



GDM

Literature Review

GESTATIONAL DIABETES MELLITUS: A review for midwives

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BACKGROUND

Historically, there has been widespread controversy over the method and benefit of screening and diagnosing gestational diabetes mellitus (GDM). This has led to a lack of international uniformity in the detection and diagnosis of GDM, which has resulted in major variation in clinical practice, research protocols and study outcomes. (1) In 2006, the Association of Ontario Midwives (AOM) endorsed the recommendations of the 2002 Society of Obstetricians and Gynaecologists of Canada (SOGC) clinical practice guideline (CPG) on *Screening for Gestational Diabetes Mellitus* (No. 121) and created AOM CPG No. 7 *Screening for Gestational Diabetes*. (2,3) The 2006 AOM endorsement of the 2002 SOGC GDM CPG also lists a series of considerations for midwifery practice.

IMPLEMENTATION TIP

Unlike a clinical practice guideline, this document does not offer recommendations for care. Instead, it is meant as a reference to help midwives interpret evidence and to incorporate clinical research into informed choice discussions with clients, as appropriate. This document considers available research from a midwifery perspective, interpreting the evidence to support pregnancy, birth, and the postpartum period as a normal physiologic process.

The AOM is committed, through our statement on Gender Inclusion and Human Rights, to reflect and include trans, genderqueer and intersex communities in all aspects of our work. In this document, there are references to sources that use gendered language to refer to populations of pregnant and birthing people. In order to accurately represent these sources, we may have maintained gendered language. We support research and knowledge translation that engages and reflects the entire childbearing population.

Two key guidelines were subsequently published:

- The 2013 Canadian Diabetes Association (CDA) guidelines include a chapter on diabetes in pregnancy developed in collaboration with the SOGC. (4)
- In 2016, the SOGC published an updated CPG *Diabetes in Pregnancy* (No. 334, replaces #121). (5) The screening recommendations in this guideline are consistent with the 2013 CDA CPG and include further recommendations about the management of pregnancies complicated by GDM. (5)

Abbreviations

ACHOIS	Australian Carbohydrate Intolerance Study in Pregnant Women Trial
ACOG	American Congress of Obstetricians and Gynecologists
ADA	American Diabetes Association
AOM	Association of Ontario Midwives
BMI	body mass index
CDA	Canadian Diabetes Association
CMO	College of Midwives of Ontario
CPG	clinical practice guideline
CS	caesarean section
CTCS	Consultation and Transfer of Care Standard
FPG	fasting plasma glucose
GCT	glucose challenge test
GDM	gestational diabetes mellitus
HAPO	Hyperglycemia and Pregnancy Outcomes study
HbA1c	glycated hemoglobin
IADPSG	International Association of Diabetes and Pregnancy Study Groups
IFG	impaired fasting glucose
IGT	impaired glucose tolerance
IMDCTC	Indications for Mandatory Discussion, Consultation and Transfer of Care document
LGA	large for gestational age
MFMU	Maternal Fetal Medicine Unit trial
NDDG	National Diabetes Data Group
NICE	National Institute for Health and Care Excellence
OGTT	oral glucose tolerance test
RCT	randomized control trial
SGA	small for gestational age
SOGC	Society of Obstetricians and Gynaecologists of Canada
WHO	World Health Organization
1hPG	1-hour plasma glucose test
2hPG	2-hour plasma glucose test

The recommendations of the 2013 CDA CPG and 2016 SOGC CPG differ significantly from those of the 2002 SOGC CPG. **The purpose of this document is to provide an overview of key research and guidance published since the AOM's 2006 endorsement of the 2002 SOGC GDM CPG. This document is not meant to provide recommendations for practice.** The SOGC's 2016 *Diabetes in Pregnancy* CPG replaces the 2002 *Screening for Gestational Diabetes* CPG; therefore, the 2006 AOM endorsement of the 2002 SOGC CPG recommendations no longer applies. GDM is on the list of CPGs to be developed by the AOM in the future. This synthesis of evidence is meant to help midwives bridge the knowledge gap in GDM research published since 2006.

Key questions

This document outlines the changes in the 2013 CDA and 2016 SOGC guidelines compared to the 2002 SOGC guideline/2006 AOM endorsement, and provides an overview of the evidence that informs these changes. Specifically, this document will address the following key questions:

1. What differences exist in terms of screening, diagnosis and management?
2. What research has guided these changes?
3. What are the implications of these changes?

Guidelines addressed in this document

AOM Clinical Practice Guideline No. 7 – Screening for Gestational Diabetes (2006) (3); *rescinded 2016*

SOGC Clinical Practice Guideline No. 121 – Screening for Gestational Diabetes Mellitus (2002) (2)

<http://sogc.org/wp-content/uploads/2013/01/121E-CPG-November2002.pdf>

CDA Clinical Practice Guideline – Diabetes and Pregnancy (2013) (4)

<http://guidelines.diabetes.ca/Browse/Chapter36>

SOGC Clinical Practice Guideline No. 334 – Diabetes in Pregnancy (2016) (5)

[http://www.jogc.com/article/S1701-2163\(16\)39087-9/pdf](http://www.jogc.com/article/S1701-2163(16)39087-9/pdf)

A note on strength of recommendations

The SOGC, AOM, and CDA CPGs assigned grades to each recommendation in order to reflect the strength of the evidence used to inform the statements. The criteria

for assigning levels of evidence and corresponding grades differ across publications. In general, the recommendations in each publication are based on research that lacks the methodological criteria required for a strong grade. All of the 2002 SOGC and AOM recommendations are based on expert opinion due to a paucity of high-quality evidence. (2,3) Many of the CDA and 2016 SOGC recommendations are also drawn from studies with important limitations or are guided by expert consensus; however, a number of recommendations are based on newer trials and observational studies. (4,5) While these studies represent an improvement in the design of available research and strength of evidence, a number of methodological limitations continue to exist in the research used to inform the CDA's and SOGC's most recent recommendations. For more information on interpreting the assigned grade of a recommendation, see the Methods chapter on the CDA website (<http://guidelines.diabetes.ca/Browse/Chapter2>) and the introduction of the SOGC CPGs. (2,5,6)

Definitions

Gestational diabetes mellitus is used to describe glucose intolerance with first onset or recognition in

pregnancy that subsequently resolves postpartum. GDM is still used to refer to diabetes that is diagnosed in pregnancy and/or falls within certain glucose thresholds.

Pregestational diabetes refers to people with type 1 or type 2 diabetes diagnosed before pregnancy (i.e., pre-existing diabetes).

Prediabetes is a term used outside of pregnancy to refer to impaired fasting glucose (IFG), impaired glucose tolerance (IGT) or a glycated hemoglobin (HbA1c) of 6.0% to 6.4% (Table 1). (7) While not all individuals with prediabetes will progress to diabetes, each of these parameters appears to place individuals at higher risk. IFG, IGT and HbA1c are not used to diagnose gestational diabetes in the CDA and SOGC CPGs; however, the term “prediabetes” is included as a risk factor for GDM in the CDA CPG and is referred to in relation to the provision of postpartum care in the CDA and SOGC CPGs, and an understanding of its definition may be helpful. For more about this term see Chapter 3 of the CDA guideline: Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome (<http://guidelines.diabetes.ca/Browse/Chapter3>). (7)

TABLE 1: DIAGNOSIS OF PREDIABETES (7)

Test	Result	Prediabetes category
Fasting plasma glucose	6.1-6.9 mmol/L	Impaired fasting glucose
2 hr plasma glucose following a 75 g oral glucose tolerance test	7.8-11.0 mmol/L	Impaired glucose tolerance
Hemoglobin A1c / glycated hemoglobin	6.0-6.4%	Prediabetes

A snapshot from BORN Ontario

The BORN Ontario database contains a limited amount of information pertaining to incidence and outcomes of diabetes among midwifery clients. GDM incidence among midwifery clients was approximately 2.5% from April 1-March 31, 2012-13 and 2013-14. Births

occurred without complication (see Table 2) for 93% of infants born to clients with GDM; the same rate of complication-free birth was observed in infants born to non-diabetic clients ($p > .05$). Midwifery clients with GDM were no more likely to have births affected by shoulder dystocia ($p > .05$).

TABLE 2: PREVALENCE AND OUTCOMES OF DIABETES AMONG MIDWIFERY CLIENTS FROM THE BORN DATABASE 2012-2014

Prevalence of diabetes		
Ontario midwifery clients, 2012-2014 (37,600 births)		%
No diabetes	35,153	93.49
GDM	937	2.49
Type I diabetes	17	0.05
Type II diabetes	27	0.07
Diabetes type unknown	8	0.02
Information on diabetes status missing	1,458	3.88
Incidence of shoulder dystocia		
Ontario midwifery clients, 2012-2014 (37,600 births)		%
All births	822 / 37,600	2.19
No diabetes	764 / 35,153	2.17
GDM	23 / 937	2.45
Type I diabetes	0 / 17	0
Type II diabetes	0 / 27	0
Type unknown	0 / 8	0
Missing data on diabetes status	35 / 1,458	2.40
Births without complications*		
Ontario midwifery clients, 2012-2014 (37,125 infants)		%
All infants	34,584 / 37,125	93.16
Infants born to clients without diabetes	32,401 / 34,759	93.22
Infants born to clients with GDM	791 / 848	93.28
Type I diabetes	12 / 12	100.00
Type II diabetes	21 / 35	60.00
Infants born to clients with diabetes status missing	1,354 / 1,471	92.05

*Complications include (but are not limited to) birth injury, brachial plexus injury, caput succedaneum, cephalohematoma, clavicular fracture, facial nerve injury, hyperbilirubinemia, hypoglycemia.

Source: BORN Ontario database. Data based on midwifery billable courses of care, April 1-March 31, 2012-13 and 2013-14.

GDM and adverse outcomes

Glucose testing during pregnancy has been widely adopted based on the perceived association of maternal hyperglycemia with a number of poor maternal and fetal outcomes. (8) It has been well established that people with type 1 or type 2 diabetes prior to pregnancy have increased rates of complications compared to the general population. (5,9) These complications can include increased rates of perinatal mortality, congenital malformation, hypertension, preterm delivery, large-for-gestational age (LGA) infants, caesarean section (CS) and neonatal morbidities. (4,5,9) Adverse outcomes related to GDM are associated with hyperglycemia and the co-existing maternal environment (5); well-controlled maternal glucose levels appear to decrease the association with adverse outcomes. The risk of adverse perinatal outcomes associated with GDM remains controversial and the benefits of treatment remain unclear. (10)

Uncertainty about the risk of adverse outcomes associated with GDM has been due to a number of factors:

1. **Confounding factors: obesity, increasing maternal age and other medical complications.**

The extent to which adverse outcomes can be attributed to confounding factors is unclear, and associations between a number of GDM-related outcomes and these confounders are well established. (11)

2. **Labeling effect**

Health-care providers may be more inclined to intervene when GDM has been diagnosed, increasing the likelihood of interventions like CS and induction of labour, which are both outcomes commonly associated with GDM. (6)

3. **Need for large sample sizes**

Many of the adverse outcomes associated with GDM are rare; therefore, large sample sizes are needed to detect significant outcomes.

