

Gestational Diabetes Screening and Treatment Guideline

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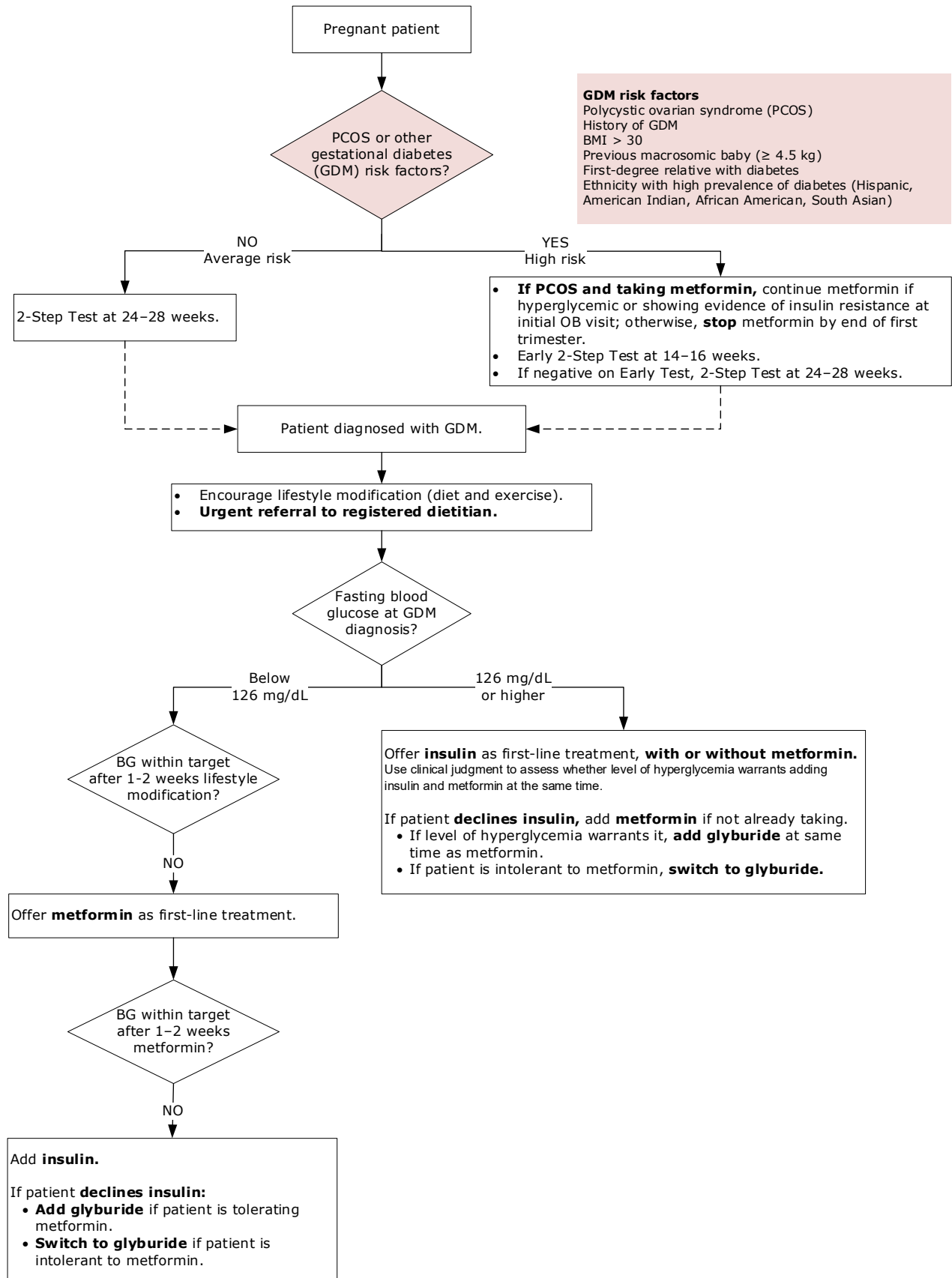
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Guidelines are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for 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 2024

