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CHAPTER 3. Guideline for Detection and Management of Diabetes in Pregnancy

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Objective: The Joslin Guideline for Detection and Management of Diabetes in Pregnancy is designed to assist internal medicine specialists, endocrinologists, and obstetricians in individualizing the care of and setting goals for women with preexisting diabetes who are pregnant or planning pregnancy. It is also a guide for managing women who are at risk for or who develop gestational diabetes mellitus (GDM). This guideline is not intended to replace sound medical judgment or clinical decision making. Clinical judgment determines the need for adaptation in all patient care situations; more or less stringent interventions may be necessary.

The objective of the Joslin Guideline for Detection and Management of Diabetes in Pregnancy is to support clinical practice and to influence clinical behaviors in order to improve clinical outcomes and assure that patient expectations are reasonable and informed. This guideline was approved November 13, 2016, and updated February 12, 2018.

3.1.0 SCREENING FOR GESTATIONAL DIABETES MELLITUS

FIGURE. See at end of Chapter 3.

3.2.0 PRECONCEPTION CARE. For preexisting type 1 diabetes (T1D) or type 2 diabetes (T2D)

3.2.1 Glucose goals prior to conception:

- Fasting and pre-meal glucose: plasma 80 to 110 mg/dL [**1C**]
- 1-hour postprandial blood glucose: plasma 100 to 155 mg/dL [**1C**]
- Glycated hemoglobin (A1C): <7% and as close to 6% as possible, without severe hypoglycemia [**1B**]
- Avoid severe hypoglycemia [**1B**]

3.2.2 Counseling:

- Educate women of childbearing age about the importance of near-normal blood glucose control prior to conception.
- Refer to a specialist in maternal–fetal medicine and/or endocrinology/diabetes for counseling, assessment

of maternal and fetal risk, and guidance in achieving management goals. This includes all women who are planning pregnancy and women who are not planning pregnancy but are using inadequate contraception and have A1C greater than 7%.

- Assess diabetes self-management, including meal planning, insulin care and use, activity program, medication schedule, self-monitoring of blood glucose (SMBG), treatment for hypoglycemia and hyperglycemia, and sick day management, utilizing diabetes educators (DEs) as appropriate. Review maternal and fetal health issues.
- Begin a multivitamin with 400 mcg of folic acid to supplement average daily intake of 400 mcg for a total daily intake of 800 mcg to 1 mg of folic acid to decrease the risk of neural tube defects. Patients with a prior pregnancy affected with a neural tube defect should take folic acid 4 mg daily.
- Strongly advise smoking and alcohol cessation.
- Refer overweight and obese women with and without known diabetes or polycystic ovary syndrome (PCOS) for medical nutrition therapy with a goal of 5% to 10% weight loss based on 2009 Institute of Medicine recommendation.

3.2.3 Medical assessment:

- Take thorough medical and obstetrical history, including comprehensive review of diabetes history and management.
- Eye evaluation: dilated comprehensive eye exam and pregnancy clearance by an ophthalmologist; should also include a discussion about the risk of developing and/or the progression of diabetic retinopathy during pregnancy.
- Kidney function assessment: random urine albumin/creatinine ratio and serum creatinine. Refer to nephrology if urine protein ≥1 gram.
- Thyroid evaluation: Check thyroid stimulating hormone level.
- Gynecology evaluation: Make sure pelvic exam and Pap smear are up to date.
- Cardiac evaluation: If asymptomatic and ≥ 35 years of age with 1 or more additional risk factors (hypertension, smoking, family history of coronary artery disease, hypercholesterolemia, albuminuria, or nephropathy), recommend 1 or more of the following: electrocardiogram (ECG), echocardiogram, or exercise tolerance test (ETT). If symptomatic, recommend ECG and echocardiogram or ETT and consider referral to cardiologist.
- Check vitamin B12 level in patients consuming more than 1 mg folic acid daily, as high-dose folic acid may mask a B12 deficiency.

