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## Opportunities to Reduce Diabetes Risk in Women of Reproductive Age: Assessment and Treatment of Prediabetes within a Large Integrated Delivery System

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#### ABSTRACT

*Background:* Preventing diabetes before pregnancy may be important to improve maternal and infant outcomes. Although the preconception period is a crucial time to focus on chronic disease prevention, little is known about preventive services for reproductive-aged women at risk of developing diabetes.

*Methods:* Using electronic health record data from patients at Kaiser Permanente Northern California, we identified 21,965 nonpregnant women aged 18 to 44 with incident prediabetes (PDM; fasting plasma glucose [FPG] = 100–125 or glycated hemoglobin A1c = 5.7%–6.4%) between 2007 and 2010. We looked for evidence of a "clinical response" to PDM in the 6 months after laboratory testing, defined as retesting of blood glucose levels, referral or attendance to health education, diagnosis of PDM, metformin initiation, or a clinical note of discussion of PDM. Multilevel models were used to examine the relationship between patient characteristics and clinical response, and to assess provider-level variation. *Results:* Fewer than one-half of women had a documented clinical response to the PDM-range laboratory result. Women with higher FPG values and body mass indexes were more likely to have a PDM diagnosis (FPG 120–125 vs. 100–119: OR, 1.96; 95% CI, 1.78–2.17; body mass index, 30–34 kg/m<sup>2</sup> vs. <25 kg/m<sup>2</sup>: OR, 1.30; 95% CI, 1.13–1.48) and have 'PDM' recorded in the notes (FPG 120–125 vs. 100–119: OR, 1.15; 95% CI, 1.06–1.26; body mass index: 30–34 kg/m<sup>2</sup> vs. <25 kg/m<sup>2</sup>: OR, 1.35; 95% CI, 1.44–1.74). Provider-level variation was modest, except for metformin initiation (intraclass correlation coefficient, 0.8; p < .01).

*Conclusions*: Low clinical response to PDM among women of reproductive age suggests there are missed opportunities for diabetes prevention among this vulnerable population.

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Preventing diabetes among women of reproductive age is an important clinical and public health goal that may improve the health of women, and their potential future offspring (Owens, Kieffer, & Chowdhury, 2006). Elevated blood sugar, even in the earliest stages of pregnancy, has well-documented teratogenic effects, and diabetes during pregnancy has been associated with several maternal, infant, and obstetric complications (Allen et al., 2007; Negrato, Mattar, & Gomes, 2012). Poor maternal outcomes

for women with diabetes include worsening of diabetic retinopathy and nephropathy, hypertension, preeclampsia, and preterm birth (American College of Obstetrics and Gynecology, 2005b; American Diabetes Association, 2015; Holmes et al., 2011). For infants, complications include miscarriage and stillbirth, birth defects, and fetal macrosomia (American College of Obstetrics and Gynecology, 2005b; American Diabetes Association, 2015; Jensen et al., 2009; Kitzmiller, Buchanan, Siri, Combs, & Ratner, 1996). Despite the documented risks of diabetes during pregnancy, data suggest that the prevalence of diagnosed diabetes in reproductive aged-women has been increasing (Hayes, Fan, Smith, & Bombard, 2011), and that more women are entering pregnancy with preexisting diabetes (Lawrence, Contreras, Chen, & Sacks, 2008). In addition, recent estimates suggest the prevalence of undiagnosed diabetes in

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nonpregnant women of reproductive age may be substantial (Razzaghi, Marcinkevage, & Peterson, 2015).

Considering the risks of diabetes to both mothers and babies, preventing type 2 diabetes before pregnancy may be an important strategy for improving maternal and neonatal outcomes (Owens et al., 2006). The prepregnancy, or preconception, period is an ideal opportunity during which modifiable risk factors that contribute to diabetes and other chronic conditions can be identified and reduced (American College of Obstetrics and Gynecology, 2005a; American Diabetes Association, 2004). In an effort to improve women's health overall as well as pregnancy outcomes, preconception care is a process of care that involves health care providers framing his or her thinking, counseling, and decision making in light of the reproductive plans and sexual and contraceptive practices of the patient (Centers for Disease Control and Prevention, 2014a; Johnson et al., 2006). Because close to one-half of all pregnancies in the United States are unintended (Finer & Zolna, 2016), it is important that diabetes prevention efforts be considered part of routine care for women in their childbearing years (Callegari, Ma, & Schwarz, 2015). Primary care providers are uniquely positioned to care for reproductive-aged women before, between, and after pregnancies, making them appropriate to offer diabetes preventive services (Callegari et al., 2015). However, despite the important role that primary care providers can play in addressing and reducing diabetes risk in reproductive-aged women, little is known about how this varies across providers.

