

Gestational Diabetes Screening and Treatment Guideline

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Guidelines are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for many patients with specific clinical problems or prevention issues, guidelines are not meant to replace the clinical judgment of the individual provider or establish a standard of care. The recommendations contained in the guidelines may not be appropriate for use in all circumstances. The inclusion of a recommendation in a guideline does not imply coverage. A decision to adopt any particular recommendation must be made by the provider in light of the circumstances presented by the individual patient.

Major Changes as of October 2015

The guideline team reviewed the 2011 Gestational Diabetes Guideline, determined there were no outstanding evidence gaps, and re-approved the guideline with no changes.

Screening Recommendations and Tests

Table 1. Recommendations for screening for previously undiagnosed diabetes and for gestational diabetes ¹			
Screen for	Eligible population	Recommended frequency	Recommended tests
Previously undiagnosed diabetes	All pregnant women ¹	Initial OB visit with nurse	HbA1c (as part of OB lab panel) If HbA1c screen is negative but diabetes is suspected due to symptoms, BMI, or ultrasound findings, a provocative test is recommended (2-hour oral glucose tolerance test with 75 g glucose load).
Gestational diabetes	Pregnant women at high risk for gestational diabetes ²	Consider screening earlier than 24–28 weeks gestation.	2-hour oral glucose tolerance test (OGTT) with 75 g glucose load
	Pregnant women not at high risk for gestational diabetes ²	Screen at 24–28 weeks gestation.	2-hour OGTT with 75 g glucose load
<p>¹ It is reasonable to exclude screening for previously undiagnosed diabetes if the woman is at low risk for diabetes and gestational diabetes. This would include women who are Caucasian, young (age < 25), thin, and with no personal or family history of diabetes.</p> <p>² Women at increased risk of diabetes or gestational diabetes include those with a history of gestational diabetes; BMI > 30; previous macrosomic baby (weighing ≥ 4.5 kg); first-degree relative with diabetes; ethnicity with high prevalence of diabetes (Hispanic, American Indian, African American, South Asian); or polycystic ovarian syndrome (PCOS).</p>			

Diagnosis

Table 2. Recommendations for confirming diabetes diagnosis		
Diagnosis	Recommended tests	Positive result parameters
Previously undiagnosed diabetes	HbA1c Confirm the diagnosis with a second test on a different day. The second test can be HbA1c, fasting plasma glucose or random plasma glucose. For more information about the diagnostic process, see the Type 2 Diabetes Guideline.	≥ 6.5%
Gestational diabetes at 24–28 weeks	2-hour glucose challenge after a 75 g glucose load	Fasting result ≥ 92 mg/dL or 1-hour result ≥ 180 mg/dL or 2-hour result ≥ 153 mg/dL ¹
<p>¹ One or more of these values from the 75 g OGTT must be equaled or exceeded for the diagnosis of gestational diabetes.</p>		

Treatment

Goals

Maintaining glycemic control will lead to improved pregnancy outcomes, including decreases in macrosomia, clinical neonatal hypoglycemia, and cesarean section rates.

Lifestyle modifications/non-pharmacologic options

Most women who have gestational diabetes can successfully control their blood glucose with diet and exercise. Initiate a trial of lifestyle modifications and provide information about diet and exercise.

Diet and nutrition

- Give simple messages about nutrition: decrease simple sugars, rely more on complex carbohydrates, and increase lean protein and vegetable consumption.
- Diet recommendations for women with gestational diabetes are different from those for non-pregnant women with diabetes, in that the diet for GDM includes both more protein and more fat.
- Among women with gestational diabetes, 75–80% can achieve normoglycemia through dietary changes.