4. **Lack of study uniformity**

Methodological differences in studies measuring the same outcome are common, especially with regard to thresholds used to identify women with GDM. The

lack of uniformity in diagnostic thresholds has led to a body of evidence that is difficult to synthesize.

5. **Correct identification of GDM vs. pre-existing type 2 diabetes**

With increasing rates of pregnant people presenting with undiagnosed type 2 diabetes, disentangling outcomes of those whose diabetes likely predated pregnancy from diabetes that began in pregnancy is a methodological and diagnostic challenge. (4)

SCREENING FOR GDM

What are the changes in the 2013 CDA and 2016 SOGC guidelines?

The 2013 CDA and 2016 SOGC CPGs recommend universal blood glucose screening for all pregnant people and do not include selective laboratory screening or non-screening as recommended options. (4) This recommendation diverges from the 2002 SOGC CPG, which stated that universal or selective laboratory screening could be performed. (2,3)

The 2013 CDA and 2016 SOGC guidelines specify two options for screening. The CDA's "preferred approach" to screening is consistent with the 2002 SOGC and 2006 AOM CPGs: a 50 g glucose challenge test (GCT) at 24 to 28 weeks followed by a 75 g oral glucose tolerance test (OGTT) if plasma glucose at one hour is ≥ 7.8 mmol/L. This guideline also suggests an "alternative approach", which is to forgo the 50 g OGCT and to proceed directly to the 75 g OGTT. (4,5)

These guidelines have also increased the 50 g GCT value considered diagnostic of GDM without further testing. Specifically, if the one-hour post-glucose measurement on a 50 g GCT is ≥ 11.1 mmol/L, they suggest that a diagnosis of GDM be made without a subsequent 75 g OGTT. (4,5)

The following chart compares the recommendations related to screening for GDM (see Table 3).

TABLE 3: CHANGES IN GUIDELINE RECOMMENDATIONS: GDM SCREENING

2002 SOGC/2006 AOM CPG (2,3)	2013 CDA CPG (4)	2016 SOGC CPG (5)
Who to screen		
<p>Informed choice principles and research evidence suggest that it is reasonable for midwives to recommend either the approach of selective screening or non-screening.</p> <p>Selective screening: routine screening at 24 to 28 weeks of women who do not fulfill the following low-risk criteria:</p> <ul style="list-style-type: none"> • Maternal age < 25 • Caucasian or member of other ethnic group with low prevalence of diabetes • Pregnant body mass index of ≤ 27 • No previous history of GDM or glucose intolerance • No family history of diabetes in first-degree relative • No history of GDM-associated adverse pregnancy outcomes 	<p>All pregnant women should be screened for GDM at 24 to 28 weeks of gestation.</p> <p>If there is a high risk of GDM based on multiple clinical factors, screening should be offered at any stage of pregnancy. If the initial screen is performed before 24 weeks and is negative, rescreen between 24 and 28 weeks.</p> <p>Risk factors include:</p> <ul style="list-style-type: none"> • Previous diagnosis of GDM • Prediabetes (see definition in key terms) • Member of a high-risk population (Aboriginal, Hispanic, South Asian, Asian, African) • Age ≥ 35 years • BMI ≥ 30 kg/m² • Polycystic ovarian syndrome, acanthosis nigricans • Corticosteroid use • History of macrosomic infant • Current fetal macrosomia or polyhydramnios 	<p>All pregnant women should be <i>offered</i> screening between 24 to 28 weeks gestation.</p> <p>If there is a high risk of GDM based on multiple risk factors, screening or testing should be offered during the first half of pregnancy and repeated at 24 to 28 weeks gestation if initially normal. If screening was missed or there is a clinical suspicion of later onset GDM, a screening or diagnostic test should be performed.</p> <p>Risk factors include:</p> <ul style="list-style-type: none"> • Age > 35 years • Pre-pregnancy BMI > 30 kg/m² • Ethnicity (Aboriginal, African, Asian, Hispanic, South Asian) • Family history of diabetes • Polycystic ovarian syndrome, acanthosis nigricans • Corticosteroid use • Previous diagnosis of GDM • Previous macrosomic infant
Screening test and cut off values		
<p>50 g GCT administered in a non-fasting state with glucose measured at one hr:</p> <ul style="list-style-type: none"> • 1hPG ≥ 7.8 mmol/L: proceed to 75 g OGTT • 1hPG ≥ 10.3 mmol/L: diagnoses GDM without 75 g OGTT 	<p>Preferred approach: Screening and diagnostic two-step approach above 50 g GCT line. 50 g GCT administered in non-fasting state with glucose measured at one hr:</p> <ul style="list-style-type: none"> • 1hrPG ≥ 7.8 mmol/L: proceed to 75 g OGTT • 1hrPG ≥ 11.1 mmol/L: diagnoses GDM without 75 g OGTT <p>Alternate approach: "one-step" Proceed directly to 75 g OGTT</p>	<p>Endorsed approach: The "preferred screening and diagnostic two-step" approach for GDM of the CDA.</p> <p>Acceptable approach: The "alternative one-step" approach of the CDA.</p> <p>It is recommended that each centre align with one of the strategies and implement protocols to ensure consistent and uniform reporting of test results.</p>
Observed incidence of GDM with screening approach	Estimated incidence of GDM with screening approach*	Estimated incidence of GDM with screening approach*
5.6%	Preferred two-step approach 8.8%. Alternative one-step approach: 16.1%	Endorsed two-step approach: 8.8%. Acceptable one-step approach: 16.1%

*Based on estimates made by applying each approach's thresholds to the Hyperglycemia and Pregnancy Outcomes study (HAPO) cohort as a whole. (5) Please see the research on diagnosis section below for further details.

The SOGC and the CDA also recommend offering early screening to people with multiple clinical risk factors “to facilitate the diagnosis of unrecognized type 2 diabetes that will benefit from earlier interventions to ensure glycemic control.” (5) The CDA classifies this recommendation as based on consensus opinion, (4) whereas the SOGC classifies their similar recommendation as being based on evidence from well-designed cohort studies. (5)

While many midwifery, obstetric and diabetes organizations (e.g., NICE, American Congress of Obstetricians and Gynecologists, Australian College of Midwives) have endorsed a screening strategy for people with risk factors, guidelines vary in terms of whom is designated “high risk” for gestational diabetes and what characteristics warrant early screening. (12–14)

The National Institute for Health and Care Excellence (NICE) recommends offering early self-monitoring of blood glucose or screening at booking (using a 75 g OGTT) to those who have had GDM in a previous pregnancy. (15) NICE suggests offering 75 g OGTT at 24 to 28 weeks’ gestation to people with other risk factors for GDM, including:

- BMI > 30 kg/m²;
- Previous infant > 4500 g;
- Family history of diabetes; or
- Ethnic background with a high prevalence of diabetes. (15)

The American Congress of Obstetricians and Gynecologists (ACOG) identifies previous GDM, known impaired glucose metabolism, and BMI > 30 kg/m² as criteria for early screening. ACOG recommends screening all pregnant people between 24 to 28 weeks’ gestation using medical history, clinical risk factors or laboratory tests. (13)

A consensus panel convened by the International Association of Diabetes and Pregnancy Study Groups (IADPSG) suggests measuring fasting plasma glucose (FPG), HbA1c or random plasma glucose at the initial prenatal visit (or < 24 weeks depending on when client comes into care) on all or only high-risk pregnant people to detect overt diabetes that existed prior to pregnancy. Noting the absence of evidence to suggest clinical benefits or cost-effectiveness of early screening, the IADPSG panel recommended that the decision whether to perform universal early testing vs. limiting early testing to people

classified as high risk (according to locally-defined criteria) should depend on local circumstances. The IADPSG panel recommends universal early testing in populations with a high prevalence of type 2 diabetes. (1)

Research on screening

Significant uncertainty and disagreement persists among professional groups and individual clinicians regarding whether to recommend universal or selective screening, and how selective screening should occur. (14,16,17) The 2014 Cochrane review on screening and management of GDM identified insufficient evidence to evaluate the effectiveness of screening (and subsequently treating) GDM. (18)

Both CDA and SOGC guidelines acknowledge that GDM screening does not meet the criteria typically used to justify mass screening programs, including availability of a reliable test that detects the condition at an early stage, agreed-upon diagnostic criteria, and availability of an acceptable and effective treatment. (19) Nonetheless, the CDA offers justification for recommending universal screening for all pregnant people using three main arguments:

- Risk factor-based screening misses GDM cases in those who do not have risk factors.
- Due to current demographic and health trends, many in the North American childbearing population would not meet the low-risk criteria and would be screened anyway. According to this argument, selective screening is unnecessarily complicated.
- Treating GDM may reduce incidence of preeclampsia, shoulder dystocia, LGA and macrosomia (birth weight > 4000 g), according to recent research (discussed below in the management section). (20–23)

The proportion of people with GDM who may be missed with selective screening is dependent on the criteria used to identify candidates for screening and the prevalence of GDM in a given population. Two retrospective studies conducted in the U.S. in the 1990s found that risk factor-based approaches would have subjected 90% of the study populations to screening and would have missed 3% to 4% of GDM diagnoses. (24,25) The Atlantic Diabetes in Pregnancy study applied NICE, American

Diabetes Association and 2010 Irish guidelines for selective screening to 5,500 participants in the Republic of Ireland who were universally screened between 2007 and 2009. (26) Each of these guidelines utilized different criteria for screening. The authors found that 5% to 20% of those with GDM had no risk factors and would not have been selected for screening and between screening and subsequently diagnosed depending on the guideline used. Approximately 50% to 75% of people included in the study had at least one risk factor (according to the different criteria used) that would have caused them to be selected for screening. (26)

50 g GCT

The 2013 CDA and 2016 SOGC guidelines have increased the threshold for diagnosis of gestational diabetes using the 50 g GCT from ≥ 10.3 mmol/L to ≥ 11.1 mmol/L. (4,5) The GCT diagnostic threshold is intended to minimize delays in treatment for those with markedly elevated glucose levels and to avoid subjecting them to the inconvenience of additional testing. However, there is currently no high-quality evidence supporting a specific value at which the 50 g GCT can be used for diagnostic purposes. (4,27) Ninety-five percent of participants with 50 g GCT values > 10.1 mmol/L went on to be diagnosed with GDM in Carpenter and Coustan's original work in the 1980s; studies since then have produced more equivocal findings. (28,29) In a retrospective cohort study of 14,771 pregnancies screened for GDM between 1988 and 2001, GDM was diagnosed by OGTT in 100% of pregnancies associated with 50 g GCT values ≥ 12.8 mmol/L and 84% of pregnancies associated with 50 g GCT ≥ 11.1 mmol/L. (29)

IMPLICATIONS

If the CDA and SOGC recommendations for universal screening are widely implemented, the proportion of pregnant people who undergo screening and testing will increase. No criteria are provided to help guide selective screening, as a list of what would identify an individual as low-risk has been removed from the guidelines. It is uncertain how an increase in screening will affect pregnancy outcomes, clients' psychological well-being, clinician workload or costs to the health-care system.