- Insulin glargine is now the preferred basal insulin at Kaiser Permanente (prior authorization not needed). Previously, NPH was the preferred basal insulin. Glargine dosing recommendations for patients with GDM are provided in Table 4.
- Glyburide is no longer recommended as the third-line treatment for GDM due to possible risks to the fetus. Women with GDM who are unwilling to take insulin may still be prescribed glyburide if they have an intolerance or failure of metformin, but information about the risks of glyburide should be provided.
- The recommended metformin dosing frequency for GDM has been changed to twice daily, to align with the dosing frequency for type 2 diabetes and improve adherence. The previous recommendation called for metformin three times daily.
- A minimum daily intake of 175 g carbohydrates is now recommended to avoid increased ketone levels in the mother and fetus.

Screening and Treatment Flowchart



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 patients 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-step oral glucose tolerance test). |
| Gestational diabetes | Pregnant patients at high risk for GDM ² | Consider screening at 14–16 weeks gestation. | 2-step oral glucose tolerance test |
| | Pregnant patients not at high risk for GDM ² | Screen at 24–28 weeks gestation. | |
| <p>¹ It is reasonable to exclude screening for previously undiagnosed diabetes if the patient is at low risk for diabetes and gestational diabetes. This would include patients who are Caucasian, young (age < 25), thin, and with no personal or family history of diabetes.</p> <p>² Patients 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 | <p>HbA1c</p> <p>Confirm the diagnosis with two tests done the same day: HbA1c and either fasting plasma glucose or random plasma glucose.</p> <ul style="list-style-type: none"> Abnormal results on both tests are diagnostic of diabetes. If only one test produces an abnormal result, that test should be repeated. <p>For more information about the diagnostic process, see the Type 2 Diabetes Guideline.</p> | ≥ 6.5% |
| Gestational diabetes at 24–28 weeks | <p>2-step oral glucose tolerance test</p> <p>Step 1 is nonfasting 1-hour 50 mg glucose tolerance test.</p> <ul style="list-style-type: none"> 1-hour result < 135 mg/dL is considered normal. No more testing required. 1-hour result between 135 mg/dL and 200 mg/dL is considered abnormal and the patient needs to move on to step 2. 1-hour result ≥ 200 mg/dL is considered diagnostic of GDM and does not require any further diagnostic tests. <p>Step 2 is fasting 2-hour 75 mg glucose tolerance test. The patient is diagnosed with GDM if any one of these three values is abnormal:</p> <ul style="list-style-type: none"> Fasting ≥ 95 mg/dL 1-hour ≥ 180 mg/dL 2-hour ≥ 162 mg/dL | |

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 patients 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 patients with gestational diabetes are different from those for non-pregnant patients with diabetes, in that the diet for GDM includes both more protein and more fat.
- Among patients 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 patients with overweight or obesity the snacks are often eliminated. 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%

Note: A minimum of 175 g carbohydrates daily is recommended to avoid increased ketone levels in the mother and fetus.

Exercise

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

- All patients, 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

Patients taking metformin for PCOS prior to pregnancy

There is insufficient evidence on which to make a strong recommendation about whether to continue metformin during pregnancy for the management of PCOS. Due to limited evidence that suggests that stopping metformin decreases the risks of adverse pregnancy outcomes, including first-trimester loss, we recommend stopping metformin by the end of the first trimester of pregnancy; however, if such a patient is found to have hyperglycemia or evidence of insulin resistance at the initial OB visit, the metformin should be continued.

Initiation of pharmacologic treatment

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

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

- Fasting plasma glucose ≥ 95 mg/dL, **or**
- 1-hour postprandial glucose ≥ 140 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 patient and clinician.

Note: While **oral anti-hyperglycemic agents** have been used for years to treat gestational diabetes, their use for this purpose has not been approved by the FDA. 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 is preferred over insulin for patients with fasting blood glucose < 126 mg/dL because, as compared to insulin, metformin use is associated with lesser maternal weight gain and lower incidences of pregnancy-induced hypertension and neonatal hypoglycemia (Society for Maternal Fetal Medicine 2018). In addition, metformin can be started immediately, unlike insulin, which usually has a delayed start due to the wait for an RN insulin teaching appointment.