3.2.4 Diabetes medications:

- Discontinue oral antihyperglycemic therapy; start insulin. An exception is metformin, which may be continued during anovulatory infertility and in the first trimester in patients with PCOS or T2D. Prior to the first prenatal visit, the patient should begin increasing doses of insulin as necessary to control blood glucose while metformin is tapered off or discontinued. Metformin should not be used beyond the first trimester or in lieu of insulin based on safety and efficacy data available at this time
    - Metformin crosses the placenta and achieves therapeutic levels in the fetus. Presently, there are no long term randomized controlled trials (RCT) regarding outcomes in offspring of mothers with preexisting diabetes treated with metformin during pregnancy. (See 3.3.3b regarding outcomes in infants exposed to metformin in utero in PCOS and GDM.).
    - Other oral medications have not been adequately studied for the treatment of preexisting T2D in pregnancy.
- The rapid-acting insulin analogs lispro and aspart lower postprandial blood glucose and decrease the risk of nocturnal hypoglycemia. Patients on lispro and aspart prior to conception may continue them during pregnancy. Patients on regular insulin may be switched to lispro or aspart if 1-hour postprandial blood glucose levels are above target and/or the patient is also experiencing pre-meal or nocturnal hypoglycemia.
- No information exists on the safety of using the insulin analogs glulisine and degludec in pregnancy. We cannot recommend their use at this time.
- A rapid-acting insulin, lispro or aspart, may be delivered either through multiple daily injections or an insulin pump.
- Detemir is a long-acting insulin analog that has been studied in T1D and is noninferior to isophane insulin in terms of safety, efficacy, and outcomes.
- Glargine, a long-acting insulin analog, is not recommended in women who are planning a pregnancy or who are currently pregnant. There is no RCT data comparing it to detemir or isophane insulins. A specific concern in the pregnant population is related to the 6- to 8-fold increased insulin-like growth factor receptor affinity and mitogenic potency compared with human insulin.
- There is inadequate safety information about the use of glucagon-like peptide-1 receptor agonists, dipeptidyl peptidase-4 inhibitors, alpha-glucosidase inhibitors, and sodium glucose co-transporter-2 inhibitors in pregnancy. Therefore, they should not be used in pregnancy.

3.2.5 Other medications

3.2.5a Hypertension and/or albuminuria management:

- Angiotensin-converting-enzyme (ACE) inhibitors

and angiotensin receptor blockers (ARBs) should be stopped preconception except as cited in 3.2.5b below, due to the increased risk of fetal injury or demise with second or third trimester use and inconsistent teratogenicity data.

- The nondihydropyridine calcium channel blocker diltiazem in extended release forms may be a useful substitute for ACE inhibitors and ARBs.
- Switch to antihypertensive agents that are safe in pregnancy (see section **3.5.0** below).

3.2.5b Diabetic nephropathy/chronic kidney disease management:

- Data on teratogenicity of ACE inhibitors and ARBs are inconsistent; therefore, risks and benefits of continuing them during preconception should be weighed. **[1B]** The benefits of preconception use of ACE inhibitors for renal protection may outweigh the uncertain risk of birth defects. In this case, ACE inhibitors should be stopped as soon as pregnancy is diagnosed in the first trimester.

3.2.5c Lipid management:

- Stop all cholesterol-lowering agents before conception, including statins. **[1B]**
- Hypertriglyceridemia: Omega-3 fatty acids may be started or continued in pregnancy. **[2B]**

3.3.0 DIABETES MANAGEMENT DURING PREGNANCY

3.3.1 Self-monitoring of blood glucose and urine ketones: preexisting diabetes and GDM:

- For gestational diabetes, check glucose levels 4 times/day: once before breakfast and 1 hour after each meal.
- For preexisting diabetes, check glucose levels before every meal and 1 hour after each meal.
- Nocturnal monitoring (around 3 am) may be necessary on an intermittent basis.
- Check fasting urine ketones daily.

3.3.2 Treatment goals

3.3.2a Preexisting diabetes:

- Fasting and pre-meal plasma glucose: 60 to 99 mg/dL. [**1C**]
- 1-hour post meal or peak postprandial plasma glucose: 100 to 129 mg/dL. [**1C**]
- Urine ketones: negative.
- Normalization of A1C to <6% if possible without resulting in severe hypoglycemia. [**2B**]
- Use standard hypoglycemia treatment for blood glucose less than 60 mg/dL: Consume 15 grams of carbohydrate, and recheck glucose in 15 minutes. If blood glucose remains less than 60 mg/dL, consume an additional 15 grams of carbohydrate.
- Avoid severe hypoglycemia (an episode in which the patient experiences coma, seizure, or suspected seizure, or impairment sufficient to require the assistance of another person). Blood glucose goals must be relaxed for patients with hypoglycemia unawareness or recurrent hypoglycemia.

