

# Counterpoint: Selective Screening for Gestational Diabetes Mellitus

**G**estational diabetes mellitus (GDM), defined as carbohydrate intolerance first diagnosed during pregnancy (1), is a common medical complication of pregnancy, affecting 1.1–14.3% of pregnant women depending on the ethnic and clinical characteristics of the population and the diagnostic test employed (2). Ever since O'Sullivan and Mahan (3) published their criteria for diagnosis of GDM using a 100-g oral glucose tolerance test (GTT), clinicians worldwide have been struggling to determine whether screening for GDM should be offered routinely in pregnancy and, if so, the optimal method of screening. There have been no adequately designed randomized controlled trials to answer the question of whether screening for GDM is both beneficial and cost effective, leading to a wide variance in screening practices worldwide. The Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS), a multicenter randomized controlled trial of GDM treatment versus routine prenatal care, found a reduction in a composite of severe perinatal outcomes in the treatment group compared with a control group receiving routine prenatal care (4). Although it was not a trial of screening, its results have convinced many practitioners to adopt some type of screening for GDM because logically, in order to treat GDM (an asymptomatic entity), one must first screen for it. Recently, the U.S. Preventive Services Task Force (USPSTF), in an update to its policy statement on screening for GDM, recognized that treatment of GDM after 24 weeks of gestation improves some maternal and neonatal outcomes but, conversely, also stated that there is still insufficient evidence to support screening of all pregnant women either before or after 24 weeks of gestation (5). Despite this, most clinicians use some method of screening for GDM.

Ideally, the chosen screening protocol should identify subjects at maximal risk of adverse pregnancy outcomes who would most benefit from intensified management and surveillance, while freeing the rest from the burden of excessive interventions. Unfortunately, the policy of universal or near-universal screening that

is recommended by numerous professional medical organizations (1,6–8) will lead to the blanket labeling of a large group of women as having GDM, without differentiating between those at high and those at low risk of pregnancy complications. It has very clearly been shown that glucose intolerance in pregnancy is not a threshold phenomenon but, rather, is linked to several adverse pregnancy outcomes along a continuum of measured glucose values in both fasting and postprandial (or glucose challenge) states (9–11). Not all of these outcomes are of equal clinical importance; to justify widespread screening, one would prefer to show a reduction in serious outcomes such as perinatal death and permanent birth injury. These are rare outcomes and, thus, are difficult to study. The best prospective data on the effect of increasing levels of glucose intolerance in pregnancy come from the Toronto Tri-Hospital Gestational Diabetes Project (9) and have been confirmed by the recently published results of the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study. The data from the Toronto Tri-Hospital Gestational Diabetes Project showed a graded increase in the risk of macrosomia and preeclampsia, the need for phototherapy, and maternal and neonatal length of stay. The HAPO study largely confirmed these data and Pederson's hypothesis (12), showing a positive association between plasma glucose values after a 75-g oral GTT, birth weight above the 90th percentile, and cord blood C-peptide levels (11). Neither of these studies was able to identify clear outcome-based thresholds that could lead to new clinically relevant diagnostic criteria for GDM.

This brings us to the current status in 2009 where we have evidence that treatment of GDM reduces some perinatal outcomes without significantly increasing the cesarean section rate but still lack a gold standard diagnostic or screening test. In North America, the most common method of screening is a two-stage test comprised of a 50-g oral glucose challenge test (GCT) at 24–28 weeks of gestation followed by either a 75-g or a 100-g oral GTT for women who screen positive

on the GCT (13). Using a cutoff of 7.8 mmol/l (140 mg/dl) for the GCT, ~14–18% will test positive and need to proceed to the diagnostic test. The reported sensitivity and specificity of this test strategy are ~80 and 90%, respectively, whereas the positive and negative predictive values vary according to the prevalence of GDM in the population tested (14). Thus, with this strategy some 20% of women with GDM will remain undiagnosed even with universal screening. In many parts of Europe, a risk factor–based approach to GDM screening is still the most common approach (15–17). Common risk factors can be found in Table 1. Overall, the performance of risk factor–based screening has been poor, with reported sensitivity and specificity of 63 and 56%, respectively (18). This poor performance is in part due to the inability to apply historic obstetric risk factors to women during their first pregnancy; thus, primiparas who develop GDM will likely remain undiagnosed unless they develop macrosomia, glycosuria, or polyhydramnios during the index pregnancy. The pragmatic utility of applying risk factor–based screening will largely depend on the frequency of these risk factors in the screened population. For example, if the screened population is mostly slim young Caucasians, then many women will be spared biochemical screening. On the other hand, in heavier, older, multiethnic obstetric populations, applying risk factor–based screening will likely lead to the majority of women undergoing biochemical screening. Studies from North America have shown that using the American Diabetes Association criteria for selective screening based on risk factors will lead to some 90% of the obstetric population still undergoing some form of biochemical screening (19). This leaves us with the question of whether it is possible to apply a form of risk factor–based screening that will spare the lower-risk population unnecessary tests while maintaining the performance of a universal screening protocol. The answer is available from a secondary analysis of data from the Toronto Tri-Hospital Gestational Diabetes Project (20). The subject population in-