Table 3. Recommended anti-hyperglycemic medications for patients with gestational diabetes

| Population | Preferred | If needed |
|--|-----------|-----------------------------|
| Fasting blood glucose 126 mg/dL or higher | Insulin | Add metformin. ¹ |
| Fasting blood glucose between 95 and 126 mg/dL and GDM not controlled by diet and exercise | Metformin | Add insulin. |

¹ Use clinical judgment to assess whether level of hyperglycemia warrants adding insulin and metformin at the same time.

Patients unwilling to take insulin

For patients with uncontrolled GDM who are unwilling to take insulin:

1. **Offer metformin.**
2. If fasting blood sugar not adequately controlled with metformin: Continue metformin and **revisit the insulin discussion; add glyburide** if still unwilling to take insulin.*
3. If intolerant to metformin and continues to be unwilling to take insulin: **Switch to glyburide.***

***Provide information about the risks of glyburide.** Compared to insulin therapy, glyburide may be associated with a higher risk of neonatal hypoglycemia, higher birth weight, macrosomia, and greater NICU admission duration. The [Society for Maternal Fetal Medicine Statement on Pharmacologic Treatment of GDM \(2018\)](#) concludes that glyburide is inferior to both insulin and metformin. Both the American Diabetic Association (2023) and American College of Obstetrics and Gynecology (2023) recommend **against** the use of glyburide as a first-line agent.

If glyburide is prescribed, the dosages are:

- Starting: 2.5–5.0 mg daily at first meal
- Titration: 2.5 mg once daily to 7.5 mg b.i.d.

Prescribing notes

- Glyburide should not be used concurrently with insulin.
- 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.

Table 4. Insulin dosing recommendations

Step 1: Control fasting hyperglycemia by initiating insulin therapy with glargine. (Goal: average weekly fasting blood glucose < 95 mg/dL—see Table 6.)

| Medication | Frequency | Starting dose | Modified dose |
|------------|--|---|---|
| Glargine | Administer once daily either each morning or bedtime | Start insulin glargine 0.2 – 0.4 u/kg: <ul style="list-style-type: none">• If fasting glucose is 95–126, start 0.2 u/kg• If fasting glucose if 126–140, start 0.3 u/kg• If fasting glucose is above 140, start 0.4 u/kg | Titration of glargine, increase by 2–4 units every week or 10 to 20% of insulin glargine titration every 3 to 5 days to achieve the fasting glucose < 95 |

Step 2: After controlling fasting hyperglycemia, control postprandial readings with insulin lispro (Goal: average weekly 1-hour postprandial readings < 140 mg/dL—see Table 6.)

| Medication | Frequency | Starting dose | Modified dose |
|----------------|--|---|---|
| Insulin lispro | If for any meal the 1-hour postprandial reading is <i>persistently</i> ≥ 140 mg/dL, add insulin lispro to be taken at that meal. | 1 unit lispro per 10 g carbohydrate at largest meal | Adjust lispro 20% titration every 2 to 3 days until 1-hour postprandial glucose goal < 140. Do not exceed 40% basal and 60% bolus. |

Step 3: If control is still not adequate, contact the Diabetes Team for advice on additional adjustments.

| Table 5. Oral medication dosing recommendations | | |
|--|-------------------|--|
| Medication | Starting dose | Titration |
| Metformin | 500 mg once daily | Metformin should be titrated as tolerated. ¹ A reasonable initial titration schedule is: <ol style="list-style-type: none"> 500 mg PO once daily x 3 days; 500 mg PO twice daily x 3 days; 1000 mg PO twice daily until delivery |
| ¹ If a patient does not experience any GI side effects, the dose may be titrated more quickly to goal of 1000 mg twice daily. If a patient develops GI side effects, consider starting insulin. Alternatively, consider prescribing the extended-release (XR) formulation for patients who have GI side effects with the immediate-release (IR) formulation. <i>Note:</i> Maximum dose for the XR formulation is 2000 mg per day, while maximum dose for the IR formulation is 2550 mg per day. | | |