3.3.2b Gestational diabetes mellitus (GDM):

TABLE 1. Diagnosing GDM

	Plasma Glucose Hadlock AC <75th percentile	Plasma Glucose Hadlock ≥75th percentile
Fasting and pre-meal glucose	60-90 mg/dL	60-79 mg/dL
1 hour post meal or peak postprandial	100-129 mg/dL	90-109 mg/dL

- Urine ketones: negative.
- Initiate insulin therapy if above levels are not maintained.
- Use standard hypoglycemia treatment for blood glucose less than 60 mg/dL: Consume 15 grams of carbohydrate, and recheck glucose in 15 minutes. If blood glucose remains less than 60 mg/dL, consume an additional 15 grams of carbohydrate.

3.3.3 Diabetes monitoring and visits

3.3.3a Preexisting diabetes:

- Medical visits (endocrinologist preferred) every 1 to 4 weeks, with additional phone contact as needed, depending on level of self-management skills and stability of blood glucose control. At each visit, review SMBG and urine ketone results; measure blood pressure; measure urine protein and ketones by dipstick.
- Check A1C level every 4 to 8 weeks.
- Education utilizing a DE, preferably a certified diabetes educator (CDE), as needed; suggest nutrition therapy (NT) by registered dietitian (RD).
- Ophthalmology exam early in first trimester; repeat dilated exam every trimester and for 1 year postpartum as indicated by the degree of retinopathy.
- Consider providing mental health counseling to assist women and/or their partners cope with the psychological and relationship changes that may result from pregnancy.

3.3.3b Gestational diabetes mellitus:

- Medical visits (endocrinologist preferred) every 1 to 4 weeks, with additional phone contact as needed, depending on level of self-management skills and stability of blood glucose control. At each visit, review SMBG and urine ketone results; measure blood pressure; measure urine protein and ketones by dipstick.
- If newly diagnosed with gestational diabetes, patient should be started on insulin, not metformin or glyburide (glibenclamide), if medication is required. **[2C]**

- Education utilizing a DE (preferably a CDE) as needed, especially for review of SMBG to increase adherence; NT should be provided by an RD.
- Glyburide is associated with a 2-fold or greater increased risk of macrosomia and neonatal hypoglycemia compared with insulin, in meta-analyses and an increased risk of neonatal hypoglycemia, in an RCT powered for neonatal outcomes. **[2B]**
- Glyburide should not be used in pregnancy, except in rare situations when insulin is not an option. **[2B]**
- Metformin is associated with high treatment failure rates and increased preterm delivery, but also with lower neonatal hypoglycemia. Infants exposed to metformin in utero, during prior PCOS or GDM RCTs, may weigh more, and demonstrate larger waist circumferences and greater fat mass at 4 and 9 years of age. **[2B]**

3.4.0 DIABETES MEDICATIONS

For **preexisting diabetes** the only diabetes medication currently used throughout pregnancy is insulin (see **Preconception Care**). Insulin does not cross the placenta. Oral agents are often insufficient and ineffective in both T1D and T2D.**[1B]**

3.5.0 HYPERTENSION MANAGEMENT

- Maintaining blood pressure in nonpregnant patients with diabetes at below 130/80 mmHg decreases end organ damage. [**2A**]
- During pregnancy, blood pressure targets are 110 to 129 mmHg systolic and 65 to 79 mmHg diastolic in women with chronic hypertension.[**2C**] These targets are lower than in those without diabetes. Antihypertensives are initiated in pregnant patients with known or suspected chronic hypertension if blood pressure is ≥130/80 mmHg 3 times during pregnancy.
- Preeclampsia requires special treatment; therefore, these guidelines and treatment strategies do not apply to preeclampsia, for which other treatment options are preferred, nor do they apply to gestational hypertension.
- Antihypertensives used during pregnancy are:
  - Alpha methyldopa
  - Beta-blockers:
    - acebutolol, betaxolol, bisoprolol, labetalol, levatol, metoprolol, nadolol, sotalol, timolol
    - NOTE: atenolol ; should not be used as it may cause fetal growth restriction)
  - Calcium channel blockers Nifedipine extended release. The nondihydropyridine calcium channel blocker diltiazem in extended-release form may be preferred in patients with microalbuminuria or nephropathy.
  - Hydralazine as second-line agent.
- Aspirin 81 mg daily is recommended from 12 weeks gestation until delivery to help reduce risk for preeclampsia in patients with T1D or T2D. **[2B]**

3.6.0 NUTRITION THERAPY

Recommendations are the same for preexisting diabetes and GDM except where noted.