DIAGNOSIS OF GDM

What are the changes in the 2013 CDA CPG and 2016 SOGC CPGs?

The recommendations in the 2013 CDA and 2016 SOGC guidelines pertaining to diagnosis of GDM (see Figure 1 in Appendix) differ from the previous 2002 SOGC CPG (see Figure 2 in Appendix) in four key ways:

1. Thresholds for diagnosis following a 75 g OGTT are different.
2. Threshold values for the 100 g OGTT are no longer included.
3. Diagnosis of GDM is based on a single OGTT value at or above threshold, rather than two or more values.
4. Preferred and alternate approaches to diagnosis are provided. (4,5)

Table 4 outlines the diagnostic criteria in the 2002 SOGC/2006 AOM CPGs and the 2013 CDA/2016 SOGC CPGs.

The diagnostic criteria used in the 2002 SOGC/2006 AOM CPGs were based on 75 g and 100 g OGTT thresholds used by the American Diabetes Association (ADA) and ACOG. (2,3) The ADA and ACOG thresholds are derived from research by O'Sullivan and Mahan in the 1960s that established an association between OGTT values above threshold and subsequent risk of developing type 2 diabetes. Later criteria (Carpenter Coustan and NDDG) adapted O'Sullivan and Mahan's original thresholds to conform to new methods of measuring glucose. (31)

The diagnostic criteria used in the newer CDA/SOGC guidelines are based on recommendations from a consensus panel convened by IADPSG and which in turn are based on findings of the Hyperglycemia and Pregnancy Outcomes study (HAPO). (1) These findings are described in further detail below. Whereas the ADA and ACOG thresholds are designed to predict adverse maternal outcomes, the diagnostic criteria used in the CDA/SOGC guidelines are designed to predict adverse perinatal outcomes.

TABLE 4: DIAGNOSTIC CRITERIA COMPARED

Threshold glucose level (mmol/L)	2002 SOGC/2006 AOM CPG (2,3)		2013 CDA/2016 SOGC CPG (4,5)	
	ADA thresholds 75 g OGTT following 50g GCT ¹	ACOG thresholds 100 g OGTT following 50 g GCT ¹ CC ² criteria NDDG ³ criteria	Preferred (two-step) approach 75 g OGTT following 50 g GCT ⁴	Alternate (one-step) approach 75 g OGTT without 50 g GCT
0h	≥ 5.3	≥ 5.3 ≥ 5.8	≥ 5.3	≥ 5.1
1h	≥ 10.0	≥ 10.0 ≥ 10.6	≥ 10.6	≥ 10.0
2h	≥ 8.6	≥ 8.6 ≥ 9.2	≥ 9.0	≥ 8.5
3h	N/A	≥ 7.8 ≥ 8.0	N/A	N/A
DIAGNOSE GDM if →	2 values met or exceeded (III-C)	2 values met or exceeded (III-C)	1 value met or exceeded (Grade B, Level 1)	1 value met or exceeded (Grade B, Level 1)

¹ with 1hPG ≥ 7.8 mmol/L

² Carpenter Coustan thresholds (28)

³ National Diabetes Data Group thresholds from (30)

⁴ with 1hPG 7.8 -11.0 mmol/L.

THE HAPO STUDY

The multicenter, prospective HAPO trial aimed to answer the question of whether hyperglycemia in pregnancy at a level less severe than GDM is associated with an increased risk of maternal, fetal or neonatal complications. HAPO recruited more than 25,000 pregnant participants in nine countries who underwent a single 75 g OGTT between 24 and 32 weeks' gestation. Those whose glucose measures exceeded specified diagnostic thresholds (FPG > 5.8 mmol/L or 2hPG > 11.1 mmol/L) were excluded from the study and given standard treatment for GDM. Those whose OGTT values were below the diagnostic criteria for diabetes according to the study design (FPG ≤ 5.8 mmol/L or 2hPG ≤ 11.1 mmol/L) remained in the study and had their glucose results blinded to them, their care providers, and HAPO study staff (N = 23,316). (11)

In an attempt to identify maternal glucose levels that predict clinically important perinatal outcomes, four outcomes commonly associated with GDM were chosen as primary outcomes for the HAPO study:

- large-for-gestational age (LGA), defined as birth weight > 90th percentile for gestational age;
- primary caesarean section (CS);
- neonatal hypoglycemia, defined by symptoms, treatment with glucose infusion or laboratory report of glucose ≤ 1.7 mmol/L in the first 24 hours or ≤ 2.5 mmol/L after the first 24 hours; and
- fetal hyperinsulinemia, defined as cord blood serum c-peptide levels above the 90th percentile.

Despite its sample size and international scope, HAPO failed to identify clear thresholds for development of useful diagnostic criteria for GDM. Analysis of HAPO findings revealed no point at which risk of perinatal complications increased significantly. Instead, the analyses indicated a continuous, linear association between increasing maternal glucose levels and LGA, CS, neonatal hypoglycemia and fetal hyperinsulinemia. (11) The strongest associations observed in the HAPO cohort were the increased incidence of LGA (adjusted odds ratios from 2.68-5.01) and fetal hyperinsulinemia (adjusted OR 2.18-11.32) among study participants with high OGTT values. These findings are consistent with the Pedersen hypothesis, which posits that maternal hyperglycemia produces fetal hyperglycemia, to which the fetus adapts by secreting increased insulin and subsequently converting excess glucose to adipose tissue, causing fetal overgrowth or macrosomia. (45)

Furthermore, the study's primary outcomes do not clearly represent clinically significant effects and their association with longer-term maternal and/or neonatal outcomes is unclear. (11) LGA and hyperinsulinemia hold little clinical relevance unless they are associated with higher risk of shoulder dystocia, CS or metabolic issues following birth. (46) In the HAPO cohort, primary CS, clinical neonatal hypoglycemia, premature delivery, shoulder dystocia/birth injury, and admission to neonatal intensive care displayed weaker or non-statistically significant associations with increasing maternal glycemia, as did hyperbilirubinemia and preeclampsia. (11) A subsequent publication from HAPO researchers found that BMI was generally more predictive of LGA incidence than glycemic status: over three-quarters (78%) of all participants giving birth to LGA infants had glucose levels that fell below diagnostic criteria for GDM. (46) More recent research on the origins of gestational diabetes suggests that maternal dyslipidemia may also influence excessive fetal growth. (47)

Research on diagnosis

The intention of the HAPO study, published in 2008, was to identify clear diagnostic threshold effects for a number of perinatal outcomes. (11) Though HAPO did not identify glucose levels at which risk increased significantly, the IADPSG used HAPO results to develop new diagnosis and screening guidelines in 2010. (1) The group produced four recommendations related to diagnosis of GDM:

- A fasting plasma glucose ≥ 7.0 mmol/L or HbA1c level $\geq 6.5\%$ found in early pregnancy should be identified as **overt diabetes** and FPG between 5.1 and 6.9 mmol/L should be diagnosed as GDM.
- **A single 75 g OGTT at 24-28 weeks' gestation** for all people not previously diagnosed with overt diabetes or GDM.
- OGTT values associated with a **1.75-fold** increased odds of infant birth weight, cord C-peptide concentration or percentage body fat above the 90th percentile in the HAPO cohort constitute a diagnosis of GDM. These values (FPG = 5.1 mmol/L, 1h = 10.0 mmol/L, 2h = 8.5 mmol/L) are reflected in the CDA's **alternate approach**.
- **Only one abnormal OGTT value is needed to diagnose GDM** since any abnormal fasting, one-hour or two-hour glucose values are associated with outcomes above the 90th percentile for infant birth weight, cord C-peptide concentration and percentage body fat (outcomes assessed in the HAPO trial).

The cut-off values used in the CDA/SOGC's preferred approach are also based on data from the HAPO trial. The preferred approach cut-offs represent the average 75 g OGTT values (following a positive screen on a 50 g GCT) in the HAPO study at which the odds of infant birth weight, cord-C peptide concentration or percentage body fat values above the 90th percentile are double the estimated odds of these outcomes at the mean glucose level (using an OR of 2.0, rather than the IADPSG's OR of 1.75). The CDA's expert committee chose their preferred approach due to predicted increases in workload and cost associated with one-step screening using thresholds determined by an odds ratio of 1.75. (4) Diagnosis of GDM using either preferred or alternate approaches is dependent on one or more value at or above the specified cut-off values.

While the IADPSG panel recommends proceeding directly to 75 g OGTT, the CDA/SOGC's preferred approach is two steps: a 50 g GCT followed by 75 g OGTT. Though a formal cost/workload analysis has not been undertaken using the cut-off values used in the preferred approach, the CDA concluded that "most cost analysis evaluations support a sequential screening approach to GDM; thus, our preferred approach is to continue with this strategy." (4) When the preferred approach thresholds are applied to the HAPO cohort as a whole, the incidence of GDM is 8.8%, almost half the incidence of GDM (16.1%) when the alternate approach thresholds (which are consistent with IADPSG cut-offs) are applied. (4) The incidence of GDM in the Ontario context using either the preferred or alternate approach is unknown. The observed incidence of GDM in Ontario doubled from 2.8% in 1996 to 5.6% in 2010, and the updated CDA/SOGC diagnostic criteria will likely increase this rate further. (32)

Historic disagreement surrounding GDM diagnosis has led to high degrees of variation in practice and research. Despite criticism of the arbitrary nature of the IADPSG recommendations, a number of professional bodies have adopted the IADPSG criteria in order to standardize international definitions of GDM. (33) The 2013 WHO guideline uses IADPSG-based thresholds and diagnostic criteria consistent with the CDA's alternate approach, but added upper limits to the FPG (11.1 mmol/L) and 2hPG (7.0 mmol/L) to differentiate between gestational diabetes and "diabetes in pregnancy" that more likely represents undiagnosed type 2 diabetes. (8) The ADA has endorsed the IADPSG strategy, but ACOG and NICE have not. ACOG's 2013 practice bulletin on GDM lists the diagnostic thresholds established by both the NDDG and Carpenter and Coustan as reasonable to use due to the "absence of clear comparative trials" and recommends a two-step testing approach. (13) The 2015 NICE guideline on diabetes and pregnancy recommends diagnosing GDM based on a FPG ≥ 5.6 mmol/L or 2hPG ≥ 7.8 mmol/L following 75 g OGTT. (15) The NICE guideline suggests that application of the IADPSG criteria would result in a substantial increase in GDM diagnoses without clear benefit in maternal or neonatal outcomes or cost-effectiveness. (15)

Table 5, in the Appendix, compares diagnostic screening for various guideline development groups at 24-28 weeks' gestation.