Additional Testing/Monitoring

Patient home glucose monitoring

Following the diagnosis of gestational diabetes, ask patients to begin home glucose monitoring as outlined in Table 6. Ask them to report the results after 1 week of monitoring and every 2–3 weeks thereafter until delivery. Let patients know that they will be informed if any changes to treatment are needed based on those results.

| Table 6. Home glucose monitoring for patients with gestational diabetes | |
|---|---------------------|
| Glucose monitoring time | Goal |
| Fasting | Average < 95 mg/dL |
| Before lunch Before evening meal | Average < 95 mg/dL |
| 1 hour after all meals | Average < 140 mg/dL |

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

However, the patient should return to the full Table 6 schedule:

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

Antenatal monitoring

There is no evidence on which to base the optimal timing for delivery, ultrasound for fetal weight and amniotic fluid index, or for non-stress testing, so the following recommendations are based on community standards and expert opinion.

| | GDM diet controlled/GDM A1 | GDM med/insulin controlled/GDM A2 | GDM poorly controlled |
|--|-----------------------------------|--|---|
| Non-stress test | Not standard practice | Start at 32 weeks/ twice weekly | Start at 32 weeks/ twice weekly |
| Ultrasound for fetal weight (estimated fetal weight) | Not standard practice | Start at 30–32 weeks Consider repeat in 4–6 weeks | Start at 30–32 weeks/ Consider repeat in 4–6 weeks |
| Amniotic fluid index/ maximum vertical pocket | Not standard practice | Start at 32 weeks/ once weekly | Start at 32 weeks/ once weekly |
| Induction of labor | Consider between 40w0d and 40w6d | Consider between 39w0d and 39w6d | Consider between 38w0d and 38w6d |

Ketone checking is *not* recommended as an antenatal test.

Follow-up after delivery

Gestational diabetes is a risk factor for type 2 diabetes. While only about 5% of patients 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.

| Eligible population | Test | Frequency/timing |
|---|-------------|-------------------------|
| All patients with gestational diabetes (place order at 4-week postpartum visit) | HbA1c | 3 months postpartum |
| All patients with a history of gestational diabetes | HbA1c | Annually |

Referral

- Family medicine providers or ARNP midwives should consult with an obstetrician if the estimated fetal weight is $\geq 4,500$ g, or if the non-stress test or amniotic fluid index is abnormal.
- Obstetricians should consider a consult with Maternal Fetal Medicine if early induction of labor is being considered (at 38 weeks gestation or earlier).
- Patients with gestational diabetes (regardless of whether they are taking insulin) do not need to be managed by an obstetrician unless specific issues arise.
- All patients diagnosed with gestational diabetes should be referred to a registered dietitian for nutritional counseling. (Order as urgent referral to avoid delays.)

Evidence Summary

The Gestational Diabetes Guideline was developed using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis.

As part of our improvement process, the Kaiser Permanente Washington guideline team is working towards developing new clinical guidelines and updating the current guidelines regularly. To achieve this goal, we are adapting evidence-based recommendations from high-quality national and international external guidelines, if available and appropriate. The external guidelines should meet several quality standards to be considered for adaptation. They must: be developed by a multidisciplinary team with no or minimal conflicts of interest; be evidence-based; address a population that is reasonably similar to our population; and be transparent about the frequency of updates and the date the current version was completed.

In addition to identifying the recently published guidelines that meet the above standards, a literature search was conducted to identify studies relevant to the key questions that are not addressed by the external guidelines.

