and plans. Goals for patients with severe health problems and reduced life expectancy should be less strict. Reduction in morbidity and mortality in the elderly may be greater if cardiovascular risk factors are controlled compared to glycemic control. Important things to consider are advanced age, reduced life expectancy, cognitive impairment, polypharmacy, multiple comorbidities, history of hyperglycemia, the ability to manage hypoglycemia, duration of diabetes, and cardiovascular risk.

Initially, a target HbA\(_1c\) value of less than 7% in type 2 diabetes was recommended as a result of the United Kingdom Prospective Diabetes Study (UKPDS), which showed the beneficial effects of glucose control on microvascular complications. Recently, the benefits of glycemic control below 7% to reduce such complications have not been demonstrated in randomized, controlled trials. Studies such as the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial found a 20% higher risk for all-cause mortality in the intensive-therapy group, which aimed to achieve HbA\(_1c\) less than 6%. The achieved median HbA\(_1c\) in that group, however, was 6.4%, and the median HbA\(_1c\) was 7.5% in the standard-treatment group, which had a lower death rate. In the Steno 2 Study of 160 patients, there was an absolute risk reduction in mortality of 20% and a 13% reduction in the absolute risk of death from cardiovascular causes with target HbA\(_1c\) of less than 6.5% and target blood pressure and lipid levels. For patients with long-standing diabetes and cardiovascular risk on insulin or multiple glycemic medications and with an HbA\(_1c\) less than 6.5%, some modification of their medications should be considered to raise their HbA\(_1c\) levels to near 7%. The American Geriatrics Society recommends HbA\(_1c\) less than 8% for patients with a life expectancy of less than 5 years.

**Lipid control** LDL cholesterol levels should be less than 100 mg/dL without coronary disease and less than 70 mg/dL with coronary disease. Triglyceride management requires initial optimization of glucose levels before initiation of pharmacotherapy.

**Blood pressure** The optimum blood pressure in patients with diabetes should be less than 130/80 mm Hg. In the elderly, isolated systolic hypertension is the most common form of hypertension and is a major risk factor for cardiovascular disease. In the Systolic Hypertension in the Elderly Program (SHEP), antihypertensive treatment lowered the risk of stroke by 36%. Uncontrolled hypertension can also accelerate the progression of diabetic neuropathy. First-line agents to reduce blood pressure include an angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker. Diuretics are useful in patients who require additional agents to lower blood pressure.

**Renal and hepatic function** Liver function, urine for microalbumin, and renal function should be tested annually. If urinary microalbumin is more than 30 mg/g, the level should be rechecked twice in 3 months.

**Case continued** Management of our patient will include medical nutrition consultation, recommendation of increased physical activity, and pharmacologic therapy to reduce cardiovascular risk factors. Counseling on medical nutrition therapy is available by a certified dietician or diabetes educator. Modest physical activity will be recommended, with a weight loss goal of 5% of body weight. Furthermore, initiation of pharmacotherapy will be appropriate at this time. Pharmacologic agents will include metformin or short-acting, low-dose secretagogues. We should be careful with using long-acting agents because the elderly are more susceptible to hypoglycemia. Metformin, acarbose, exenatide, sitagliptin, and human amylin analog are all associated with weight loss or weight maintenance. Unless the patient has symptoms of congestive heart failure, metformin would be the drug of choice because it does not cause hypoglycemia and is...
### Table 2. Pharmacotherapy for diabetes mellitus (continued)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Usual starting dose for the elderly</th>
<th>Usual maximum clinically effective dose per day</th>
<th>Contraindications</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synthetic analog of human amylin</td>
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<tr>
<td>pramlintide acetate injection (adjunct to insulin)</td>
<td>60 mcg subcutaneously immediately before meals</td>
<td>120 mcg subcutaneously immediately before meals</td>
<td>Gastroparesis</td>
<td>Nausea</td>
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<td></td>
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<td></td>
<td>Poor compliance with diabetes management</td>
<td>Vomiting</td>
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<td></td>
<td></td>
<td></td>
<td>Recurrent hypoglycemia</td>
<td>Anorexia</td>
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<tr>
<td>Thiazolidinediones</td>
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</tr>
<tr>
<td>pioglitazone</td>
<td>15-30 mg qd</td>
<td>45 mg qd</td>
<td>Moderate to severe CHF</td>
<td>Weight gain Edema Mild anemia Rare macular edema</td>
</tr>
<tr>
<td>rosiglitazone</td>
<td>4 mg qd or bid</td>
<td>4 mg bid or 8 mg qd</td>
<td>Moderate to severe CHF</td>
<td>Increased risk of MI and CV death Weight gain Edema Mild anemia Rare macular edema</td>
</tr>
</tbody>
</table>

Abbreviations: bid, twice daily; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CV, cardiovascular; ESRD, end-stage renal disease; LFT, liver-function test; MI, myocardial infarction; qd, daily; tid, three times daily; URI, upper respiratory infection.

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Data derived from ICSI guidelines.1

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not expensive. A comprehensive approach would include periodic ophthalmic evaluation and treatments, foot examinations, and control of lipid values and blood pressure. A blood pressure target of less than 130/80 mm Hg and an LDL cholesterol less than 100 (≤70 if she has coronary artery disease) should be goals for care. The guidelines recommend daily aspirin, unless the patient has a contraindication, and administration of the pneumococcal vaccine. Finally, Mrs. M. should be screened for depression, which is more common in diabetics than in the general population.

### Conclusion

The Diagnosis and Management of Type 2 Diabetes Mellitus in Adults health care guideline sponsored by the ICSI is a comprehensive guideline for the management of prediabetes and diabetes in adults 18 to 75 years old. The ICSI updates the guideline every 1 to 3 years, depending on new developments in the field. The guideline provides little reference to the management of diabetes in the elderly. This is primarily because of the lack of available data in the literature regarding management of diabetes in the elderly, and even less so in the frail elderly. Much of our current management of diabetes in the elderly is primarily extrapolated from data in adults. As the population of elderly with diabetes continues to increase, further research will be needed to direct our care of these patients.

### References


than being able to increase energy expenditure by 8 to 10 kcal per minute during exercise, middle-aged women may be able to burn only 6 to 8 kcal per minute. This has an important impact on how women can use exercise to maintain body weight as they age. Because the rate at which energy can be expended decreases gradually with aging, maintaining the same level of total exercise energy expenditure may require an increase in the amount of exercise time.

Do physically active women gain less weight than sedentary women during peri- and postmenopause? Exercise can prevent weight gain in peri- and postmenopausal women, but factors related to menopause and aging make weight maintenance a challenge. Even though regular exercise does not come with a guarantee against weight gain, prospective studies of perimenopausal women indicate that the most active women gain the least weight. Most important, women should not abandon their exercise habits if they become discouraged by what they perceive as a lack of effectiveness of exercise to prevent weight gain. Exercise has numerous health benefits that are independent of its effects on body weight regulation.

DISCLOSURE: Dr. Kohrt reports: Research support—National Institutes of Health.

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References


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