3.6.1 Counseling and education:

- All pregnant women should receive NT counseling by a RD, preferably an RD/CDE.
- All pregnant women should receive SMBG training by a DE (CDE preferred).
- Daily food records and SMBG records are required to assess effectiveness of NT.
- Carbohydrate counting skills are taught for either a consistent carbohydrate intake or a personalized insulin-to-carb ratio, so the patient can adjust insulin based on carbohydrate intake.
- At least 3 encounters with a CDE are recommended:
  - Visit 1 (60-90 minute individual or group visit with RD) for assessment and meal planning. This could include SMBG instruction if RD has received appropriate training.
  - Visit 2 (30-45 minutes) with RD or RN 1 week after initial visit to assess and modify plan.
  - Visit 3 (15-45 minutes) with RD or RN in 1 to 3 weeks to further assess and modify plan, as needed.
- Additional visits every 2 to 3 weeks and, as needed, with RD or RN until delivery, and one visit 6 to 8 weeks after delivery.

3.6.2 Calories:

TABLE 2.

WHO BMI Range (kg/m²)	Energy Needs (kcals/kg) Based on Pre-Gravid kg		Total Weight Gain Range (pounds)		Rates of Weight Gain (pounds/week) 2nd & 3rd Trimesters
	Single	Multiple	Single	Multiple	
Underweight (<18.5)	36-40	42-50	28-40	[a]	1.0 (1-1.3)
Normal (18.5-24.9)	30	40-45	25-35	37-45	1.0 (0.8-1)
Overweight (25-29)	24	30-35	15-25	31-50	0.6 (0.5-0.7)
Obese (>30)	insufficient information[b]		11-20	25-42	0.5 (0.4-0.6)

BMI indicates body mass index; kcal, kilocalorie; kg, kilogram; WHO, World Health Organization

[a]Insufficient information was available to develop a provision guideline for underweight women with multiple fetuses.

[b]Insufficient information was available to address needs (kcal/kg) in the obese category.

Guide to Calculating Energy Needs

Estimated Energy Requirements (EER) for pregnancy:
EER in pregnancy = EER pre-pregnancy (see below) + additional energy expended during pregnancy + energy dispostion, as follows:

First trimester:	EER prepregnancy + 0
Second trimester:	EER prepregnancy + 340 singleton
Third trimester:	EER prepregnancy + 452 singleton

Calculate EER prepregnancy, for women aged 19 years and older, as follows:
EER = 354 – (6.91 x age [years] + PA x [(9.36 x weight in kg + 726 x height in m), where PA is physical activity coefficient (see below).

PA = 1.0 for sedentary (physical activity level [PAL] is >1.0 but <1.4)
PA = 1.12 for low activity (PAL is ≥ 1.4 but < 1.6)
PA = 1.27 for active (PAL is ≥1.6 but < 1.9) PA = 1.45 for very active (PAL is ≥1.9)

3.6.2a Distribution of calories:

- Individualize distribution of calories based on usual intake, preferences, and medication regimen.
  - Consistent timing of 3 meals and 2 to 4 snacks per day; smaller frequent meals decrease postprandial hyperglycemia.
- Weight should be monitored at each visit; each patient's weight gain should be tracked on prenatal weight gain chart.