External guidelines eligible for adapting

- [Updated ACOG Guidance on Gestational Diabetes 2023](#)
- [American Diabetes Association ADA 2023: Management of Diabetes in Pregnancy](#) (ElSayed 2023)
- [National Institute for Health and Care Excellence \(NICE\) Diabetes in Pregnancy 2023](#)
- [American Association of Clinical Endocrinology \(AACE\) Clinical Practice 2022: Developing a Diabetes Mellitus Comprehensive Care Plan—2022 Update](#) (Blonde 2022)
- [Gestational diabetes mellitus \(GDM\)](#) (Queensland Clinical Guidelines 2022)
- [Society of Obstetricians and Gynecologists \(SOGC\) of Canada Guideline No. 393-Diabetes in Pregnancy](#) (Berger 2019)
- [Diabetes and Pregnancy](#) (Diabetes Canada Clinical Practice Guidelines Expert Committee 2018)

Key questions

1. **In pregnant women with gestational diabetes (GDM), what is the comparative effectiveness and safety of metformin versus insulin on short- and long-term maternal and fetal outcomes? (Outcomes include preventing macrosomia and reducing the risk of preeclampsia, cesarean section, intrauterine fetal death, and neonatal complications, including shoulder dystocia and birth trauma.)**
 - The ADA 2023 and ACOG 2023 guidelines recommend against the use of metformin as a first-line agent in women with GDM who need pharmacological therapy.
 - More recently published meta-analyses, including Wu 2024 and Zhang 2024, do not add or change the findings of the earlier 2021 evidence review.
 - Overall, the results of the meta-analyses showed no statistically significant differences between metformin and insulin in glycemic control in women with GDM, and suggest that metformin may have short-term advantages over insulin for several maternal and neonatal outcomes, including the reduction of maternal weight gain, pregnancy-induced hypertension, incidence of neonatal hypoglycemia, macrosomia, and NICU admission.
 - The short-term follow-up data from the studies included in the two meta-analyses limits the ability to assess the long-term safety of metformin for the child.
 - Very weak evidence from small observational follow-up studies with limitations (Paavilainen 2020 and 2023) suggests that the use of metformin versus insulin for the management of women with GDM may not be associated with clinically significant long-term adverse effects on the offspring in terms of development, anthropometrical measures, and cognitive and neuropsychological function.
 - In the MiGTOFU offspring follow-up study (Rowan 2018), no differences were found between the offspring of mothers with GDM treated with metformin versus those treated with insulin in terms of

total and abdominal body fat percent and metabolic measures at 7–9 years. Metformin-exposed children, however, were larger at 9 years.

- More evidence is needed to determine the long-term effect of metformin on children exposed to the drug in the womb.

2. In pregnant women with GDM, what is the comparative effectiveness and safety of glyburide versus insulin on short- and long-term maternal and fetal outcomes?

- The ADA 2023 and ACOG 2023 guidelines recommend against the use of glyburide as a first-line agent to women with GDM who need pharmacological therapy.
- The Li 2022 meta-analysis evaluated the safety and effectiveness of oral hypoglycemic agents used in women with GDM. The meta-analysis included 26 trials (5 trials compared insulin to glyburide, 4 compared glyburide to metformin, and 17 compared insulin to metformin). There was significant heterogeneity between the studies for many of the outcomes, and the number and size of studies on glyburide were relatively small and insufficient to provide statistical power to detect significant differences between the use of glyburide and insulin or metformin.
- The studies comparing maternal and neonatal outcomes with glyburide versus insulin in women with GDM were limited in number and size, which for many outcomes did not provide sufficient power to detect significant differences between the two therapies. However, some authors interpreted the therapies as being similar in effectiveness and safety.
- There is a lack of studies with long-term follow-up to determine the long-term safety of the drugs on the mother and her offspring.
- There are some variations between the published studies and meta-analyses in the short-term efficacy and safety outcomes of glyburide versus insulin.
- The overall results suggest that:
 - Compared to insulin therapy, glyburide may be associated with a higher risk of neonatal hypoglycemia, higher birth weight, macrosomia, and NICU admission duration (Zeng 2014, Song 2017, Guo 2018, Helal 2020).
 - The limited number of published studies comparing metformin to glyburide suggest that metformin may be associated with a lower incidence of induction of labor and lower gestational weight gain, but glyburide may be superior in controlling fasting blood glucose.
- More evidence is needed to determine the long-term effect of glyburide on children exposed to the drug in the womb.