HbA1c and pregnancy

HbA1c refers to glycated hemoglobin, produced when blood glucose molecules bind to hemoglobin. Because glycation is irreversible, HbA1c values reflect the average level of plasma glucose to which the cell has been exposed throughout its lifespan. HbA1c values therefore provide an overall snapshot of plasma glucose values over a period of eight to 12 weeks. In the non-pregnant population, an HbA1c value $\geq 6.5\%$ is used to diagnose diabetes mellitus. The HbA1c test is also used to identify individuals with impaired glucose tolerance and to assess glycemic control in known diabetics. (34,35)

The IADPSG guideline recommends measuring fasting plasma glucose, HbA1c or random plasma glucose at first prenatal visit to detect overt diabetes existing prior to pregnancy. The IADPSG guideline acknowledges that the clinical value or cost-effectiveness of universal testing to detect overt diabetes early in pregnancy is unclear. (1)

The recently updated NICE guideline recommends measuring HbA1c in all pregnant people with newly diagnosed GDM, as a means of identifying those who likely had pre-existing diabetes. (14) However, reference ranges for HbA1c testing in pregnancy have not been established. Typical hematologic changes in pregnancy, such as increased red blood cell turnover and high prevalence of anemia, may limit the

applicability of cut-off values used in a non-pregnancy population. (15)

Researchers have suggested that HbA1c testing may have value as an early predictor of GDM. Studies suggest that high HbA1c levels in the first half of pregnancy are associated with an increased likelihood of subsequent GDM diagnosis. (36,37) In one study, nearly one-third of participants with first trimester HbA1c levels suggestive of impaired glucose tolerance (5.7%-6.4%) were subsequently diagnosed with GDM by routine screening at 24 to 28 weeks, compared to fewer than 10% of participants with HbA1c $<5.7\%$. (36) Researchers have not established what proportion of GDM cases could be identified with early HbA1c screening. The NICE guideline recommends against using HbA1c (and plasma glucose measures) to assess risk of GDM.

HbA1c has limited efficacy as an alternative to OGTT for the diagnosis of GDM in the third trimester. (14,38,39) Because of its poor specificity and sensitivity, NICE and U.S. Preventative Services Task Force recommend against using HbA1c to diagnose GDM during screening at 24 to 28 weeks' gestation. (14,23)

IMPLICATIONS

The 2013 CDA and 2016 SOGC guidelines propose a preferred (two-step) and an alternate (one-step) approach to the diagnosis of GDM. These diagnostic thresholds are based on findings of the HAPO study.

Adopting new diagnostic criteria that require one rather than two or more abnormal results on an OGTT will increase the incidence of GDM. Specific incidence will vary depending on the population screened and the thresholds used. Research suggests that the incidence of GDM when applying the “alternate approach” criteria to a population of pregnant people cared for in hospitals in Toronto is about 15%. (42) Adoption of the “preferred approach” criteria (50 g GCT, followed by a 75 g GTT if needed) is estimated to result in a GDM incidence of 8.8% based on a retrospective analysis of the HAPO cohort. (11) The incidence of GDM in Ontario using the new criteria is unknown, but will likely be similar. (4)

The 2013 CDA/2016 SOGC diagnostic criteria are based on neonatal outcomes (increased risk of infant birth weight, cord C-peptide concentration or percentage body fat above the 90th percentile) that could be interpreted as neonatal adaptation to maternal hyperglycemia, rather than an overt pathological outcome with clear long-term implications. The threshold values used to diagnose GDM do not reflect increasing risks of harder endpoints such as longer-term morbidity or CS.

The 2013 CDA/2016 SOGC thresholds represent a shift from diagnostic criteria designed to predict adverse maternal outcomes to criteria designed to predict adverse perinatal outcomes. **It is unclear whether the new diagnostic criteria will, in fact, result in clinically significant improvements in neonatal outcomes.**

MANAGEMENT OF GDM

CPG recommendations

2002 SOGC CPG

SOGC guidance for the management of pregnant people diagnosed with GDM is limited to recommending a reassessment of glucose tolerance at six to 12 weeks postpartum. (2)

2006 AOM CPG

The 2006 AOM guideline endorses the same postpartum reassessment of glucose tolerance as the 2002 SOGC CPG. At the time the 2006 AOM CPG was written, diagnosis of GDM required consultation with a physician per the College of Midwives’ (CMO) Indications for Mandatory Discussion, Consultation and Transfer of Care (IMDCTC) document. The CMO’s Consultation and Transfer of Care Standard (CTCS) replaced the IMDCTC in 2015.

The CTCS states that for clients diagnosed with GDM (hyperglycemia), a consultation with a physician is necessary in the event that hyperglycemia is not responsive to nutritional therapy. (48)

2013 CDA CPG and 2016 SOGC CPG

The 2013 CDA and 2016 SOGC guidelines are more prescriptive regarding management of GDM. It should be noted that all of these recommendations are based on expert opinion and consensus, unless otherwise stated. (4,5)

The CDA recommends that during the **prenatal period**, those with GDM should:

- perform self-monitoring of blood glucose before (fasting) and after meals (postprandially, PP) [Grade B, Level 2] and should strive for **target glucose values of:**

Fasting	< 5.3 mmol/L [Grade B, Level 2]
1hPP	< 7.8 mmol/L [Grade B, Level 2]
2hPP	< 6.7 mmol/L [Grade B, Level 2]
- avoid ketosis during pregnancy [Grade C, Level 3];
- receive nutritional counselling from a registered dietician [Grade C, Level 3];

- gain weight within recommended ranges based on pre-pregnancy BMI [Grade D, Consensus];
- receive insulin therapy if glycemic targets are not reached within two weeks [Grade D, Consensus].

No recommendations are given in the CDA CPG related to monitoring of fetal growth or timing of labour in the presence of GDM, nor how management may differ with diet-controlled GDM compared to insulin-dependent GDM. (4)

The SOGC CPG refers to the CDA recommendations for maternal glycemic control described above and also recommends the following for clients with **GDM and pre-gestational diabetes**:

- Care be provided by a multidisciplinary team and aimed at attaining and maintaining euglycemia. (II-2B)
- Serial assessment of fetal growth every three to four weeks, starting at 28 weeks as a baseline, to assess the effect of maternal glycemic control on fetal growth and to assess amniotic fluid volume. (II-2B)
- Initiation of weekly assessment of fetal well-being at 36 weeks for pre-gestational diabetes mellitus and medically-managed GDM. The guideline suggests it is also reasonable to consider weekly fetal assessment

for those with diet controlled GDM beginning at 36 weeks. Acceptable methods of assessment of fetal well-being near term can include the non-stress test + amniotic fluid index, biophysical profile, or a combination of these. (III-A)

- If comorbid factors are present, such as obesity, evidence of suboptimal glycemic control, previous stillbirth, hypertension, or suspected LGA (> 90%) or SGA (< 10%), earlier onset and/or more frequent fetal health surveillance is recommended. In specific cases in which fetal growth restriction is suspected, the addition of umbilical artery and fetal middle cerebral artery Doppler assessment may be helpful. (II-2A)
- Offer induction between 38 to 40 weeks gestation depending on glycemic control and other co-morbidity factors. (II-2B)

During the **intrapartum period**, the CDA recommends:

- close monitoring of maternal blood glucose (recommended maternal blood glucose between 4.0 and 7.0 mmol/L) to minimize the risk of neonatal hypoglycemia [Grade D, Consensus]; and
- providing adequate glucose to clients during labour to meet their energy demands [Grade D, Consensus]. (4)

The following is recommended in the **postpartum period**. See Figure 3 in Appendix for the 2016 SOGC postpartum testing algorithm, with suggested glycemic values.

RECOMMENDATION / INDICATION	CDA 2013 (4)	SOGC 2016 (5)
Chest/breastfeed immediately after birth to avoid neonatal hypoglycemia	Yes [Grade D, Level 4]	Yes
Continue chest/breastfeeding to prevent childhood obesity and maternal hyperglycemia	At least three months [Grade C, Level 3]	At least six months
Offer 75 g OGTT between six weeks and six months postpartum to detect prediabetes and diabetes (see Table 6 for postpartum testing algorithm)	Yes [Grade D, Consensus]	Yes* (II-2A)

*See postpartum glycemic values for normal, prediabetes and type 2 DM suggested by the SOGC in Figure 3, in Appendix.

Research on management

Antenatal treatment

Two recent randomized controlled trials and four meta-analyses suggest that treatment of pregnant people with varying degrees of elevated glucose diagnosed using older GDM criteria (such as the criteria used in the 2002 SOGC and 2006 AOM CPGs) can decrease incidence of preeclampsia, macrosomia, LGA and shoulder dystocia. (20,21,23,49–51) The findings of these studies have been used as justification for universal screening, since GDM can exist asymptotically. (4) **It is not certain that treatment will benefit people with GDM identified using newer diagnostic criteria.**

Initial treatment of GDM typically involves nutritional counseling, self-monitoring of blood glucose levels and moderate exercise, with 7% to 20% of people diagnosed with GDM requiring insulin or oral antidiabetic medication. (12,20,21,23)

Benefits of treating GDM

The SOGC's 2016 CPG identifies five goals of treatment of GDM: reducing the risks of macrosomia (and optimizing fetal growth) and reducing risk of intrauterine fetal death, preeclampsia, CS, and neonatal complications (including shoulder dystocia, birth trauma and hypoglycemia). (5) The guideline's recommendations draw on two pivotal trials published in the past decade: the Australian Carbohydrate Intolerance Study (ACHOIS trial, N = 1000) and the Maternal Fetal Medicine Unit trial (MFMU, N = 958). (20,21) Both of these trials used a two-step diagnostic process to identify people with hyperglycemia, half of whom were randomly selected to receive treatment (individualized diet counselling and glucose monitoring, with insulin therapy as needed).

