

Joslin Diabetes Center and Joslin Clinic Guideline for Detection and Management of Diabetes in Pregnancy

11/10/2016 corrected 01/11/17

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 pre-existing 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 objectives of the Joslin Guideline for Detection and Management of Diabetes in Pregnancy are to support clinical practice and to influence clinical behaviors in order to improve clinical outcomes and assure that patient expectations are reasonable and informed. Guidelines are developed and approved through the Clinical Oversight Committee that reports to the Chief Medical Officer of the Joslin Diabetes Center. The Guideline is established after careful review of current evidence, medical literature and sound clinical practice. This Guideline will be reviewed periodically and modified as clinical practice evolves and medical evidence suggests.

SCREENING FOR GESTATIONAL DIABETES MELLITUS

See *Screening Strategy to Detect GDM* on page 7.

PRECONCEPTION CARE

Pre-existing type 1 or type 2 diabetes

Glucose Goals Prior to Conception	<ul style="list-style-type: none"> • Fasting and pre-meal blood glucose: Plasma 80-110 mg/dl • 1 hour postprandial blood glucose: 100-155 mg/dl • A1C: < 7% and as close to 6% as possible without resulting severe hypoglycemia • Avoid severe hypoglycemia
Counseling	<ul style="list-style-type: none"> • Educate women of childbearing age about the importance of near normal blood glucose control prior to conception • Refer to a maternal fetal-medicine and/or endocrinologist/diabetes specialist 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 a glycosylated hemoglobin A1C greater than 7%. • Assess diabetes self-management, including meal plan, insulin care and use, activity program, medication schedule, self- monitoring of blood glucose (SMBG), treatment for hypo and hyperglycemia, and sick day management, utilizing diabetes educators (DE) 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 mgs 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 5-10% weight loss based on Institute of Medicine (IOM) 2009 recommendation.
Medical Assessment	<ul style="list-style-type: none"> • 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: TSH level • GYN evaluation: pelvic exam, Pap smear up to date • Cardiac evaluation: if asymptomatic, ≥ 35 years of age with one or more additional risk factors (hypertension, smoking, family history of CAD, hypercholesterolemia, albuminuria or nephropathy) recommend one or more of the following: EKG, echocardiogram or exercise tolerance test (ETT). If symptomatic, recommend EKG and echocardiogram or ETT and consider referral to cardiologist. • Check a B12 level in patients consuming more than 1 mg folic acid, as high dose folic acid may mask B12 deficiency

Diabetes Medications	<ul style="list-style-type: none"> Discontinue oral antihyperglycemic therapy; start insulin. An exception is metformin, which may be continued during the first trimester in patients with PCOS or type 2 diabetes, and anovulatory infertility. At 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 until randomized controlled studies evaluating safety and efficacy have been completed. <ul style="list-style-type: none"> Metformin crosses the placenta and achieves therapeutic levels in the fetus. Presently, there are no long term randomized controlled safety data in infants whose mother's were treated with metformin in pregnancy. Other oral medications have not been adequately studied for the treatment of preexisting type 2 diabetes 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. There is no information on the safety of using the insulin analogs, glulisine and degludec in pregnancy. We cannot recommend their use at this time. The rapid-acting insulins, lispro or aspart may be delivered either through multiple daily injections (MDI) or an insulin pump Detemir is a long-acting insulin analog that has been studied in type 1 diabetes and is non-inferior to NPH insulin in terms of safety and 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 information on its safety in pregnancy. A specific concern in the pregnant population is related to the 6 to 8 fold increased IGF-1 receptor affinity and mitogenic potency compared with human insulin.. There is inadequate safety information about the use of GLP-1agonists, DPP-4 inhibitors, alpha-glucosidase inhibitors, and SGLT2 inhibitors in pregnancy. They should therefore not be used in pregnancy.
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Other Medications	<p>Hypertension and/or albuminuria management:</p> <ul style="list-style-type: none"> ACE-inhibitors and ARBs should be stopped pre conception due to the increased risk of fetal injury or demise with 2nd or 3rd trimester use. Data on teratogenicity of ACE-inhibitors and ARBs is inconsistent therefore risks and benefits of continuing them should be weighed. <ul style="list-style-type: none"> The non-dihydropyridine 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 below). <p>Diabetic nephropathy/chronic renal disease management:</p> <ul style="list-style-type: none"> 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. <p>Hyperlipidemia management:</p> <ul style="list-style-type: none"> Stop all cholesterol-lowering agents before conception, including statins Hypertriglyceridemia: omega 3 fatty acids may be started or continued in pregnancy
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DIABETES MANAGEMENT DURING PREGNANCY