3. In pregnant women with polycystic ovarian syndrome (PCOS) whose HbA1c at the first prenatal visit did not detect DM, what is the comparative efficacy of screening for GDM at 12–14 weeks gestation versus the routine 24–28 weeks?

There is insufficient published evidence to determine whether screening women with PCOS for GDM prior to the standard screening for GDM at 24 weeks gestation would improve the maternal and fetal pregnancy outcomes.

4. In pregnant women with PCOS, what is the comparative safety and effectiveness of continuing the use of preconception metformin during pregnancy versus discontinuing it, adding insulin, or replacing it with insulin?

- There is insufficient evidence from published, well-designed, large randomized controlled trials (RCTs) to determine the efficacy and safety of continuing, discontinuing, or adding insulin to preconception metformin therapy in women with PCOS who become pregnant.
- The published trials and meta-analyses mainly investigated the use of metformin therapy initiated in the first trimester in women with PCOS.
- Only one systematic review with meta-analysis of both RCTs and observational studies (Cheshire 2023) investigated the effect on pregnancy outcomes of continuing preconception metformin through at least the first trimester in women with PCOS. However, those findings were published only in the article abstract and were not critically appraised. Based on the pooled results, the authors concluded that continuing metformin treatment until at least the end of first trimester can increase the clinical pregnancy rate and reduce the risk of miscarriage, and that stopping it once

pregnant could be harmful and increase the risk of miscarriage. The effectiveness and safety of continuing metformin throughout the remainder of the pregnancy is unclear.

- The overall results of qualitative and quantitative systematic reviews of studies investigating the maternal and offspring effects of metformin therapy initiated early in pregnancy in women with PCOS (Kanda 2023, Zhu 2022, Zhao 2022) suggest that:
 - The use of metformin during pregnancy in women with PCOS is associated with a significantly lower risk of pregnancy-induced hypertension and preeclampsia, preterm delivery, and macrosomia.
 - Metformin may improve insulin resistance in the mothers.
 - The effects of metformin therapy on increasing the rate of live birth and lowering the rate of miscarriage, risk of GDM, and need for adding insulin therapy were inconsistent among the published reviews.
- The analyses showed that, for the offspring, the use of metformin during pregnancy increased the risk of larger head circumference at birth and may be associated with higher BMI and obesity in the long term.
- High-quality RCTs with larger sample size are needed to provide evidence on the effectiveness and safety of continuing or stopping preconception metformin therapy after pregnancy in women with PCOS.

5. In women with GDM, what is the comparative safety and efficacy of tight versus liberalized intrapartum glycemic control on maternal and neonatal blood glucose level after birth?

- There is insufficient good-quality evidence from large multicenter RCTs to determine the optimal intrapartum glycemic control regimen in mothers with GDM.
- Very weak evidence from one single-center small RCT (Hamel 2019) suggests that tight intrapartum glycemic control in women with GDM may not be superior to liberalized glycemic control in lowering the risk of hypoglycemia in the newborn.
- Due to lack of evidence from larger published RCTs to determine the optimal glucose level during labor, the published guidelines vary in their recommendations, from advocating tight control (4.0–7.0 mmol/L), to a more liberal range (5.0–8.0 mmol/L), to making no specific recommendation.

6. In women with GDM, what is the comparative safety and efficacy of continuous glucose monitoring (CGM) monitoring versus conventional self-monitoring of blood glucose (SMBG) on maternal and composite neonatal outcomes?

- There is insufficient published evidence to support the use of CGM on improving overall health outcomes in women with GDM and their neonates.
- The AACE and NICE guidelines consider using CGM only for insulin-treated patients who experience severe hypoglycemic events.

7. In women with GDM, what is the comparative safety and effectiveness of low versus higher carbohydrate intake during pregnancy on short- and long-term maternal and fetal outcomes?