The American MFMU trial, which restricted participation in the study to participants with mild hyperglycemia (fasting plasma glucose < 5.3 mmol/L), did not find a statistically significant difference in their composite perinatal primary outcome (perinatal mortality, hypoglycemia, hyperbilirubinemia, neonatal hyperinsulinemia or birth trauma) between treatment and control groups. Select secondary outcomes (birth weight > 4000 g, LGA, CS, shoulder dystocia and preeclampsia or gestational hypertension) occurred less frequently in the treatment group. (20)

The ACHOIS trial found that treatment reduced the incidence of “serious perinatal complication” (a composite measure including death, shoulder dystocia, bone fracture and nerve palsy) from 4% to 1% (adjusted RR 0.33; 95% CI 0.14-0.75). The ACHOIS trial was criticized for combining shoulder dystocia with death as part of the composite outcome; shoulder dystocia accounted for the majority of the events in the composite outcome (7 events, 1% incidence) in the treatment group vs. 16 events (3% incidence) in the control group (p = .07). (21) None of the outcomes included in the composite measure were significantly different between groups. ACHOIS trial researchers calculated a number needed-to-treat of 34 for the composite perinatal outcome (52)

As the MFMU and ACHOIS trials were designed to assess the outcome of *any* treatment, they do not permit conclusions about the value of a *particular* treatment. Diet counselling and glucose monitoring were provided to all study participants in the treatment arms of the two trials. Eight percent of the treatment group in the MFMU cohort and 20% of the ACHOIS cohort also received insulin therapy. Neither study analyzed outcomes based on blood glucose measures at entry into the study. Thus, it is not clear from these trials whether one type of treatment (diet or insulin therapy) is particularly effective, or whether treatment is particularly beneficial at particular levels of hyperglycemia.

A 2013 systematic review and meta-analysis by Hartling et al. analyzed the MFMU and ACHOIS trials plus three additional RCTs and six retrospective cohort studies. (23) All studies in this review diagnosed GDM at or after 24 weeks' gestation (if reported) and compared treatment (diet modification, glucose monitoring and insulin as needed) with standard care. The review's authors were not able to report on the outcomes of diet and glucose monitoring alone – the findings discussed below compare *any* treatment to standard care.

Hartling et al.'s meta-analysis found moderate-quality evidence that treatment was associated with reduced incidence of preeclampsia (3 RCTs; RR 0.62, 95% CI 0.43-0.89), shoulder dystocia (3 RCTs; RR 0.42, 95% CI 0.23-0.77), LGA (3 RCTs; RR 0.56, 95% CI 0.45-0.69), and macrosomia (birth weight > 4000 g) (5 RCTs; RR 0.50, 95% CI 0.35-0.71). (23) The authors note that these outcomes may be intermediate to more clinically important outcomes, such as preterm birth

and brachial plexus injury, or less frequent outcomes for which studies have been too small to show significant differences between treatment and control groups. They also highlight that most cases of preeclampsia, shoulder dystocia and macrosomia occur in pregnant people without GDM, and that other factors such as maternal weight and gestational weight gain are more strongly associated with these outcomes. (23)

Hartling et al.'s meta-analysis did not detect differences between treatment and control groups in either RCTs or retrospective cohort studies for other outcomes: maternal weight gain, maternal or infant birth trauma, maternal BMI at delivery, birth weight > 4500 g, brachial plexus injury, clavicle fracture, hyperbilirubinemia, perinatal death, respiratory complications, Apgar scores at one and five minutes, or long-term effects on glucose tolerance or BMI in offspring. (23) Maternal weight gain at delivery showed conflicting results between studies in Hartling et al.'s meta-analysis. The ACHOIS and MFMU trials showed less weight gain with treatment (mean difference (95% CI): -1.40 kg (-1.74 to -1.66) and -2.20 kg (-2.71 to -1.69), respectively, but two older RCTs found no difference with treatment. (20,21,53,54)

While intrauterine fetal death was not assessed in the trials discussed above, it is another adverse outcome underlying the SOGC's recommendations regarding management of pregnancies complicated by GDM. The SOGC CPG cites a recent analysis of population-level California data suggesting an elevated risk of stillbirth in pregnancies affected by diet- or insulin-controlled GDM (overall rate 17.1/10 000 deliveries with GDM vs 12.7/10 000 deliveries without GDM). Stillbirth rates were also examined at each week of gestation; from 36 to 39 weeks, pregnancies with GDM had a higher risk of stillbirth than pregnancies without GDM (RRs 1.45 to 1.84). (55) Due to the limitations of the dataset, the researchers did not adjust for confounders such as obesity or HDP, which are associated with GDM as well as increased stillbirth risk, nor were the researchers able to take glycemic control into account. The findings of the California study diverge from previous assessments of stillbirth risk in GDM pregnancies: studies from Italy, Sweden and Israel have failed to establish a clear association between GDM and stillbirth, those studies tended to involve homogenous populations with a lower prevalence of GDM and one study limited participation

to individuals with diet-controlled GDM. (56–58) Rates of stillbirth are also increased in those with diabetes pre-dating pregnancy. (59)

Harms of treating GDM

It has been hypothesized that aggressive surveillance and increased intervention occurring as a result of a GDM diagnosis may lead to induction of labour, CS or small for gestational age (SGA) infants and create additional costs associated with laboratory testing and patient/clinician time. Moderate quality evidence from four RCTs showed no difference in incidence of SGA based on treatment, potentially due to a small number of events and inadequate power to detect differences. (23) Cost and resource allocation was assessed in two RCTs that reported an increase in the number of prenatal visits among study participants receiving treatment. (23) Increased surveillance and intervention due to care provider apprehension following a GDM diagnosis was discussed but not directly examined in the MFMU and ACHOIS trials. The MFMU trial found a reduced incidence of CS with treatment (RR 0.79, 95% CI 0.64–0.99) and no difference in induction of labour. (20) The ACHOIS trial found an increased incidence of induction of labour with treatment (RR 1.31, 95% CI 1.10–1.56) and no difference in CS. (21)

Identifying and treating GDM may also produce maternal stress and anxiety. The ACHOIS study is the only major trial to address maternal anxiety and depression related to GDM diagnosis. This study found no difference in anxiety six weeks after study entry or three months after delivery in treatment and control groups, but did find lower rates of depression in the treatment group at three months after birth (RR 0.50, 95% CI 0.31–0.79). (21) Another study showed that people diagnosed with GDM had higher anxiety levels at time of diagnosis compared to those without GDM, though this difference did not persist to delivery. (60) Yet another study found that people with GDM exhibited more concern about their own health and their child's health compared to matched controls three to five years after diagnosis. (61) More research is necessary to determine how increasing rates of GDM diagnosis will affect people emotionally or psychologically.

Antenatal fetal assessment

Scant research underlies the SOGC's recommendations regarding antenatal fetal assessment. There is consensus

that enhanced surveillance may benefit pregnancies in which diabetes is likely to affect fetal growth and well-being. (13,10,62,63) Accelerated – or in some cases, restricted – fetal growth increases the likelihood of many of the adverse perinatal outcomes associated with diabetes in pregnancy. While existing methods of antenatal fetal weight estimation have poor accuracy, fetal surveillance could theoretically identify fetuses at risk and lead to earlier treatment or intervention. (64)

The 2007 SOGC guidelines on fetal health surveillance include diabetes pre-dating pregnancy and GDM managed with insulin as conditions associated with increased perinatal morbidity/mortality; antenatal fetal surveillance may therefore be beneficial.(63) The 2013 ACOG guidelines also recommend fetal surveillance for GDM with suboptimal glucose control. (13)

There is little consensus about the issue of fetal surveillance in pregnancies affected by diet-controlled GDM, a topic that was not addressed in either the 2002 SOGC CPG or the 2013 CDA CPG. In a 2002 analysis, Landon and Vickers argued that the value of surveillance was limited in pregnancies with well-controlled GDM, since stillbirth rates, at that point in time, were thought to be comparable to the general pregnant population. (62) Another American commentator cited in the recent SOGC guideline recommends that testing not be initiated until 40 weeks' gestation in those with well-managed diet-controlled GDM, given the lack of data suggesting any increased perinatal risk in this population. (10) Noting a lack of consensus regarding the value of fetal monitoring with well-controlled GDM, the 2013 ACOG guidelines suggest that surveillance can be guided by local practice. (13)

Citing newer California research that suggests that diet-controlled GDM may also increase risk of perinatal mortality, particularly after 38 weeks' gestation, the SOGC suggests that cases of diet-controlled GDM “should not be excluded from a protocol for antenatal fetal surveillance applicable to high-risk pregnancies.” (5,55,65)

Assessment of fetal growth

For individuals with pre-gestational and gestational diabetes, the SOGC guideline recommends assessment of fetal growth every three to four weeks beginning at 28 weeks' gestation. This recommendation, they point out, matches protocols used research studies assessing

management of diet-controlled GDM. (5,66,67) This recommendation is also consistent with the NICE CPG, which recommends monthly monitoring of growth and amniotic fluid volume in all individuals with diabetes in pregnancy from 28 to 36 weeks. (68) . While available research suggests that monthly US monitoring may lower risk of LGA and SGA, other outcomes have not been definitively demonstrated. (67)

Because polyhydramnios may develop with poor glycemic control or fetal macrosomia, the SOGC recommends measuring amniotic fluid volume as part of the ultrasound assessment of fetal growth. (5)

Assessment of fetal well-being

The SOGC CPG recommends weekly assessment of fetal well-being beginning at 36 weeks for pregnancies complicated by pre-gestational or gestational diabetes managed with insulin or oral hyperglycemics. The guideline also suggests it is “reasonable to consider” extending weekly monitoring to cases of diet-controlled GDM. Earlier initiation and/or more frequent monitoring is recommended for pregnancies in which comorbid factors are present (obesity, suboptimal glycemic control, LGA or SGA, hypertension or previous stillbirth). (5)

Possible methods of fetal assessment include the non-stress test (NST), NST plus amniotic fluid index, and biophysical profile, either alone or in combination. These methods of assessment have not been well studied in the context of gestational diabetes. The SOGC CPG refers to a retrospective study in which participants with diet- and insulin-controlled GDM underwent twice-weekly NSTs. Atypical and abnormal NST findings (specifically, absence of variability and presence of decelerations) were found to be predictive of later fetal distress in labour, though not to an improvement in GDM-related outcomes specifically, leading the researchers to suggest that NST is an effective method of monitoring fetal well-being in diabetic pregnancies. (69) While the utility of BPP has not been thoroughly assessed in the context of diabetes in pregnancy, if SGA is suspected the SOGC guideline recommends performing umbilical artery and middle cerebral artery Doppler as part of the assessment of fetal well-being and placental function. (5)

Timing of delivery

The SOGC CPG recommends offering induction of labour between 38 to 40 weeks' gestation depending on glycemic control and other co-morbidity factors.