TABLE 3. Calorie Distribution

	GDM	Preexisting T1D or T2D
Carbohydrate	40% to 55% total calories	40% to 55% total calories
Breakfast	15-30 g[a,b]	consistent carb intake or individualized, per usual intake and BG levels
Lunch/Dinner	45 g each	consistent carb intake or individualized, per usual intake and BG levels
Daytime snacks (mid-morning/ mid-afternoon)	15-20 g each	
HS Snack	15-30 g	15-30 g
Fiber	Calculate 14 g of fiber/1000 kcals per day (25-30 g/ day) based on provider assessment	
Protein	Calculate 1.1 g of protein/kg/day, based on provider assessment Multiple-fetus pregnancies: an additional 50 grams of protein/day, above nonpregnant DRI for protein, during 2nd and 3rd trimesters	
Fat	30% to 40% total calories with <10% total calories from saturated fat for both GDM and preexisting diabetes Encourage use of monounsaturated and polyunsaturated fats such as olive oil, canola oil, soybean oil, nuts, seeds, avocado, and fish, particularly those high in omega-3 fatty acids; discourage intake of saturated fats	

BG indicates blood glucose; DRI, daily reference intake; GDM, gestational diabetes mellitus; g, grams; HS, bedtime; kcal, kilocalorie; kg, kilogram; T1D, type 1 diabetes; T2D, type 2 diabetes.

Other Dietary Guidelines for Pregnancy

Nutritive and nonnutritive sweeteners. The safety of nonnutritive sweeteners has not been established.

Vitamin and mineral supplements. Prenatal multivitamin and mineral supplements should include: (1) iron, 30 mg/ day; (2) potassium iodide 150 mcgs (3) folic acid, 400 mcg to supplement 400 mcg from daily dietary intake. Start the prenatal vitamin preconception, ideally, to boost folic acid to decrease the risk of neural tube defects; (4) added calcium to reach 1000 mg/day, or 1300 mg/day if aged 18 years or less; (5) vitamin D, 600 IUs/day, with tolerable upper intake of 4000 IU/day for 12 weeks.

Caffeine/Fluids. Limit caffeine to <200 mg/day (equivalent of 1 cup of coffee or 4 cups of black tea). Excess caffeine consumption during pregnancy may increase the risk of miscarriage. Three liters of water per day for adequate hydration, or about 10 cups per day, in total beverage intake is recommended.

3.7.0 PHYSICAL ACTIVITY

Regular physical activity is recommended after a provider gives clearance.

- 30 minutes of moderate exercise on most days, for 150 minutes per week
- Unless contraindications are present, women who were previously inactive or active should be encouraged to be active.

Benefits of exercise include reducing insulin resistance postprandial hyperglycemia, and excessive weight gain.

Activity after meals can reduce postprandial hyperglycemia.

3.8.0 ALCOHOL AND TOBACCO USE

Alcohol and tobacco use should be discouraged during pregnancy.

3.9.0 POSTPARTUM CARE

Breastfeeding is encouraged in patients with preexisting or gestational diabetes.

Enalapril and captopril may be used to treat hypertension and albuminuria in nursing mothers of full-term infants.

Appointments with the following specialists should be completed 6 to 8 weeks postpartum: ophthalmology, RD or registered nurse, and endocrinology.

For women who developed GDM

- A 2-hour, 75-gram oral glucose tolerance test (OGTT) should be performed at 6 weeks to evaluate for persistent diabetes.
  - Normal: fasting glucose level <100 mg/dl
  - Impaired: fasting glucose level 100 to 125mg/dl
  - Diabetes: fasting glucose level ≥126 mg/dl
  - Normal glucose tolerance: 2-hour OGTT value <140 mg/dl
  - Impaired glucose tolerance: 2-hour OGTT value 140 to 199mg/dl
  - Diabetes: 2-hr OGTT value ≥200mg/dl

- Counsel women with GDM on the roles of lifestyle management and weight loss to reduce the risk of future T2D; approximately 50% of women with GDM will develop T2D in the next 7 to 10 years.
- Review nutrition guidelines and establish exercise goals. For women with BMI greater than 25 (or BMI >23 in Asians), target a 5% to 7% weight loss from the preconception weight.
- Discuss family planning/contraceptive issues. Medroxyprogesterone (Depo-Provera) and progestin-only oral contraceptives are less preferred in patients who have had gestational diabetes, as they can accelerate the development of T2D. In patients with preexisting diabetes, medroxyprogesterone may worsen glycemic control. The intrauterine device is preferred in monogamous partnerships because it is a metabolically neutral and highly effective form of contraception.
- Assist women with GDM with the transfer of care back to the primary care physician for longer-term diabetes screening and diabetes risk reduction interventions. This includes a 75-gram, 2-hour OGTT at 1 year postpartum and every 3 years, a fasting glucose or A1c yearly on alternate years, , and a yearly discussion of risk reduction options and lifestyle management strategies afterwards.