Calorie distribution

Opinions regarding the optimal distribution of calories vary. Most programs suggest three meals and three snacks; however, in overweight and obese women the snacks are often eliminated. Listed below are recommendations for caloric distribution:

- Breakfast: 10% of total caloric allotment (Carbohydrate intake at breakfast is limited since insulin resistance is greatest in the morning.)
- Lunch: 30% of calories
- Dinner: 30% of calories
- Snacks: 30% of calories

Recommended overall total caloric distribution:

- Carbohydrate: 33–40%
- Protein: about 20%
- Fat: about 40%

Exercise

Moderate exercise is recommended by the American Diabetes Association (ADA):

- All women, including those who are pregnant, are encouraged to exercise 1 hour daily.
- The current intensity and type of exercise should be modified for obvious safety issues (e.g., activities involving balance, direct contact sports).

Pharmacologic options

Patient home glucose monitoring

Following the diagnosis of gestational diabetes, ask the patient to begin home glucose monitoring as outlined in Table 3. Ask her to report the results after 1 week of monitoring and every 2–3 weeks thereafter until she delivers. Let the patient know that she will be informed if any changes to her treatment are needed based on those results.

Glucose monitoring time	Goal
Fasting	Average < 90 mg/dL
Before lunch Before evening meal	Average < 90 mg/dL
1 hour after all meals	Average < 120 mg/dL

If the patient is maintaining good glucose control, consider decreasing her home monitoring to twice a day: fasting and 1 hour after the biggest meal.

However, the patient should return to the full Table 3 schedule:

- If, at any time, her average readings are not below target, and
- Periodically throughout pregnancy as her dietary needs change.

Initiation of pharmacologic treatment

Pharmacologic treatment is initiated if lifestyle measures are inadequate for reaching target blood glucose.

The glucose level for which pharmacotherapy's benefits clearly outweigh its disadvantages or harms has not been clearly established. The Hyperglycemia and Adverse Pregnancy Outcome trial (HAPO), a large observational trial, demonstrated that a fasting glucose level of > 105 mg/dL is associated with a five-fold increase in the risk of macrosomia compared to a fasting glucose level of < 75 mg/dL (25% versus 5%) (HAPO Study Cooperative Research Group 2008). Lower glucose levels were associated with better primary outcomes, but there were no obvious thresholds at which the risks increased. Since the HAPO trial, more organizations are recommending lower glucose targets.

This guideline recommends initiating pharmacologic treatment if, **during the previous week**, the patient's average readings are:

- Fasting plasma glucose: ≥ 90 mg/dL, **or**
- 1-hour postprandial glucose: ≥ 120 mg/dL

There is no direct evidence on which to establish treatment thresholds; therefore, if the patient would prefer a higher threshold before initiating pharmacotherapy—after a conversation about the risks of gestational diabetes and the benefits of tight glucose control has occurred—a higher target can be negotiated between the patient and her clinician.

Table 4. Recommended anti-hyperglycemic medications		
Population	Line	Medication
All women with gestational diabetes not controlled by diet and exercise	1 st	Insulin
Women with gestational diabetes not controlled by diet and exercise and unwilling to take insulin See “Prescribing notes.”	1 st	Metformin
	2 nd	Glyburide
Women taking metformin prior to pregnancy for the management of polycystic ovarian syndrome (PCOS)	See “Prescribing notes.”	

Prescribing notes for Table 4

Oral anti-hyperglycemic agents

Currently, the use of oral anti-hyperglycemic agents has not been approved by the FDA for treatment of gestational diabetes. Reserve oral diabetes agents for women who fail nutritional therapy and cannot or refuse to take insulin. If oral diabetes agents are used, patients should be clearly informed that these drugs cross the placenta and may have unknown risks to the fetus.

Metformin

There is insufficient evidence on which to base recommendations for continuing metformin during pregnancy for the management of PCOS. The harms of discontinuation include possible increased risk of miscarriage. If metformin is stopped, monitor glucose with the goal of FPG < 90 mg/dL and 1-hour postprandial < 120 mg/dL.