The 2015 NICE guidance suggests advising individuals with GDM “to give birth no later than 40+6 weeks, and offer[ing] elective birth (by induction of labour, or by caesarean section if indicated) to those who have not given birth by this time.” If maternal or fetal complications are present, NICE suggests “consider[ing] elective birth before 40+6 weeks.” (12) Given the lack of research available at the time of publication, the 2013 ACOG guideline concluded that “no evidence-based recommendation can be made regarding timing of delivery in women with GDM that is controlled either with a diet and exercise regimen or with medication.” (13)

The SOGC's recommendation is based on research that suggests lower rates of macrosomia and shoulder dystocia with induction of labour (without a concomitant increase in rates of CS), and possible decreased rates of stillbirth if birth occurs before 40 weeks' gestation. (5)

The SOGC CPG refers to a 2009 systematic review of studies comparing induction of labour and expectant management in pregnancies complicated by GDM. One RCT and four observational studies were included in the review. While the findings of this review were limited by the small sample sizes and heterogeneity of the studies included, the researcher noted a reduced rate of fetal macrosomia with induction of labour. (70) These findings are supported by a recent large RCT comparing induction of labour and expectant management for suspected fetal macrosomia, which found a reduced risk of shoulder dystocia and no difference in risk of CS with induction of labour between 37+0 and 38+6 weeks. Approximately 10% of participants included in each arm of the study had diet-controlled GDM. (71)

A recent study based on data from Ontario's BORN database compared outcomes among approximately 8,000 people with GDM who were either induced or expectantly managed at 38 or 39 weeks' gestation. Compared to expectant management, induction of labour at 38 or 39 weeks was associated with lower odds of CS. Induction of labour at 38 weeks was also associated with higher odds of NICU admission. No

other outcomes were different between induction and expectant management groups. (72)

The SOGC's suggestion that a policy of induction by 40 weeks may decrease rates of stillbirth in people with diet-controlled GDM and “may be beneficial in this population” is based on retrospective analysis of just under 200,000 births at an Israeli hospital where individuals with GDM were routinely induced at 40 weeks' gestation. People with diet-controlled GDM had consistently lower rates of perinatal mortality than people without GDM. (56) Because they observed higher rates of obstetric and perinatal complications in study participants with diet-controlled GDM (including abnormal fetal heart rate patterns, Apgar score less than 7 at one minute, macrosomia, shoulder dystocia and CS), the researchers expected to see excess perinatal mortality in the GDM group. The researchers attributed the lower-than-expected rate of stillbirth to their policy of inducing people with diet-controlled GDM by 40 weeks. (56) However, the lower rate of perinatal mortality observed in the GDM group may also reflect the effects of a general policy of induction at term, rather than any effects related to diet-controlled GDM specifically. (73)

On the whole, the association between GDM (diet or insulin-controlled) and perinatal mortality remains unclear. While a recent California study identified higher rates of perinatal mortality in a GDM population, previous large retrospective studies in Sweden and Italy did not find any significant association between GDM and stillbirth and perinatal or neonatal mortality rates. (55,57,58) Like the Israeli research described above, the California, Swedish and Italian studies demonstrated higher rates of congenital anomalies and other maternal and perinatal complications with GDM, compared to control groups without GDM. Only the California study found a concomitant increase in risk of perinatal or neonatal mortality, a finding the authors suggest may be attributable to the higher rate of GDM observed in their study population (4.6% in California vs 0.8% and 0.9% in Sweden and Italy, respectively). Differences in mortality outcomes may also be attributable to access or quality of care in these different settings.

Differential management of pregnancies affected by GDM is another factor that may explain why some of these studies have not demonstrated excess perinatal mortality risk – pregnancies with GDM may be more thoroughly monitored and involve earlier delivery than pregnancies

without GDM. Management-related factors cannot easily be considered in studies that use retrospective, population-level data. Additionally, none of the California, Swedish or Italian studies were able to assess differences in outcomes based on diet vs insulin treatment or poor vs good glycemic control.

Intrapartum management

Close monitoring of maternal blood glucose during labour (recommended maternal blood glucose between 4.0 and 7.0 mmol/L) is primarily concerned with preventing neonatal hypoglycemia attributable to fetal hyperinsulinemia developed during gestation. Studies done to determine the effect of intrapartum maternal glycemia on infant metabolic outcomes have found a continuous relationship between mean maternal glucose levels during labour and risk of neonatal hypoglycemia, but like HAPO these studies have found no clear point at which risk of hypoglycemia rises dramatically.

These studies have generally been done on people with pregestational diabetes or insulin controlled diabetes; therefore, results should be assessed with caution, as they may not be applicable to clients diagnosed with GDM who have good glucose control with diet modification and exercise alone. (4)

Postpartum management

Postpartum management recommendations are focused on decreasing the risk of later diabetes diagnosis and obesity in individuals with GDM and their offspring. These recommendations are largely based on consensus opinion as the evidence linking GDM to these outcomes is relatively weak.

Protective effects of chest/breastfeeding

The CDA and SOGC guidelines recommend chest/breastfeeding immediately after birth and for at least three to six months postpartum to protect against neonatal hypoglycemia, childhood obesity and maternal hyperglycemia. (4,5) This recommendation draws from four major studies. Chertok et al. sought to examine the benefit of early feeding to reduce the risk of fetal hypoglycemia following birth. The study compared timing of chest/breastfeeding and type of infant feeding and found that infants born to people with GDM who were fed human milk within 30 minutes of delivery had higher mean blood glucose levels compared to those not

chest/breastfed early in the postpartum period. Infants fed human milk also had significantly higher mean blood glucose levels compared to infants who were fed formula for their first feed. (74)

Schaefer-Graf et al. demonstrated an association between chest/breastfeeding and lower rates of childhood obesity in children born to individuals with GDM. Increased duration of chest/breastfeeding and feeding human milk for more than three months was shown to reduce the risk of overweight in childhood by 40% to 50%. In this study, exclusive chest/breastfeeding was an independent predictor for normal weight in childhood after adjusting for confounders such as parental obesity and high birth weight. (75)

Chest/breastfeeding has also been shown to exhibit a protective effect for maternal glycemia in both the short- and long-term. Gunderson et al.'s study on lactation intensity, maternal glucose tolerance and insulin resistance in individuals with GDM observed lower glucose and insulin levels in participants who were exclusively and mostly chest/breastfeeding compared to those who were inconsistently chest/breastfeeding or mostly formula feeding at six to nine weeks postpartum. The authors hypothesized that feeding with human milk preserves pancreatic β -cells, due to a roughly 50 g/day diversion of glucose and lipids into milk production via non-insulin mediated pathways of mammary gland uptake. (76) A long-term study that followed 304 participants with GDM for up to 19 years after the birth of their infant found that chest/breastfeeding decreased the long-term risk of developing postpartum type 2 diabetes by more than 40%. This reduction was most pronounced when chest/breastfeeding duration was at least three months. (77)

While chest/breastfeeding has been associated with benefits for both mothers and infants, the authors of the CDA CPG suggest that people with GDM may have more difficulty chest/breastfeeding due to the increased incidence of obesity in those with GDM and the higher likelihood that they will experience operative delivery. (4)

Longer-term risks to offspring

Some studies have shown increased incidence of insulin resistance in children born to those with GDM, potentially due to intrauterine hyperglycemia exposure that modifies fetal islet cells, hormone production and adipose tissue accretion. (78–80) This association was first examined

by Pettitt et al. in the 1980s, who found that the children of Pima American Indian individuals diagnosed with diabetes before or during pregnancy had significantly increased rates of obesity and diabetes detected between ages five to 19, independent of both maternal obesity and birth weight. (81) Studies conducted among this population have noted increased odds of developing type 2 diabetes in siblings born after diabetes was diagnosed (OR 3.7). (4) Similar associations have been noted in a number of different populations. Clausen et al.'s study of a primarily Caucasian population reported higher rates of abnormal glucose tolerance in offspring of people with GDM (21%) compared to the background population (4%) and Silverman et al.'s work found impaired glucose tolerance in 19.3% of offspring of individuals with pregestational diabetes and GDM compared to 2.5% of age- and sex-matched controls. (82,83)

The independent contribution of GDM to offspring obesity was minimal in two recent studies: a prospective longitudinal study of 16 year olds and a follow-up of HAPO cohort offspring at age 2, both of which showed no increased risk of obesity in children exposed to maternal hyperglycemia in the absence of maternal obesity. (84,85) A follow-up study of children four to five years after the ACHOIS trial found no difference in BMI between offspring of mothers in the treatment and control groups, despite the latter having an increased rate of macrosomia. (86)

There remains uncertainty on the appropriate time at which to assess the effects of gestational diabetes on offspring. Social, environmental and sex-specific factors also remain poorly understood. While hyperglycemia in utero may play a role in the development of offspring diabetes and obesity, it is likely that other factors, such as maternal weight gain and/or obesity, also play an important role. (46)

Longer-term maternal risks

Impaired secretion and action of insulin can persist postpartum and increase the risk of developing impaired fasting glucose, impaired glucose tolerance and type 2 diabetes following pregnancy. (4) A meta-analysis of 20 retrospective and prospective cohort studies found that participants with GDM (N = 32,000) had a roughly 7-fold greater risk of developing type 2 diabetes later in life (unadjusted pooled RR 7.43, 95% CI 4.79-11.51).

(32,87) Feig et al. determined that the incidence of type 2 diabetes following GDM in a large Canadian population was 18.9% at nine years after pregnancy, compared to 1.9% in people without GDM. (32) The criteria used to diagnose GDM in these studies were more conservative than the CDA's current diagnostic criteria. It is uncertain whether the relationship between GDM and type 2 diabetes will change with widespread adoption of the CDA's lower diagnostic thresholds. Expanding the definition of GDM to encompass people with milder forms of hyperglycemia may result in a decline in the proportion progressing to type 2 diabetes. (33,46,88)

The recommendation to retest glucose levels with a 75 g OGTT between six weeks and six months postpartum is based on the increased risk of developing type 2 diabetes following pregnancy. The CDA guideline's authors note that many people do not receive proper postpartum follow-up and that caregivers should explicitly communicate the importance of postpartum care, facilitate blood glucose testing, and continue to discuss lifestyle and diet modification. (4)

IMPLICATIONS

Evidence from two major RCTs and a meta-analysis indicate treating GDM through diet modification, glucose monitoring and insulin as needed is associated with decreased incidence of preeclampsia, LGA, shoulder dystocia and macrosomia; however, benefits are modest and these outcomes occur more often in pregnant people who do not have GDM. Participants in these studies were selected using more restrictive diagnostic criteria than those proposed in the 2013 CDA and 2016 SOGC CPGs and treatment may not have the same benefits when GDM has been identified using lower diagnostic thresholds. Treatment of GDM is not associated with differences in maternal weight gain, maternal or infant birth trauma, maternal BMI at delivery, birth weight > 4500 g, brachial plexus injury, clavicle fracture, hyperbilirubinemia, perinatal death, and respiratory complications, Apgar scores at one and five minutes, or long-term effects on glucose tolerance or BMI in offspring.

There is currently little evidence on short-term harms associated with GDM treatment. A single RCT shows a mild increase in short-term maternal anxiety, but no long-term difference based on GDM diagnosis. Other observational studies have shown increased long-term anxiety in individuals diagnosed with GDM compared to matched controls.