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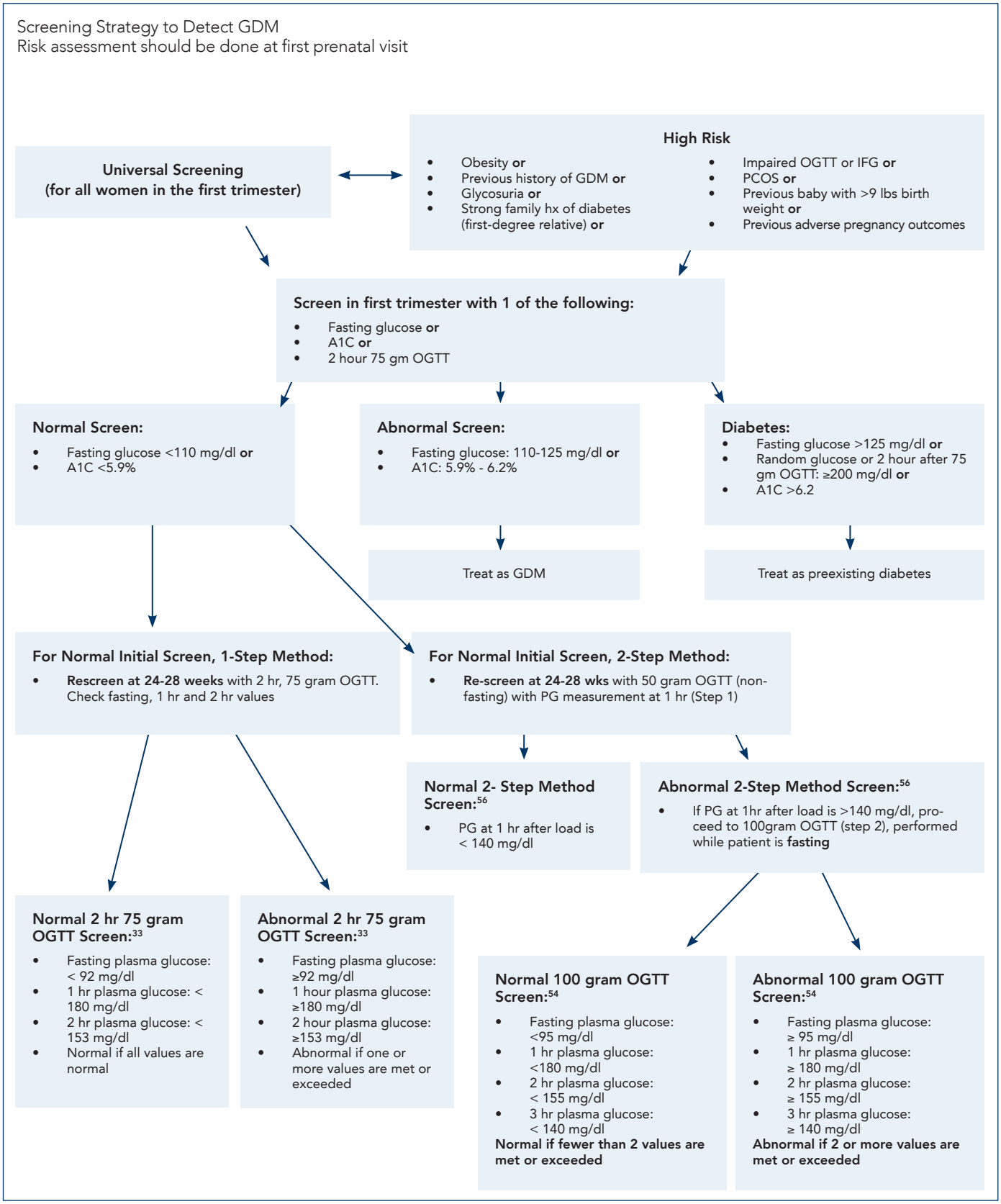
FIGURE. Gestational Diabetes Mellitus (GDM)



A1C indicates glycated hemoglobin; hx, history; lbs, pounds; IFG, impaired fasting glucose; OGTT, oral glucose tolerance test; PCOS, polycystic ovary syndrome; PG, plasma glucose; wks, weeks.