CONDUCT PRACTICE-BASED SCREENING

A process is in place to identify patients seen in the practice who are at high risk for Type 2 diabetes, according to American Diabetes Association (ADA) recommendations for testing for diabetes or prediabetes in asymptomatic adults. Screening occurs at primary care, endocrinology, cardiology, nephrology, and other specialty visits (as determined by the group), and appropriate follow-up is provided. The EHR is used to identify patients who already meet the clinical criteria for type 2 diabetes but lack a diagnosis or problem list entry.

One-fourth of Americans who have Type 2 diabetes—and nearly twice that proportion among Asian and Hispanic Americans—are unaware they have it. Screening asymptomatic adults (practice-based case detection) is therefore an essential population health strategy.

According to the American Diabetes Association’s Standards of Care:

- All patients 45 years of age or older should be tested, with repeat testing every 3 years if the results are normal, every year for people who have prediabetes; and
- Testing should be considered in adults younger than 45 who are overweight (BMI ≥ 25, or ≥ 23 in Asian Americans) and have additional risk factors.

TIPS FOR EFFECTIVE SCREENING

- Conduct screening in a practice-based setting, where patients can receive individualized treatment and support.
- Use hemoglobin A1c (HbA1c), fasting plasma glucose, or a two-hour oral glucose tolerance test for screening. Equivocal results should be confirmed through repeat testing or a different test.
- Identify people with diabetes who are “hiding in plain sight.” These are patients who already have lab results that are diagnostic for diabetes or who are being treated for glycemic control but do not have the diagnosis on their problem list.
- Address “clinical inertia” to improve the effectiveness of identifying, documenting, and treating patients with diabetes or at risk to develop the condition.

- Organizations should consider addressing policy, system, and environmental factors through community interventions to promote healthy lifestyles.
- Create care pathways for those newly diagnosed with Type 2 diabetes or pre-diabetes:
  - For people found to have Type 2 diabetes, therapy should be individualized.
  - For people who have “pre-diabetes” (HbA1c 5.7–6.4%, impaired fasting glucose, or impaired glucose tolerance), retesting should occur at least once a year.
    - Clinicians should provide full diagnostic disclosure that promotes shared decision-making. This may include creation of a “roadmap” for aggressive lifestyle interventions to prevent or delay the onset of overt Type 2 diabetes.
    - Consider referral to programs that meet the guidelines of the Centers for Disease Control and Prevention’s National Diabetes Prevention Program.
    - Other modifiable risk factors should be addressed, including smoking cessation and treatment of hypertension.
    - Clinicians should discuss the benefits and risks of medications for glycemic control for people at the upper end of the range for prediabetes who are obese or have additional risk factors. Shared decision-making is recommended for these patients.
TOOL: SCREENING AND DIAGNOSIS ALGORITHM

SCREENING AND DIAGNOSIS

Timely, accurate screening and diagnosis is important because it can:

- **Identify those at risk for diabetes.** Therapeutic lifestyle changes may delay or prevent development of diabetes in people with prediabetes.
- **Prevent or delay diabetes complications.** The length of time between the onset of hyperglycemia and appropriate treatment for the condition can be a significant factor in the development and severity of complications. Type 2 diabetes is often asymptomatic, and at the time of diagnosis a significant number of type 2 patients already have complications such as neuropathy, nephropathy, or retinopathy.
- **Identify those at risk for other causes of hyperglycemia.** Hyperglycemia can be chronic, pathogenic, asymptomatic, and can be caused by conditions other than diabetes. Screening for hyperglycemia can also detect patients at risk for complications from vascular, neurological, and renal conditions.

Screening

This CPM recommends:

- **Routine screening for type 2 diabetes.** Note that in addition to testing the patients specified in the algorithm on page 4, physicians should consider testing adults older than age 30 every 3 to 5 years. This is a cost-effective strategy; the benefits of early detection of type 2 diabetes include a reduced incidence of myocardial infarction and microvascular complications.\(^{44}\)
- **No routine screening for type 1 diabetes.** People with type 1 typically present with acute symptoms and markedly elevated blood glucose, and most cases are diagnosed soon after the onset of hyperglycemia.

For pregnant patients, routine screening for gestational diabetes is recommended per the Intermountain care process model Management of Gestational Diabetes.

