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PRE-DIABETES: BORDERLINE NO MORE

OVER THE YEARS, it's been called "impaired glucose tolerance," "borderline diabetes," and "impaired glucose homeostasis." Whatever you call it, pre-diabetes presents us with both a challenge and an opportunity: it's common, it has a high probability of leading to diabetes and it's treatable.

Pre-diabetes is broadly defined as a condition marked by impaired fasting glucose (IFG)—a fasting plasma glucose of 110–125 mg/dl—or impaired glucose tolerance (IGT)—a plasma glucose of 140–199 mg/dl 2 hours after a 75gm glucose load on an oral glucose tolerance test (OGTT).<sup>1</sup> From a practical standpoint, there are some shortcomings to this definition. For instance, there is no threshold for diagnosis based on a random glucose measurement. (When was the last time you ordered an OGTT on someone who wasn't pregnant?) Still, identifying people with pre-diabetes provides them, and us, a chance to forestall a potentially debilitating chronic disease.

Individuals with pre-diabetes, who typically have glucose levels persistently above normal but below the diabetes threshold, are at high risk for developing diabetes in the future. How high is the risk? For someone with IFG or IGT, but not both, the five-year cumulative incidence of diabetes is 20–34%. For someone with both IFG and IGT the

cumulative incidence skyrockets to 38–65%. This compares with a cumulative risk of about 4–5% in normoglycemic adults.<sup>1</sup> Nationwide, 23% of overweight persons 45–74 years of age, almost 12 million people, are thought to have pre-diabetes.<sup>2</sup> As if that's not enough, CDC estimates that, among adults 20 or older, 12.3 million Americans meet the definition for pre-diabetes based on the presence of IFG alone.<sup>3</sup> Add in all those people with IGT and the estimate goes much higher. Even if we limit ourselves to folks who are overweight and older than 45, in Oregon, that translates to about 152,000 adults who likely have pre-diabetes, and could benefit from interventions to prevent them from developing type 2 diabetes.

**DOES HAVING PRE-DIABETES MATTER?**

Pre-diabetes is a serious issue. The high risk of progression to overt diabetes among those with this condition is nothing to take lightly. Even in the absence of diabetes, elevated blood glucose levels can increase a person's risk of heart attack or stroke by 50%, and the risk of cardiovascular death is also higher.<sup>1</sup>

**WHO IS AT RISK?**

In addition to age and weight, there are several other risk factors that might make screening someone for pre-diabetes a good idea. Family history of diabetes (in a parent or sibling), African

American, Native American, Asian American, Latino, or Pacific Islander heritage, history of gestational diabetes, or history of bearing an infant weighing nine pounds or more at birth all can be associated with higher incidence of pre-diabetes. These risks can be taken into account when making decisions about screening for the condition. The table shows the distribution of some of these risk factors among Oregonians without known diabetes.

Recognizing some other risk factors may be a bit more complex. For instance, the triad of hypertension, hyperlipidemia, and abdominal obesity in a person suggests the presence of the so-called "metabolic syndrome," a condition also associated with a fourth metabolic abnormality, insulin resistance.<sup>4</sup>

The American Diabetes Association (ADA) recommends screening for pre-diabetes in individuals ≥45 years of age, particularly in those with a BMI ≥25 kg/m<sup>2</sup>. They further suggest that, "screening should be considered for people who are ≤45 years of age and are overweight if they have another risk factor for diabetes."<sup>1</sup>

**HOW CAN PRE-DIABETES BE DIAGNOSED?**

A fasting plasma glucose or an OGTT is the quickest way to a diagnosis. OGTT is the more sensitive test for diagnosing pre-diabetes or diabetes, while a fasting plasma glucose, as the sole screening test, will miss some patients with IGT or diabetes. Unfortunately, OGTT is also more time consuming and more expensive. Clearly, we need to pay attention to patients with abnormally high plasma glucoses on incidental testing as well; however, we can't "make the call" that a person meets the criteria for IGT based on these values.