- If the patient received clear instructions from her prescribing specialist about what to do if she became pregnant while on metformin, she should continue following that advice.
- For those who did not receive clear advice, the decision about tapering or changing medications should be individualized between the patient and her physician. It is likely that a transition to insulin would be accompanied by a tapering of metformin as plasma glucose levels are monitored.

Table 5. Insulin dosing recommendations			
Long-acting insulin analogs (insulin glargine, insulin detemir) are not recommended, as they have not been studied extensively in pregnancy.			
Step 1: Control fasting hyperglycemia by initiating insulin therapy with NPH. (Goal: average weekly fasting blood glucose < 90 mg/dL—see Table 3.)			
Medication	Frequency	Starting dose	Modified dose
NPH	The entire dose is taken at bedtime.	0.2 units/kg	Every 4 days; if 4-day average is ≥ 90 mg/dL, increase dose by 2 units until 4-day average fasting blood glucose is < 90 mg/dL.
Step 2: After controlling fasting hyperglycemia, control postprandial readings with insulin aspart. (Goal: average weekly postprandial readings < 120 mg/dL—see Table 3.)			
Medication	Frequency	Starting dose	Modified dose
Insulin aspart	If for any meal the 1-hour postprandial reading is <i>persistently</i> ≥ 120 mg/dL, add insulin aspart to be taken at that meal.	1 unit aspart per 10 g carbohydrate	Increase aspart to 2 units per 15 g carbohydrate until 1-hour postprandial reading is < 120 mg/dL.
Step 3: If control is still not adequate, contact diabetes expert David McCulloch, MD for advice on additional adjustments.			

Table 6. Oral medication options for glycemic control for women who will not take insulin

Eligible population	Medication	Starting dose	Titration
Pregnant women unable or unwilling to take insulin	Metformin See "Prescribing notes."	250 mg once daily	500 mg b.i.d. to 850 mg t.i.d.
	Glyburide See "Prescribing notes."	2.5–5.0 mg daily at first meal	2.5 mg once daily to 7.5 mg b.i.d.
Pregnant women above goal on oral medication	Switch to insulin.	—	—

Prescribing notes for Table 6**Metformin**

Metformin should be titrated as tolerated. A reasonable initial titration schedule is:

- a) 500 mg ½ tab (250 mg) PO once daily x 7 days;
- b) 500 mg 1 tab PO once daily x 7 days;
- c) 500 mg 1 tab PO b.i.d.

If a patient does not experience any GI side effects after 2–3 days, the dose may be titrated to goal more quickly.

If a patient develops GI side effects, reduce the dose and reassess. Consider a more conservative titration schedule starting with 500 mg ¼ tab (125 mg) PO once daily; alternatively, consider prescribing the XL formulation for patients who cannot tolerate ideal dose with regular release formulation. Some patients (young, obese, and without GI side effects) may tolerate metformin up to 3,000 mg daily; consider consultation with a diabetes expert.

Glyburide

While the maximum dose is glyburide 10 mg b.i.d., the medication's effectiveness has been found to plateau at 5.0–7.5 mg b.i.d.

Additional Testing/Monitoring

Monitoring before delivery

The following antenatal tests are **not recommended**:

- Ultrasound to estimate fetal weight
- Ketone checking

Timing of delivery

There is no evidence on which to base the optimal timing for delivery.

- For women with good glucose control, induction before 40 weeks is not indicated.
- For women on insulin, consider induction at 39 weeks and no later than 41 weeks.

Follow-up after delivery

Gestational diabetes is a risk factor for type 2 diabetes. While only about 5% of women who have gestational diabetes develop type 2 diabetes within 6 months of delivery, about 60% will develop type 2 diabetes within 10 years (Hartling 2012). Encourage a healthy diet, exercise, and weight control to prevent type 2 diabetes.

Table 7. Recommended follow-up testing		
Eligible population	Test	Frequency/timing
All women with gestational diabetes (place order at 4-week postpartum visit)	HbA1c	3 months postpartum
All women with a history of gestational diabetes	HbA1c	Annually

Referral

- Consider a consult with an obstetrician if the estimated fetal weight is $\geq 4,500$ g.
- Unless additional issues arise, women taking insulin for gestational diabetes do not need to be managed by an obstetrician.