Diagnosis

Recommended diagnostic tools for type 2 diabetes include:

- **Hemoglobin A1c (HbA1c).**\(^{44}\) HbA1c measurement does not require the patient to fast or undergo a glucose tolerance test, and the required specimens are stable at room temperature. Further, the results are not affected by intercurrent illness or stress and correlate with the development of subsequent retinopathy. Limitations of this test are that HbA1c’s normal range is modestly higher in certain ethnic groups (e.g., African-Americans, Asian Indians) and it increases with age. HbA1c is elevated in patients with untreated hypothyroidism, and among U.S. adults with diabetes it tends to be slightly higher in winter.\(^{44}\) False negative values can occur in patients with rapid red cell turnover, some anemias, and recent onset of diabetes.
- **Fasting plasma glucose (FPG).** The FPG is more convenient for patients, more reproducible, less costly, and easier to administer than the 2-hour OGTT.
- **Other acceptable diagnostic tests include a two-hour, 75-gram oral glucose tolerance test (OGTT).** This test may be required when evaluating patients with impaired fasting glucose (IFG) or if diabetes is still suspected despite a normal FPG or HbA1c result.

Diagnostic criteria for diabetes are listed in note (d) on the algorithm on the following page. Note that in the absence of unequivocal hyperglycemia, repeat testing is required to make a diagnosis of diabetes.\(^{44}\) In an outpatient with new onset of hyperglycemia, causes of hyperglycemia other than diabetes should be considered. The differential diagnosis of hyperglycemia includes type 1 and type 2 diabetes. Cushing’s syndrome, electrolyte abnormalities, acromegaly, pheochromocytoma, and pancreatic cancer.

PROFILES: TYPE 2, TYPE 1, LADA

Most new diabetes patients over the age of 30 will have type 2. Nevertheless, when the type of diabetes is uncertain by clinical presentation, we recommend antibody testing. Key considerations:

Type 2:
- Onset is usually slow.
- Occurs mainly in older adults, but can occur in children.
- Common features at diagnosis are obesity, insulin resistance, and neuropathy.
- Family history usually includes a first-degree relative with type 2 diabetes.
- Condition usually responds to oral medications for years.

Type 1:
- Onset is usually rapid (over the course of days or weeks).
- Occurs primarily in children and younger adults.
- Common features at diagnosis are DKA, recent weight loss, and insulin deficiency.
- Family history including a first-degree relative with diabetes is less common.
- Condition requires insulin from onset.

LADA (latent autoimmune diabetes in adults)

- Onset is slow.
- Occurs in adults age 30 and older (does not occur in children).
- Prevalence among patients with adult-onset diabetes is about 10%,\(^{44}\)
- In LADA patients, glutamic acid decarboxylase (GAD) antibodies are present close to 90% of the time, with only a small additional fraction of patients having other autoantibodies.\(^{44}\)
- In comparison to diabetic patients without autoantibodies, LADA patients are more often female, younger at diagnosis, have a smaller waist circumference (are overweight but not obese), and do not exhibit DKA.
- Family or personal history often includes autoimmune disorder.
- Condition may initially respond to oral medications and other therapies, but will eventually require insulin.

To order antibody testing:
- GAD antibody: ARUP #0070211, Sunquest code GADAB, CPT 83519
- If GAD is negative, then order insulinoma associated-2 antibodies and/or Zinc transporter 8 antibodies
TOOL: SCREENING AND DIAGNOSIS ALGORITHM (CONTINUED)

INTERMOUNTAIN HEALTHCARE

ALGORITHM: SCREENING AND DIAGNOSIS

Patient appropriate for SCREENING or with symptoms (a)

TEST by measuring one of the following:
- Plasma glucose (not capillary glucose): FPG or 2-hour OGTT
- HbA1c

NORMAL
- HbA1c <5.7%
- FPG <100 mg/dL
- 2-hour OGTT <140 mg/dL

ABNORMAL (b) but below diagnostic threshold
- HbA1c 5.7%–6.4%
- FPG 100–125 mg/dL
- 2-hour OGTT 140–199 mg/dL

ABNORMAL (b) meets criteria for diagnosis
- HbA1c ≥6.5%
- FPG ≥126 mg/dL
- 2-hour OGTT ≥200 mg/dL

EDUCATE on lifestyle management
REPEAT TESTING every 3 years or more frequently if overweight or other risk factors

In the absence of unequivocal elevated blood glucose, REPEAT same or alternative test using a new blood sample

Meets criteria for DIAGNOSIS (d)?

no

yes

PREDIABETES (c)

DIABETES MELLITUS

If suspected type 1 or LADA (see profiles page 3), CONSIDER ANTIBODY TESTS (e)

Refer to Prediabetes Care Process Model for follow-up plan

See ALGORITHM: Treatment of Type 2, page 11

Indicates an Intermountain measure
Algorithm Notes

(a) Diabetes Screening

Screen these patients at least every 3 years or more frequently depending on initial results and risk status:

- Adults ≥45 years
- Adults of any age who are overweight or obese (BMI ≥25 kg/m² or ≥23 kg/m² in Asian Americans) and have any of these additional risk factors:
  - Hypertension >140/90 mm Hg or on therapy for hypertension
  - Family history: first-degree relative with diabetes
  - Habitual physical inactivity
  - High-risk ethnicity (African American, Latino, Native American, Asian American, Pacific Islander)
  - Previous GDM or delivery of baby >9 pounds
  - Dyslipidemia (HDL-cholesterol <35 mg/dL and/or triglycerides >250 mg/dL)
  - Polycystic ovary syndrome (PCOS)
  - History of vascular disease
  - Other clinical conditions associated with insulin resistance, e.g., acanthosis nigricans, sleep apnea, multiple skin tags, peripheral neuropathy, and gout.
  - Use of second-generation antipsychotic medication (SGAs); see page 17

Screen these patients annually:

- History of elevated HbA1c ≥5.7%, impaired fasting glucose (≥100 mg/dL), or impaired glucose tolerance (≥140 mg/dL)

(b) Investigating Abnormal Values

- Ensure the integrity of plasma glucose values: must be obtained from a correctly collected/stored specimen, NOT from finger stick.
- If repeat testing is indicated by an abnormal value, use ICD-9 code 790.6 Abnormal Chemistry to order follow-up test. DO NOT use ICD-9 code 250.xx or your patient will be labeled a diabetic regardless of the test result.
- Hemoglobinopathy: If patient has hemoglobinopathy and diabetes is suspected based on blood glucose or symptoms, measure two FPG values for confirmation.

(c) Prediabetes

Prediabetes is not a clinical entity of itself. It is the term used for individuals with impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT), which are risk factors for developing diabetes and cardiovascular disease in the future. The Prediabetes Care Process Model provides system-wide support for helping patients prevent these conditions. Criteria for prediabetes include:

- HbA1c <5.7%–6.4% OR
- FPG <100–125 mg/dL OR
- 2-hour OGTT <140–199 mg/dL

(d) Criteria for Diabetes Diagnosis

Criteria for diabetes diagnosis:

- TWO HbA1c values ≥6.5% OR
- TWO FPG values ≥126 mg/dL OR
- TWO 2-hour OGTT values ≥200 mg/dL

Remember: Plasma glucose values must NOT come from a finger stick.

(e) Antibody Testing

- Glutamic acid decarboxylase (GAD) antibodies account for 90% of diabetes-associated autoantibodies.
- Insulinoma associated-2 antibodies and zinc transporter 8 antibodies account for only the remaining 10%.
- See sidebar on page 4 for more further discussion of LADA and information on ordering tests.
Screening for type 2 diabetes
The United States Preventative Services Task Force (USPSTF) recommends only adults with blood pressure readings > 135/80 mm Hg be screened for diabetes. Relying on this as a sole criterion for screening, however, may identify only half of those who have diabetes. We recommend following guidelines from the American Diabetes Association (ADA) for screening. The ADA recommends adults who are overweight (BMI > 25) and possess at least one additional risk factor (listed below) be screened for DM. The ADA also recommends screening be performed in all adults age > 45 years even in the absence of other risk factors. Appropriate tests used for screening include the hemoglobin A1c (A1c), fasting blood glucose (FBG), or the 75-gram oral glucose tolerance test (OGTT). If normal, screening should be repeated every 3 years or more frequently depending on results.

<table>
<thead>
<tr>
<th>Physical inactivity</th>
<th>First-degree relative with diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk race/ethnicity (African-American, Latino, Native American, Asian American, Pacific Islanders)</td>
<td></td>
</tr>
<tr>
<td>Women with history of GDM or having delivered an infant weighing &gt; 9 lbs</td>
<td></td>
</tr>
<tr>
<td>HTN (BP &gt; 140/90 mm Hg or treatment)</td>
<td></td>
</tr>
<tr>
<td>HDL &lt; 35 or triglycerides &gt; 250 mg/dl</td>
<td></td>
</tr>
<tr>
<td>Women with history of polycystic ovarian syndrome</td>
<td></td>
</tr>
<tr>
<td>History of A1c ≥ 5.7%, impaired fasting glucose, or impaired glucose tolerance (ie, “pre-diabetes”)</td>
<td></td>
</tr>
<tr>
<td>Clinical signs of insulin resistance, such as severe obesity or acanthosis nigricans</td>
<td></td>
</tr>
<tr>
<td>History of cardiovascular disease</td>
<td></td>
</tr>
</tbody>
</table>

The ICD codes for diabetes screening are V77.1 (ICD-9) and Z13.1 (ICD-10). Medicare allows annual screening with a single FBG in those with HTN, obesity (BMI >30), or dyslipidemia. Medicare also allows annual screening in those with two of the following: overweight (BMI 25-30), age >65, history of GDM, history of delivering baby weighing > 9 lbs. In addition, Medicare allows screening twice in a calendar year for those previously found to have “pre-diabetes”.