**IS THERE A CASE FOR TREATING PRE-DIABETES?**

Happily, several recent intervention trials<sup>6,7</sup> demonstrate that, once individuals with pre-diabetes are identified, develop-

**Frequency of select risk factors for pre-diabetes among Oregonians age 18 and older without diabetes<sup>1</sup>**

Age ≥45 years old <i>and</i> overweight (BMI ≥25 kg/m <sup>2</sup> )	30%
Family history of diabetes	25%
Inactive lifestyle <sup>2</sup>	46%
Told by doctor had high blood pressure	23%
Told by doctor had high cholesterol	32%

<sup>1</sup> Oregon Behavioral Risk Factor Surveillance System (BRFSS) self-report survey, 2002 (prevalence of inactive lifestyle derived from BRFSS 2001).

<sup>2</sup> Did not report attaining in a usual week at least 30 minutes per day of moderate physical activity on at least five or more days of the week.



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ment of type 2 diabetes can be delayed and, better yet, prevented with modest lifestyle changes. Two of these studies followed persons with pre-diabetes for an average of about 3 years and compared rate of progression to frank diabetes in a control group with the rate of progression in a group involved in an exercise and weight reduction regimen. In the Diabetes Prevention Program (DPP),<sup>6</sup> a 5–7% weight reduction plus 30 minutes of modest physical activity five days a week decreased progression to diabetes by 58%. The Finnish Diabetes Prevention Study (DPS)<sup>7</sup> produced similar reductions in progression to diabetes, using similar methods. This means that your patients do not need to become the next supermodel or world-class athlete to decrease their diabetes risk.

It is important to note that these levels of risk reduction were achieved through intensive intervention, including training in diet, exercise, and behavior modification from case managers who met with each participant for at least 16 sessions in the first 24 weeks monthly thereafter. While we recognize that these intensive interventions may not be feasible for you in your office, taking the time to share information on modest lifestyle changes with pre-diabetic patients might motivate those individuals who are ready to make those lifestyle modifications. These modifications can also lead to a decreased risk of cardiovascular disease and other diabetes-related complications.

Several studies have suggested that medications such as metformin also delay diabetes onset and may ultimately have a role in this setting.<sup>6,8</sup> However,

ADA does not recommend routine use of medication to prevent diabetes due to the lower efficacy when compared with exercise and weight loss, the risk of medication-related adverse effects, and the lack of data regarding possible effects on cardiovascular disease risk.<sup>1</sup>

#### WHAT CAN YOU DO?

Once you've identified a patient with pre-diabetes, there are a some issues to consider:

- Monitoring for progression to diabetes. Regular screening with a fasting plasma glucose or OGTT (perhaps every 1–2 years) and periodic follow-up visits for patients with pre-diabetes will allow early detection and intervention if diabetes develops.
- Diabetes prevention. While there aren't formal clinical guidelines for treatment of pre-diabetes, based on findings from the DPP and the DPS, modest weight loss and regular physical activity delayed and in some cases may have prevented progression to diabetes. These appear to be reasonable goals to work toward with patients.
- Patients are not always eager to embark on a major change in eating or exercise habits. Many have heard the suggestions before (possibly even from you), but they may need additional support. Consider referring patients to lifestyle modification classes or services.

Though written materials may not equate to the “full-court press” that participants in DPP had available to them (or were subjected to, depending on how you look at it) there is a new resource available through the Oregon Diabetes Program that may be useful to you and your

patients. It's called “Small Steps, Big Rewards,” and it lays out a strategy for screening and diagnosing patients with pre-diabetes. It also contains helpful materials for patients that walk through, step by step, on how they can make lifestyle changes to decrease their risk of diabetes. For copies of these materials, contact Jamie Klein of the Oregon Diabetes Program at 503/731-4273.

As of this printing, the *Expert Committee on Diagnosis and Classification of Diabetes Mellitus* has recommended lowering the diagnostic level for IFG (and therefore pre-diabetes) to 100mg/dl. This new cut point will increase the sensitivity and specificity of the fasting plasma glucose test and reduce false negatives. For more information see: <http://care.diabetesjournals.org/cgi/reprint/26/11/3160.pdf>

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