- There is insufficient published evidence to determine the comparative safety and effectiveness of low-, moderate-, and high-carbohydrate diets on the pregnancy and fetal outcomes in women with GDM.
- Weak evidence from a recently published meta-analysis (Wong 2024) of RCTs with limitations suggests that there are no significant differences between a low-carbohydrate diet and usual care, or between a low glycemic index diet and usual care in the maternal or pregnancy outcomes examined. The only significant difference observed was the lower rate of macrosomia in women following a low glycemic load diet compared to those on usual care.
- To determine the optimal carbohydrate intake for the health of mother and newborn, there is a need for prospective RCTs with more reliable diet reporting and control of confounders (such as medication, energy intake, physical activity, and dietary adherence) that compare low-carbohydrate diets and higher-carbohydrate energy-balanced diets in women with GDM.

8. In women with GDM on a low-carbohydrate diet, what is the threshold for restricting carbohydrate intake that is safe for the pregnant woman and her offspring? What level of carbohydrate restriction leads to increased ketone levels in the mother and higher exposure of the fetus to the maternal ketones?

- There is insufficient published evidence to determine the threshold for restricting carbohydrate intake that is safe for the pregnant woman and her offspring.
- There is insufficient published evidence to determine the effects of a carbohydrate intake below the recommended 175 g/d on increasing the ketone levels in pregnant women with diabetes or GDM, and the effects of exposing the fetus to maternal ketones on the short- and long-term outcomes.

References

Berger H, Gagnon R, Sermer M. Guideline No. 393-Diabetes in Pregnancy [published correction appears in *J Obstet Gynaecol Can*. 2020 Oct;42(10):1288. doi: 10.1016/j.jogc.2020.08.012]. *J Obstet Gynaecol Can*. 2019;41(12):1814-1825.e1. doi:10.1016/j.jogc.2019.03.008

Blonde L, Umpierrez GE, Reddy SS, et al. American Association of Clinical Endocrinology Clinical Practice Guideline: Developing a Diabetes Mellitus Comprehensive Care Plan-2022 Update [published correction appears in *Endocr Pract*. 2023 Jan;29(1):80-81. doi: 10.1016/j.eprac.2022.12.005]. *Endocr Pract*. 2022;28(10):923-1049. doi:10.1016/j.eprac.2022.08.002

Cheshire J, Garg A, Smith P, P-665. Timing of metformin treatment in women with polycystic ovarian syndrome and associated pregnancy outcomes: a systematic review and meta-analysis. *Human Reproduction*. June 2023;38(S1). <https://doi.org/10.1093/humrep/dead093.991>

Diabetes Canada Clinical Practice Guidelines Expert Committee, Feig DS, Berger H, et al. Diabetes and Pregnancy [published correction appears in *Can J Diabetes*. 2018 Jun;42(3):337. doi: 10.1016/j.jcjd.2018.04.006]. *Can J Diabetes*. 2018;42 Suppl 1:S255-S282. doi:10.1016/j.jcjd.2017.10.038

EISayed NA, Aleppo G, Aroda VR, et al. 15. Management of Diabetes in Pregnancy: Standards of Care in Diabetes-2023. *Diabetes Care*. 2023;46(Suppl 1):S254-S266. doi:10.2337/dc23-S015

Guo L, Ma J, Tang J, Hu D, Zhang W, Zhao X. Comparative Efficacy and Safety of Metformin, Glyburide, and Insulin in Treating Gestational Diabetes Mellitus: A Meta-Analysis. *J Diabetes Res*. 2019;2019:9804708. Published 2019 Nov 4. doi:10.1155/2019/9804708

Hamel MS, Kanno LM, Has P, Beninati MJ, Rouse DJ, Werner EF. Intrapartum Glucose Management in Women With Gestational Diabetes Mellitus: A Randomized Controlled Trial. *Obstet Gynecol*. 2019;133(6):1171-1177. doi:10.1097/AOG.0000000000003257

Helal KF, Badr MS, Rafeek ME, Elnagar WM, Lashin ME. Can glyburide be advocated over subcutaneous insulin for perinatal outcomes of women with gestational diabetes? A systematic review and meta-analysis. *Arch Gynecol Obstet*. 2020;301(1):19-32. doi:10.1007/s00404-019-05430-3