There is consensus that enhanced surveillance may benefit pregnancies in which diabetes is likely to affect fetal growth and well-being. Adverse outcomes associated with diabetes in pregnancy are substantially associated with hyperglycemia and the coexisting metabolic environment. Extending enhanced antenatal surveillance to cases of diet-controlled GDM will lead to increased use of surveillance methods such as ultrasound and NST, increased utilization costs, and possibly increased rates of intervention.

The SOGC CPG recommends offering induction of labour between 38 to 40 weeks' gestation depending on glycemic control and other co-morbidity factors. This recommendation will likely increase use of induction of labour, which may in turn increase NICU utilization, as demonstrated in one Ontario study.

The scant research that suggests possible benefit to enhanced surveillance and induction of labour before 40 weeks' gestation in pregnancies with GDM comes from studies that typically use diagnostic criteria that are more strict than the criteria suggested in the 2013 CDA and 2016 SOGC CPG. These possible benefits may not be seen with GDM diagnosed using the looser criteria recommended in the 2013 CDA and 2016 SOGC CPGs.

Research suggests that GDM is associated with increased risk of insulin resistance in offspring in childhood and adolescence. Maternal weight gain may confound this association and social and environmental factors may also play a role. Uncertainty remains regarding the appropriate time to assess possible effects of gestational diabetes on offspring.

Impaired secretion and action of insulin can persist postpartum and increase the risk of developing impaired fasting glucose, impaired glucose tolerance and type 2 diabetes following pregnancy. It is uncertain whether the relationship between GDM and type 2 diabetes will change with widespread adoption of the 2013 CDA and 2016 SOGC's lower diagnostic thresholds. Expanding the definition of GDM to include people with milder forms of hyperglycemia may result in a decline in the proportion progressing to type 2 diabetes. (33,46,88)

2013 CDA/2016 SOGC guidelines recommend chest/breastfeeding immediately after birth and for at least three to six months postpartum to protect against neonatal hypoglycemia, childhood obesity and maternal hyperglycemia.

CONCLUSION AND KEY POINTS

Methodological challenges face researchers studying GDM, and wide variation in professional guidelines, practitioner opinion, and population demographics make it difficult to generalize findings.

Serious hyperglycemia (markedly elevated GCT, OGTT or pregestational diabetes) can benefit from identification and therapy; identifying and treating milder hyperglycemia should be considered in a context of some uncertainty surrounding potential benefits and harms of testing and treatment. (46)

Universal blood glucose screening will increase the proportion of people who undergo testing. It is uncertain how an increase in screening will affect pregnancy outcomes, clients' psychological well-being, clinician workload, management approaches to GDM, and costs to the health-care system.

The 2013 CDA and 2016 SOGC guidelines propose a preferred (two-step) and an alternate (one-step) approach to the diagnosis of GDM, along with new diagnostic criteria that require a single abnormal result rather than two or more abnormal OGTT results. Rates of GDM in Ontario doubled from 1996-2010; adoption of the newer diagnostic criteria in the context of increasing population-level rates of obesity and diabetes outside of pregnancy will likely increase the incidence of GDM further. The health-system effects of increasing rates of GDM are unknown.

While researchers have failed to identify clear thresholds for development of diagnostic criteria for GDM, recent studies have noted a consistent linear association between increasing maternal glucose levels and fetal birth weight > 90th percentile, cord c-peptide levels and hyperinsulinemia. However, the downstream effects of these outcomes, including shoulder dystocia, CS, labour induction, hypoglycemia, birth trauma, and later development of obesity and diabetes are less clear. Most

cases of LGA, shoulder dystocia and macrosomia occur in pregnant people without GDM.

Treatment for hyperglycemia (diet therapy and insulin as required) appears to modestly reduce the incidence of some adverse perinatal outcomes, including preeclampsia, shoulder dystocia, LGA and macrosomia. There is low-quality or inconclusive evidence for the benefit of treatment on more clinically important outcomes such as brachial plexus injury or long-term metabolic outcomes. These findings are based on research that used more restrictive diagnostic criteria than those proposed in the 2013 CDA and 2016 SOGC CPGs. Treatment may not have the same benefits when GDM has been identified using lower diagnostic thresholds. There is currently little evidence on possible harms associated with GDM treatment.

The 2016 SOGC CPG includes recommendations that are likely to increase surveillance and intervention in pregnancies affected by gestational diabetes, including pregnancies with well-managed, diet-controlled GDM. The SOGC's recommendation to offer induction between 38 and 40 weeks' gestation is based on research that suggests lower rates of macrosomia and shoulder dystocia with induction of labour without a concomitant increase in rates of CS, and possibly decreased rates of stillbirth. This recommendation differs from those of both NICE and ACOG. Past research suggests that individuals with GDM have an increased risk of developing type 2 diabetes following pregnancy. The criteria used to diagnose GDM in these studies were more conservative than the current diagnostic criteria. Expanding the definition of GDM to encompass pregnant people with milder forms of hyperglycemia may result in a decline in the proportion progressing to type 2 diabetes. The independent effect of GDM on the development of diabetes and obesity in the offspring of those with GDM is still uncertain, and it is unclear if treating GDM will prevent metabolic consequences in offspring. (89)

APPENDIX

FIGURE 1: GESTATIONAL DIABETES SCREENING AND DIAGNOSIS ALGORITHM
2002 SOGC CPG (2)

"A single approach of testing for GDM cannot be recommended at the present as there is not enough evidence-based data proving the beneficial effect of a large screening program. Until a large prospective RCT shows a clear benefit for screening and consequently treating GDM, recommendations will by necessity be based on consensus or expert opinion. Each of the following is acceptable."

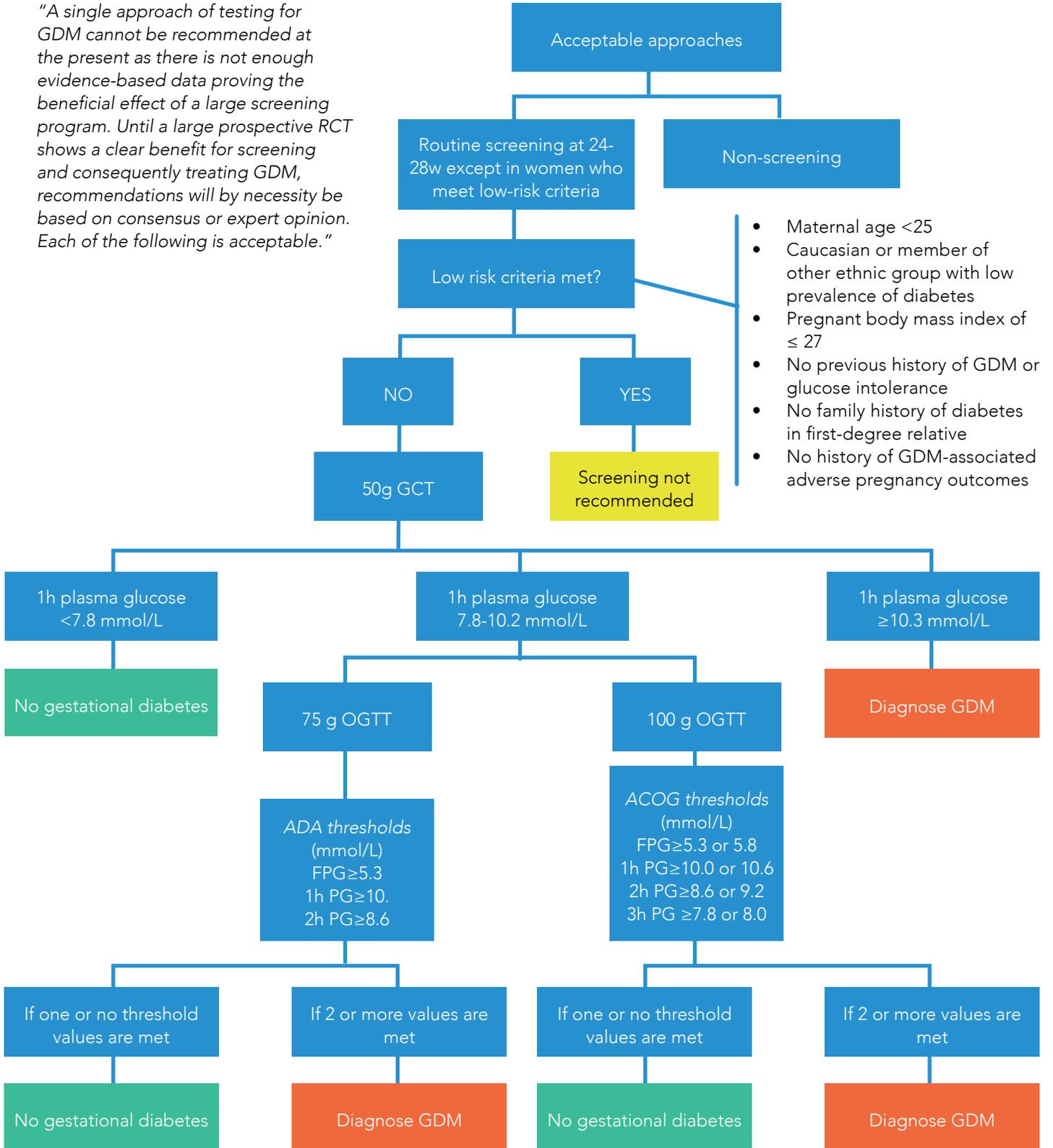


FIGURE 2: GESTATIONAL DIABETES SCREENING AND DIAGNOSIS ALGORITHM
2013 CDA AND 2016 SOGC CPGS (4,5)