Reproductive-aged women with prediabetes (PDM) are particularly vulnerable to developing diabetes, and may be an important target for preventive care. People with PDM have an increased risk of developing type 2 diabetes, and without intervention, up to 30% will develop the condition within 5 years (Knowler et al., 2002; Tuomilehto et al., 2001). The Diabetes Prevention Program has shown that type 2 diabetes can be prevented or delayed via lifestyle modification and metformin use in people with PDM (Knowler et al., 2002; Tuomilehto et al., 2001). Current American Diabetes Association guidelines recommend that patients with PDM be referred to an intensive behavioral lifestyle program modeled on the Diabetes Prevention Program, and that metformin therapy should be considered for patients with additional risk factors (American Diabetes Association, 2017). Research suggests the number of women of reproductive age with PDM is substantial. One study examining women ages 18 to 44 presenting at a family planning clinic found that close to a third had PDM, mirroring the prevalence for the adult population in the United States (Centers for Disease Control and Prevention, 2014b; Robbins et al., 2013). Although the available evidence suggests that screening and treatment for PDM in the general population is low (Carve & Hayward, 2010; Mainous, Tanner, & Baker, 2016; Schmittdiel et al., 2014), little is known about PDM clinical practice for women of reproductive age. The factors associated with the follow-up, management, and treatment of PDM in this important population vulnerable to poor outcomes are largely unknown. Available evidence suggests that patient characteristics, such as demographics, may be associated with PDM management and treatment in the general population, but studies have focused on different treatment outcomes and none have specifically examined women of reproductive age (Cloney, Galer-Unti, & Barkley, 2011; Hooks-Anderson, Crannage, Salas, & Scherrer, 2015; Moin et al., 2015).

Using a cohort of reproductive-aged female patients with PDM in a large integrated health delivery system with a robust information technology infrastructure, the primary objectives of this study were to 1) examine the association between patientlevel characteristics and PDM identification and treatment and 2) assess primary care provider-level variation in PDM identification and treatment.

#### **Materials and Methods**

#### Study Design and Population

This retrospective cohort study analyzed data from Kaiser Permanente Northern California, a large integrated health delivery system serving approximately 650,000 women of reproductive age annually. Data in this study were drawn primarily from the patient electronic health record (EHR), which combines diagnosis, use, pharmacy, and laboratory records from across the care system. Our study population consisted of nonpregnant female patients, aged 18 to 44 with laboratory-defined PDM (fasting plasma glucose [FPG] 100-125 mg/dL or glycated hemoglobin A1c [HbA1c] 5.7%-6.4%) between January 1, 2007, and December 31, 2010. For the small number of patients with both an elevated FPG and HbA1c, the FPG value was used to classify PDM status. To capture women with incident PDM, we excluded patients who tested in this range in the previous 2 years, those with a preexisting diagnosis of diabetes (International Classification of Diseases, 9th edition [ICD-9] code 250.\*) or PDM (ICD-9 code 790.2\*), and those on DM medication in the 2 years before the index laboratory date (e.g., first elevated FPG or HbA1c value) or on insulin 3 months after the index laboratory result. All patients in the cohort had at least 2 years of continuous health plan enrollment before the index laboratory test and for 6 months after the index date. Finally, we excluded the small number of patients who did not have a primary care provider documented in the health record (n = 48). In this specific health care delivery system, primary care providers typically have a specialty in internal or family medicine, and female patients usually have both a primary care and women's health provider.

#### Measures

The identification and treatment of incident PDM was defined as a "clinical response" to the PDM-range FPG or HbA1c value within 6 months of the initial laboratory test. The 6-month time frame was chosen as a reasonable window in which outcomes could be conceptualized as a response to the index laboratory result, rather than unrelated care delivery occurring over time. Several clinical response outcomes were examined: 1) retesting of blood glucose levels ("follow-up lab"), 2) a referral to or attendance of health education or nutrition services, 3) a recorded diagnosis of PDM/hyperglycemia (ICD-9 code 790.2X), 4) a metformin prescription fill (metformin initiation), or 5) a clinical note regarding discussion of PDM. For the clinical note, we used text-string searches within the EHR clinical progress notes to look for documentation that the clinician discussed PDM or its management with the patient. Key search terms included exercise, physical activity, diet, nutrition, weight loss, lifestyle modification/change, healthy lifestyles, diabetes, and prediabetes. These clinical response outcomes were selected to capture a range of possible clinical actions that could occur following a laboratory result indicating PDM, and reflect American Diabetes Association guidance for PDM treatment as well as other relevant outcomes that could be captured by the EHR (American Diabetes Association, 2017; Schmittdiel et al., 2014).

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