Evidence Summary

To develop the Gestational Diabetes Screening and Treatment Guideline, the guideline team has adapted recommendations from the following externally developed evidence-based guidelines:

- Scottish Intercollegiate Guideline Network (SIGN). *Management of diabetes: a national clinical guideline*. Edinburgh: SIGN 2010 (SIGN publication no.116, cited September 2010).
- International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care*. 2010;33(3):676-682.
- National Institute for Health and Care Excellence (NICE). *Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period*. London: NICE 2015 (NICE guideline NG3).
- Moyer VA for the U.S. Preventive Services Task Force. Screening for gestational diabetes mellitus: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014 Mar 18;160(6):414-420.

Treatment

Oral hypoglycemics

Metformin

There is insufficient evidence to determine exactly how safe and effective metformin is for the treatment of gestational diabetes. Metformin has been found to cross the placenta (Charles 2006). A recent randomized controlled trial evaluating the safety and efficacy of metformin compared to insulin for the treatment of gestational diabetes found no significant difference between the two groups in the primary outcome measure, which was a composite of neonatal hypoglycemia, respiratory distress, need for phototherapy, birth trauma, 5-minute Apgar score < 7, and prematurity. However, 46.3% of women in the metformin group needed supplemental insulin to control their GDM (Rowan 2008). Another randomized controlled trial compared metformin to glyburide for controlling blood glucose. There was no significant difference in blood glucose levels; however, significantly more patients in the metformin group required insulin therapy to control blood glucose levels (Moore 2010).

Glyburide

There is insufficient evidence to determine exactly how safe and effective glyburide is for the treatment of gestational diabetes. Early studies reported little to no transfer of glyburide across the umbilical cord; however, a recent prospective cohort study found that umbilical cord plasma concentrations of glyburide averaged 70% of maternal concentrations (Hebert 2009). The effect of glyburide and insulin on neonatal body composition was evaluated in a recent randomized controlled trial. There was no significant difference between the groups in the primary outcome measure of percentage neonatal fat mass; however, mean birth weight and the rate of macrosomia were significantly higher for neonates whose mothers were treated with glyburide compared to neonates whose mothers were treated with insulin (Lain 2009).

Follow-up

Screening for type 2 diabetes

There is good evidence from a meta-analysis of 20 cohort studies that women with a history of GDM are at increased risk of developing type 2 diabetes (RR 7.43; 95% CI, 4.79–11.51) and should be screened for the development of type 2 diabetes (Bellamy 2009). Results from a recent cohort study indicate that for women with a history of gestational diabetes the probability of developing diabetes was 3.7% at 9 months after delivery, 4.9% at 15 months, 13.1% at 5.2 years, and 18.9% at 9 years. For women without a history of GDM, the probability of developing diabetes at 9 years after delivery was 1.95% (Feig 2008).

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Guideline Development Process and Team

Development process

To develop the Gestational Diabetes Screening and Treatment Guideline, the guideline team adapted recommendations from externally developed evidence-based guidelines.

This edition of the guideline was approved for publication by the Guideline Oversight Group in October 2015.

Team

The Gestational Diabetes Screening and Treatment Guideline development team included representatives from Clinical Improvement & Prevention and Obstetrics/Gynecology.

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Disclosure of conflict of interest

Kaiser Permanente requires that team members participating on a guideline team disclose and resolve all potential conflicts of interest that arise from financial relationships between a guideline team member or guideline team member's spouse or partner and any commercial interests or proprietary entity that provides or produces health care-related products and/or services relevant to the content of the guideline.

Team members listed above have disclosed that their participation on the Gestational Diabetes Guideline team includes no promotion of any commercial products or services, and that they have no relationships with commercial entities to report.