Diagnostic criteria
The diagnosis of DM is based on assessment of the A1c, FBG, or the 2-hour post OGTT blood glucose level. Because of ease of testing, A1c via blood draw is the preferred method. Point of care A1c testing is generally not recommended for use in establishing the diagnosis of DM due to variability in quality control. The diagnostic “cut-offs” are based on levels associated with increased risks of microvascular complications, such as retinopathy and nephropathy.

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>“Pre-diabetes”</th>
<th>Diabetes Mellitus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Blood Glucose</td>
<td>&lt;100 mg/dl</td>
<td>100 - 125 mg/dl</td>
<td>&gt; 126 mg/dl</td>
</tr>
<tr>
<td>2-hr Post Challenge</td>
<td>&lt;140 mg/dl</td>
<td>140 - 199 mg/dl</td>
<td>&gt; 200 mg/dl</td>
</tr>
<tr>
<td>A1c</td>
<td>&lt;5.7%</td>
<td>5.7 – 6.4%</td>
<td>&gt; 6.5%</td>
</tr>
</tbody>
</table>
The diagnosis of DM is established when two criteria are met (i.e., FBG > 126 mg/dl, 2-hr post challenge BG > 200 mg/dl, or A1c > 6.5%). If FBG and A1c are done simultaneously, and both are consistent with DM, the diagnosis is established. If two tests are performed and only one is consistent with DM, the abnormal test should be confirmed 1-3 months later. If only one test is performed (FBG or A1c) and the results are “marginal”, a confirmatory test should be done 1-3 months later.

Management of “Pre-diabetes”
“Pre-diabetes” (Pre-DM) refers to a condition recognized as abnormal glucose homeostasis, but not to the degree to be considered consistent with diabetes or its associated risks of retinopathy or nephropathy. This entity consists of those with “impaired fasting glucose” (FBG 100 - 125 mg/dl), “impaired glucose tolerance” (2-hr post challenge BG 140 - 199 mg/dl), or an A1c of 5.7 – 6.4%. Individuals with Pre-DM have a marked increased risk of developing overt DM in the future. Studies have suggested that the 5-year risk of developing DM approaches 25% for those with A1c values of 5.5 – 6.0%, and as high as 50% for those in A1c values of 6.0 – 6.5%.

It should be emphasized that lifestyle modification with diet, exercise and weight loss is paramount to improving insulin sensitivity and preventing or delaying the development of DM. Results from the Diabetes Prevention Program (DPP) suggest that such behavioral modifications with resultant weight loss of 7% may decrease the risk of developing overt diabetes by as much as 58% after 3 years.

Various oral agents have been studied as possible therapy to prevent or delay the development of DM, and each studied agent demonstrated some measurable benefit. However, studied agents did not seem to out-perform lifestyle modification. One of the most widely prescribed medications for Pre-DM, metformin, resulted in a 35% risk reduction in the DPP. Metformin was no more effective than placebo in those age > 60 years, but was equally effective as lifestyle modification in women with a history of GDM.

We recommend that all patients with Pre-DM begin moderate daily activity. We also recommend patients be counseled or referred for a diet that limits the caloric intake to a level that promotes weight loss. We also suggest the diet limit carbohydrates to 40% of daily calories, and consist of increased vegetables and fruits. We suggest metformin, if used, be reserved for patients < age 60 who have advancing BG or A1c levels despite the above maneuvers. Even so, the patient should receive ongoing counseling for weight loss.

It appears that the risks for CVD in Pre-DM may equal those in overt DM. The Honolulu Heart Study found the risks for CAD began at any level of FBG that exceeded 90 mg/dl. Further, those with Pre-DM tend to have added risk factors of hyperlipidemia and hypertension (HTN). Therefore, we recommend patients with Pre-DM be treated with an angiotensin converting enzyme inhibitor (ACE-i) or angiotensin receptor blocker (ARB) if there is concomitant HTN. Reasonably, statin therapy may be suitable in attempt to lower the LDL <130 mg/dl, and possibly <100 mg/dl.