**Table 1—Risk factors for GDM**

Current pregnancy
Age (different thresholds)
BMI (different thresholds)
Race/ethnicity
Polyhydramnios
Suspected macrosomia
Historical
GDM in previous pregnancy
Macrosomia in previous pregnancy
Unexplained stillbirth
Medical/familial
Type 2 diabetes in a first-degree relative
Polycystic ovary syndrome
Metabolic syndrome

Adapted from Berger et al., *J Obstet Gynaecol Can* 2002;24:894–912.

cluded a derivation group and a validation group involving 3,131 women who underwent a 50-g GCT at 26 weeks followed by a 100-g oral GTT at 28 weeks of gestation regardless of the results of the screening test. Based on the derivation group data, using multivariate analysis, a simple clinical risk scoring system was created using the clinical characteristics of maternal age, BMI, and race (Table 2). The scoring system was then applied to the validation group showing that the incidence of GDM increased with increasing clinical score values ranging from 0.9 in women who scored  $\leq 1$  to 18.7% in women who scored  $\geq 6$ . A screening strategy was then developed where women with clinical scores  $\leq 1$  were not screened; women with scores 2–3 were screened, and the current cutoff of 7.8 mmol/l (140 mg/dl) was retained, whereas for women with scores  $\geq 4$ , two thresholds were ex-

**Table 2—Scoring system for GDM screening based on clinical risk factors**

Risk factors	Score
Age (years)	
$\leq 30$	0
31–34	1
$\geq 35$	2
BMI (kg/m <sup>2</sup> )	
$\leq 22.0$	0
22.1–25	2
$\geq 25.1$	3
Race	
Caucasian	0
Black	0
Asian	5
Other	2

Adapted from Naylor et al., *N Engl J Med* 1997;337:1591–1596.

amined: 128 and 130 mg/dl. This strategy was then applied to the validation group with the results showing that although it achieved sensitivity and specificity similar to those associated with universal screening, selective screening allowed 34.6% of women to avoid screening altogether and maintained a detection rate of  $>80\%$ . If we apply this simple strategy of asking a woman her age and ethnicity and calculating her BMI to the most recent North American birth statistics,  $\sim 1.4$  million women in North America could avoid routine screening for GDM (21). Although some cases of GDM will be missed in the lower-risk category, more cases will be diagnosed in the higher-risk category as a result of the lower thresholds applied to this population. The economic analysis of this strategy has not been evaluated yet; however, assuming that the impact of not diagnosing GDM in the low-risk population is minimal in terms of health care USD, it is likely to result in savings of close to 4 billion USD per year (22,23).

The main limitation of this method of selective screening is that it is more complex than universal screening and its implementation adds an additional burden to the health care provider. But what is the actual burden? The data regarding age, ethnicity, and BMI are collected routinely at the first prenatal visit. All the clinician needs to do is to determine at that point whether the patient is in the low-risk category and thus can avoid screening. For the remainder of patients who undergo a GCT, the linkage between this clinical dataset and the laboratory can easily be incorporated into the laboratory reporting system, similar to what currently occurs with prenatal screening for trisomy 21, allowing for the accurate application of different glucose threshold values based on the individual clinical scores.

In summary, there is still a wide gap between screening practices in European countries and North America. Regardless of the screening method employed, the decision whether to provide selective screening or universal screening is largely based on personal preference, expert opinion, and clinical guidelines given that there is limited supporting evidence from well-designed randomized clinical trials supporting one method over the other. Until better evidence is available, those who employ universal screening need to ask themselves whether it is justified to subject all pregnant women to GDM screening; although universal screening will arguably identify more cases of GDM

in the low-risk population, these cases might have less clinical significance. By applying selective screening strategies, one can increase the detection of GDM in the higher-risk population (increased maternal age and BMI), especially if lower threshold criteria are applied to the GCT in this select population. By doing this, we will be able to focus our resources on identifying cases where making the diagnosis of GDM will have an effect on significant perinatal outcomes, while perhaps avoiding increased maternal anxiety (24) and higher cesarean section rates (25) in the low-risk population.

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