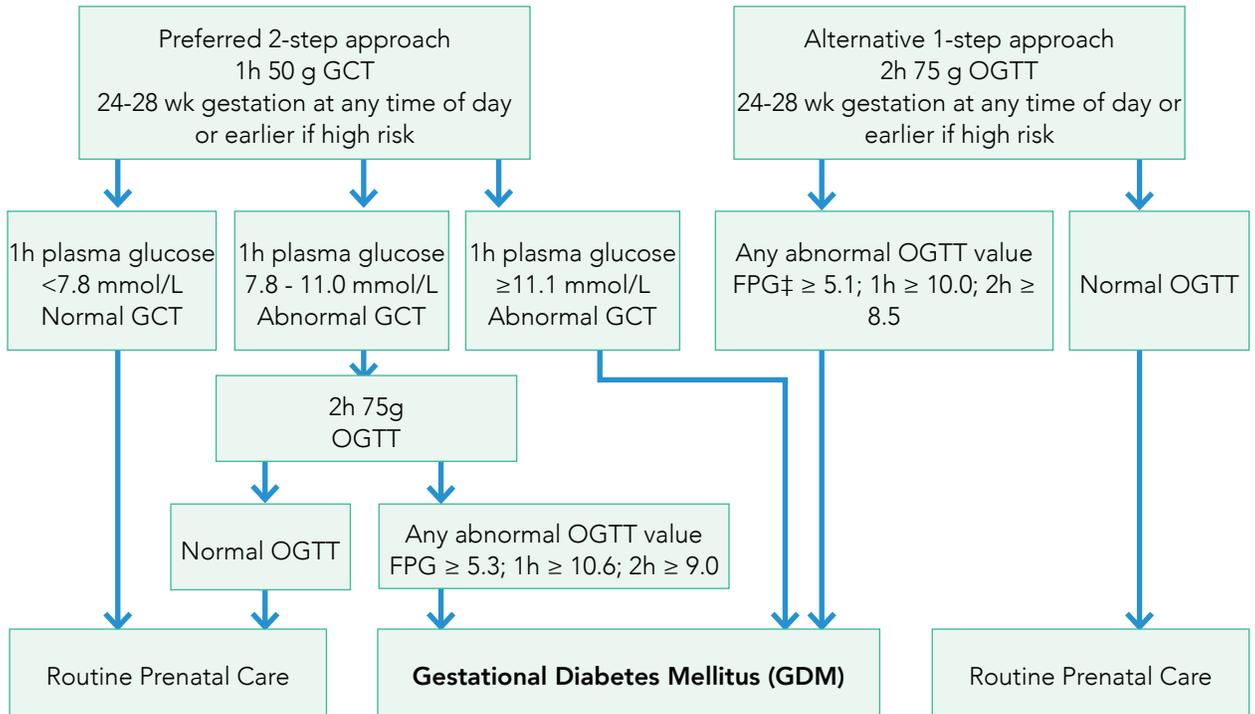


FIGURE 3: POSTPARTUM TESTING ALGORITHM WITH SUGGESTED GLYCEMIC VALUES
2016 SOGC CPG

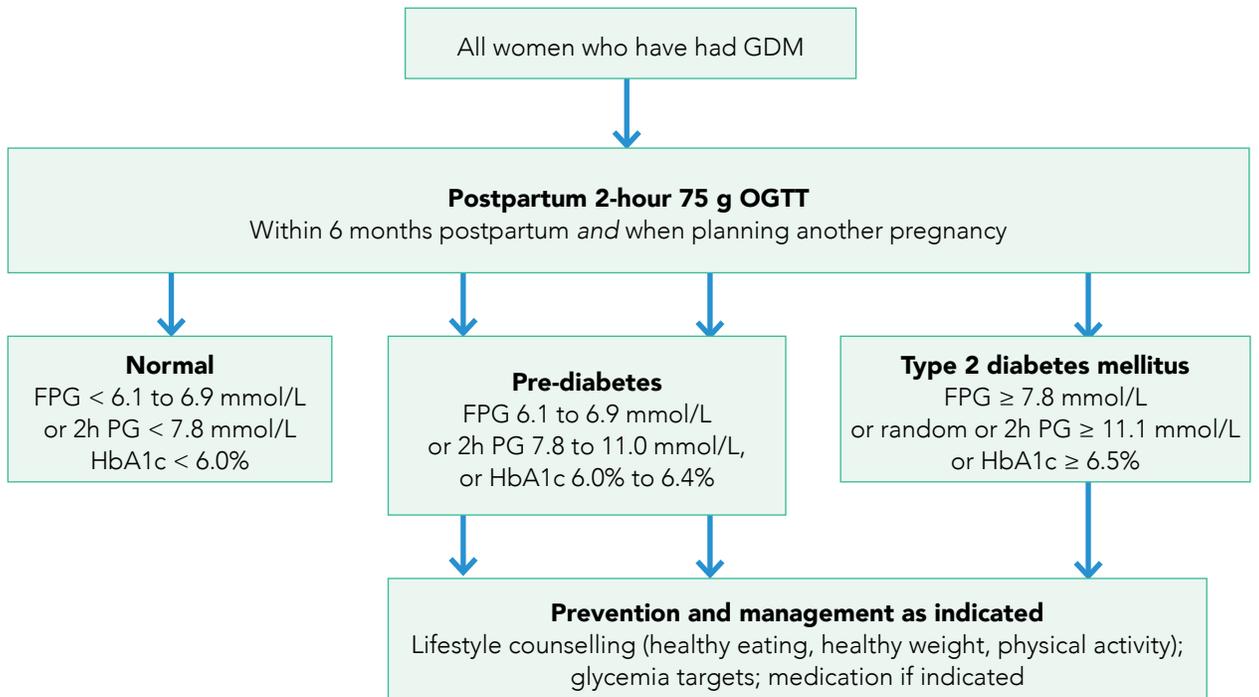


TABLE 5: A COMPARISON OF DIAGNOSTIC CRITERIA FOR GDM SCREENING AT 24-28 WEEKS

	Who is screened?	Test	GDM diagnosis threshold (equal to or greater than) (mmol/L)				Abnormal values required	Predicted incidence of GDM
			0h	1h	2h	3h		
<p>CDA and SOGC Preferred approach <i>Diabetes and Pregnancy, 2013 (4)</i> <i>Diabetes in Pregnancy, 2016 (5)</i></p> <p>Cut-offs represent glucose values associated with a doubling of odds for HAPO's primary outcomes (OR 2.0). The CDA's "preferred approach" that is "endorsed" by the SOGC involves sequential screening (50 g GCT followed by 75 g OGTT) and is less expensive and offers the same diagnostic power as one-step screening.</p>	<p>All clients (CDA) All clients offered screening (SOGC)</p>	<p>Two step: 50 g GCT ↓ 75 g OGTT</p>	5.3	10.6	9.0	-	One	3%-10% (5,40)
<p>CDA and SOGC Alternate approach <i>Diabetes and Pregnancy, 2013 (4)</i> <i>Diabetes in Pregnancy, 2016 (5)</i></p> <p>The CDA's "alternative one-step approach", termed "acceptable" by the SOGC, represents cut-off glucose values associated with a 1.75-fold increase (OR 1.75) in select pregnancy outcomes (based on HAPO)</p>	<p>All clients (CDA) All clients offered screening (SOGC)</p>	<p>One step: 75 g OGTT</p>	5.1	10.0	8.5	-	One	9%-16.1% (41-43)
<p>IADSPG <i>Recommendations on the Diagnosis and Classification of Hyperglycemia in Pregnancy, 2010 (1)</i></p> <p>Thresholds represent glucose values associated with a 1.75-fold increase in select adverse pregnancy outcomes (based on HAPO). A single abnormal value is required for diagnosis of GDM.</p>	<p>All clients without overt diabetes or GDM at early screening</p>	<p>One step: 75 g OGTT</p>	5.1	10.0	8.5	-	One	16.1% (1)
<p>SOGC <i>Screening for Gestational Diabetes Mellitus, 2002 (2)</i></p> <p>Guideline predates IADSPG recommendations. Glucose cut-offs are based on thresholds specified by the ADA (75 OGTT) or those specified by NDDG or Carpenter and Coustan.</p>	<p>Clients who do not meet criteria for low risk.* A policy of non-screening is also considered acceptable.</p>	<p>Two step: 50 g GCT ↓ 75 g OGTT or 100 g OGTT</p>	75 g				Two	Not known
			5.3	10.0	8.6	-		
			100 g					Not known
			5.3 or 5.8	10.0 or 10.6	8.6 or 9.2	7.8 or 8.0		
<p>NICE <i>Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period, 2015 (15)</i></p> <p>Threshold values were chosen based on health economic analyses showing that IADPSG criteria would result in a substantial increase in GDM diagnoses without clear benefit in maternal or neonatal outcomes or cost- effectiveness. The FPG cut-off represents a mid-point between the IADPSG criteria (5.1 mmol/L) and the WHO 1999 criteria used in the previous NICE guideline (6.1 mmol/L).</p>	<p>People with risk factors for GDM**</p>	<p>One step: 75 g OGTT</p>	5.6	7.8	-	One	Not known	

	Who is screened?	Test	GDM diagnosis threshold (equal to or greater than) (mmol/L)				Abnormal values required	Predicted incidence of GDM
			0h	1h	2h	3h		
<p>ACOG <i>Practice Bulletin No 137: Gestational Diabetes Mellitus, 2013 (13)</i></p> <p>States that application of IADPSG criteria and move to a one-step testing approach that requires only one abnormal value will increase the proportion of women who are diagnosed with GDM without clear evidence of significant benefit to maternal or neonatal outcomes. Diagnostic thresholds established by NDDG or Carpenter and Coustan (CC) are reasonable for continued use "in the absence of clear comparative trials."</p>	All pregnant people should be screened by medical history, clinical risk factors or laboratory screening tests.	Two step: 50 g GCT ↓ 100 g OGTT	5.3 or 5.8	10.0 or 10.6	8.6 or 9.2	7.8 or 8.0	Two	4%-7% (13)
<p>National Institutes of Health (NIH) <i>Consensus Development Conference Statement: Diagnosing Gestational Diabetes Mellitus, 2013 (17)</i></p> <p>Application of IADPSG criteria and move to a one-step testing approach that requires only one abnormal glucose value will increase the proportion of women who are diagnosed with GDM without clear evidence of benefit. Identifies potential consequences of higher rates of diagnosis, including "an increase in caesarean delivery and more intensive newborn assessments...increased patient costs, life disruptions, and psychosocial burdens." Recommends the two-step approach be continued until uncertainties about the value of the one-step approach are resolved.</p>	Not addressed	Two step: 50 g GCT ↓ 100 g OGTT	Recommends that professional organizations adopt a single standard for diagnostic thresholds (NDDG or CC)				N/A	Not known
<p>ADA <i>Diagnosis and Classification of Diabetes Mellitus, 2013 (44)</i></p> <p>Based on IADPSG criteria. ADA acknowledges that adopting IADPSG thresholds and would significantly increase the incidence of GDM but suggests that changes are warranted given "worrisome worldwide increases in obesity and diabetes rates [and] the intent of optimizing gestational outcomes for women and their babies."</p>	All people not known to have diabetes	One step: 75 g OGTT	5.1	10	8.5	-	One	4% to > 18% (44)
<p>WHO <i>Diagnostic Criteria and Classification of Hyperglycemia First Detected in Pregnancy, 2013 (8)</i></p> <p>Based on IADPSG criteria. Upper limits were added to aid identification of hyperglycemia likely associated with undiagnosed type 2 diabetes.</p>	All pregnant people should be screened by medical history, clinical risk factors or laboratory screening tests.	One step: 75 g OGTT	5.1 to 6.9	10.0	8.5 to 11	-	One	18% (8)

* SOGC - criteria for low risk: Maternal age < 25, Caucasian or member of other ethnic group with low prevalence of diabetes, pregnant body mass index of ≤ 27 kg/m², no previous history of GDM or glucose intolerance, no family history of diabetes in first-degree relative, no history of GDM-associated adverse pregnancy outcomes

** NICE - risk factors for GDM: BMI > 30kg/m², previous macrosomic baby, previous GDM, family history of diabetes, ethnic background with a high prevalence of diabetes

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