Kanda S, Chatha U, Odoma VA, et al. Effect of Metformin (MTF) Intervention During Pregnancy in Women With Polycystic Ovarian Syndrome (PCOS): A Systematic Review. *Cureus*. 2023;15(8):e44166. Published 2023 Aug 26. doi:10.7759/cureus.44166

Li C, Gao C, Zhang X, Zhang L, Shi H, Jia X. Comparison of the effectiveness and safety of insulin and oral hypoglycemic drugs in the treatment of gestational diabetes mellitus: a meta-analysis of 26 randomized controlled trials. *Gynecol Endocrinol*. 2022;38(4):303-309. doi:10.1080/09513590.2021.2015761

Paavilainen E, Niinikoski H, Parkkola R, et al. Metformin versus insulin for gestational diabetes: Adiposity variables and adipocytokines in offspring at age of 9 years. *Diabetes Res Clin Pract*. 2023;202:110780. doi:10.1016/j.diabres.2023.110780

Paavilainen E, Nyman A, Niinikoski H, et al. Metformin Versus Insulin for Gestational Diabetes: Cognitive and Neuropsychological Profiles of Children Aged 9 years. *J Dev Behav Pediatr*. 2023;44(9):e642-e650. doi:10.1097/DBP.0000000000001233

Queensland Clinical Guidelines. *Gestational diabetes mellitus (GDM). Guideline No. MN21.33-V6-R26*. Queensland Health. 2022.

- Rowan JA, Rush EC, Plank LD. Metformin in Gestational Diabetes The Offspring Follow Up (MiGTOFU): Associations between maternal characteristics and size and adiposity of boys and girls at nine years. *Aust N Z J Obstet Gynaecol.* 2023;63(6):825-828. doi:10.1111/ajo.13739
- Song R, Chen L, Chen Y, et al. Comparison of glyburide and insulin in the management of gestational diabetes: A meta-analysis. *PLoS One.* 2017;12(8):e0182488. Published 2017 Aug 3. doi:10.1371/journal.pone.0182488
- Wong MMH, Yuen-Man Chan M, Ng TP, Louie JCY. Impact of carbohydrate quantity and quality on maternal and pregnancy outcomes in gestational diabetes mellitus: A systematic review and meta-analysis. *Diabetes Metab Syndr.* 2024;18(1):102941. doi:10.1016/j.dsx.2024.102941
- Wu R, Zhang Q, Li Z. A meta-analysis of metformin and insulin on maternal outcome and neonatal outcome in patients with gestational diabetes mellitus. *J Matern Fetal Neonatal Med.* 2024;37(1):2295809. doi:10.1080/14767058.2023.2295809
- Zeng YC, Li MJ, Chen Y, et al. The use of glyburide in the management of gestational diabetes mellitus: a meta-analysis. *Adv Med Sci.* 2014;59(1):95-101. doi:10.1016/j.advms.2014.03.001
- Zhang L, Mai Y, Wang X, Liu D, Cui J, Sun J. Comparative Study of the Impact of Metformin Versus Insulin on Adverse Pregnancy Outcomes in Women Diagnosed with Gestational Diabetes Mellitus: A Meta-Analysis. *Altern Ther Health Med.* 2024;30(1):460-465.
- Zhao Q, He J. Efficacy and safety of metformin in pregnant women with polycystic ovary syndrome: a systematic review with meta-analysis of randomized and non-randomized controlled trials. *Gynecol Endocrinol.* 2022;38(7):558-568. doi:10.1080/09513590.2022.2080194
- Zhu D, Chen Y, Huang J, et al. Effects of metformin on pregnancy outcome, metabolic profile, and sex hormone levels in women with polycystic ovary syndrome and their offspring: a systematic review and meta-analysis. *Ann Transl Med.* 2022;10(7):418. doi:10.21037/atm-22-909

Guideline Development Process and Team

Development process

To develop the Gestational Diabetes Screening and Treatment Guideline, the guideline team adapted recommendations from external developed evidence-based guidelines and/or recommendations organizations that establish community standards. The guideline team reviewed additional evidence in several areas. For details, see Evidence Summary and References.

This edition of the guideline was approved for publication by the Guideline Oversight Group in October 2024.

Team

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