Self Monitoring of Blood Glucose and Urine Ketones	<p><u>Pre-existing diabetes and GDM</u></p> <ul style="list-style-type: none"> For gestational diabetes, check glucose levels 4 times/day: before breakfast and 1 hour post-meals For pre-existing diabetes, check glucose levels pre-meals and 1 hour post-meal Nocturnal monitoring (~3 AM) may be necessary on an intermittent basis Check fasting urine ketones daily
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Treatment Goals	<p><u>Pre-existing Diabetes</u></p> <table border="0" style="width: 100%;"> <tr> <td style="width: 60%;"></td> <td style="text-align: right;">Plasma glucose</td> </tr> <tr> <td>• Fasting and pre-meal plasma glucose</td> <td style="text-align: right;">60-99 mg/dl</td> </tr> <tr> <td>• 1-hour post-meal or peak post-prandial plasma glucose</td> <td style="text-align: right;">100-129 mg/dl</td> </tr> </table> <ul style="list-style-type: none"> Urine ketones: negative Normalization of glycohemoglobin A1C to < 6% if possible without resulting severe hypoglycemia Use standard hypoglycemia treatment for blood glucose less than 60 mg/dl (15 grams of carbohydrate – recheck in 15 minutes; repeat with 15 grams of carbohydrate if blood glucose is still less than 60 mg/dl) Avoidance of severe hypoglycemia (episode in which 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. 		Plasma glucose	• Fasting and pre-meal plasma glucose	60-99 mg/dl	• 1-hour post-meal or peak post-prandial plasma glucose	100-129 mg/dl
	Plasma glucose						
• Fasting and pre-meal plasma glucose	60-99 mg/dl						
• 1-hour post-meal or peak post-prandial plasma glucose	100-129 mg/dl						

	<p><u>Gestational Diabetes</u></p> <table border="0" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 50%;"></th> <th style="width: 25%; text-align: center;">Plasma glucose Hadlock AC < 75th percentile</th> <th style="width: 25%; text-align: center;">Plasma glucose Hadlock AC ≥ 75th percentile</th> </tr> </thead> <tbody> <tr> <td>• Fasting and premeal blood glucose</td> <td style="text-align: center;">60-95 mg/dl</td> <td style="text-align: center;">60-79 mg/dl</td> </tr> <tr> <td>• 1-hour post meal or peak post prandial</td> <td style="text-align: center;">100-129 mg/dl</td> <td style="text-align: center;">90-109 mg/dl</td> </tr> </tbody> </table> <ul style="list-style-type: none"> • Urine ketones: negative • Initiate insulin therapy if above levels are not maintained • Use standard hypoglycemia treatment for blood glucose less than 60 mg/dl (15 grams of carbohydrate – recheck in 15 minutes; repeat with 15 grams of carbohydrate if blood glucose is still less than 60 mg/dl) 		Plasma glucose Hadlock AC < 75th percentile	Plasma glucose Hadlock AC ≥ 75th percentile	• Fasting and premeal blood glucose	60-95 mg/dl	60-79 mg/dl	• 1-hour post meal or peak post prandial	100-129 mg/dl	90-109 mg/dl
	Plasma glucose Hadlock AC < 75th percentile	Plasma glucose Hadlock AC ≥ 75th percentile								
• Fasting and premeal blood glucose	60-95 mg/dl	60-79 mg/dl								
• 1-hour post meal or peak post prandial	100-129 mg/dl	90-109 mg/dl								
<p>Diabetes Monitoring and Visits</p>	<p><u>Pre-existing Diabetes</u></p> <ul style="list-style-type: none"> • Medical visits (endocrinologist preferred) every 1-4 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 4-8 weeks • Education utilizing a diabetes educator (DE), preferably a Certified Diabetes Educator (CDE), as needed; nutrition therapy (NT) by registered dietitian (RD) • Ophthalmology exam early in first trimester; with 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. <p><u>Gestational Diabetes</u></p> <ul style="list-style-type: none"> • Medical visits (endocrinologist preferred) every 1-4 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. • Education utilizing a DE (preferably a CDE) as needed for review of SMBG to increase adherence; NT by registered dietitian (RD) • Glyburide is associated with a 2 fold or greater increased risk of macrosomia and neonatal hypoglycemia compared with insulin, in a meta-analysis. • Glyburide should not be used in pregnancy, except in rare situations when insulin is not an option. • Metformin is associated with high treatment failure rates, increased preterm delivery although lower neonatal hypoglycemia. Long term safety data is not available. If insulin is not an option, metformin is preferred over glyburide 									
<p>Diabetes Medications</p>	<p><u>Preexisting Diabetes</u></p> <ul style="list-style-type: none"> • The only diabetes medication currently used throughout pregnancy is insulin (see Preconception Care). 									
<p>Hypertension Management</p>	<ul style="list-style-type: none"> • Maintaining blood pressure in non-pregnant patients at < 130/80mmHg decreases end organ damage. • Target blood pressure is 110-129 systolic and 65-79 diastolic in women with chronic hypertension during pregnancy. Antihypertensives are initiated in pregnant patients with known or suspected chronic hypertension if blood pressure is ≥ 130/80mmHg three times during pregnancy. • Pre-eclampsia needs special treatment; therefore, these guidelines and treatment strategies do not apply to pre-eclampsia for which other treatment options are preferred, or to gestational hypertension when high blood pressure exposure is limited • Antihypertensives that are used during pregnancy are: <ul style="list-style-type: none"> ○ Alpha methyl dopa (category B) ○ Beta-blockers: <ul style="list-style-type: none"> ▪ acebutolol, sotalol are category B ▪ betaxolol, bisoprolol, labetalol, levatol, metoprolol, nadolol, timolol are category C ▪ atenolol is category D and should not be used as it may cause fetal growth restriction ○ Calcium channel blockers are all category C. The nondihydropyridine calcium channel blocker diltiazem in extended-release form may be preferred in patients with microalbuminuria or nephropathy. ○ Hydralazine is category C • Aspirin 81 mg daily is recommended from 12-36 weeks to help reduce risk for preeclampsia in patients with type1 or 2 diabetes. 									

NUTRITION THERAPY (NT) AND

Recommendations are the same for pre-existing diabetes and GDM except where noted.

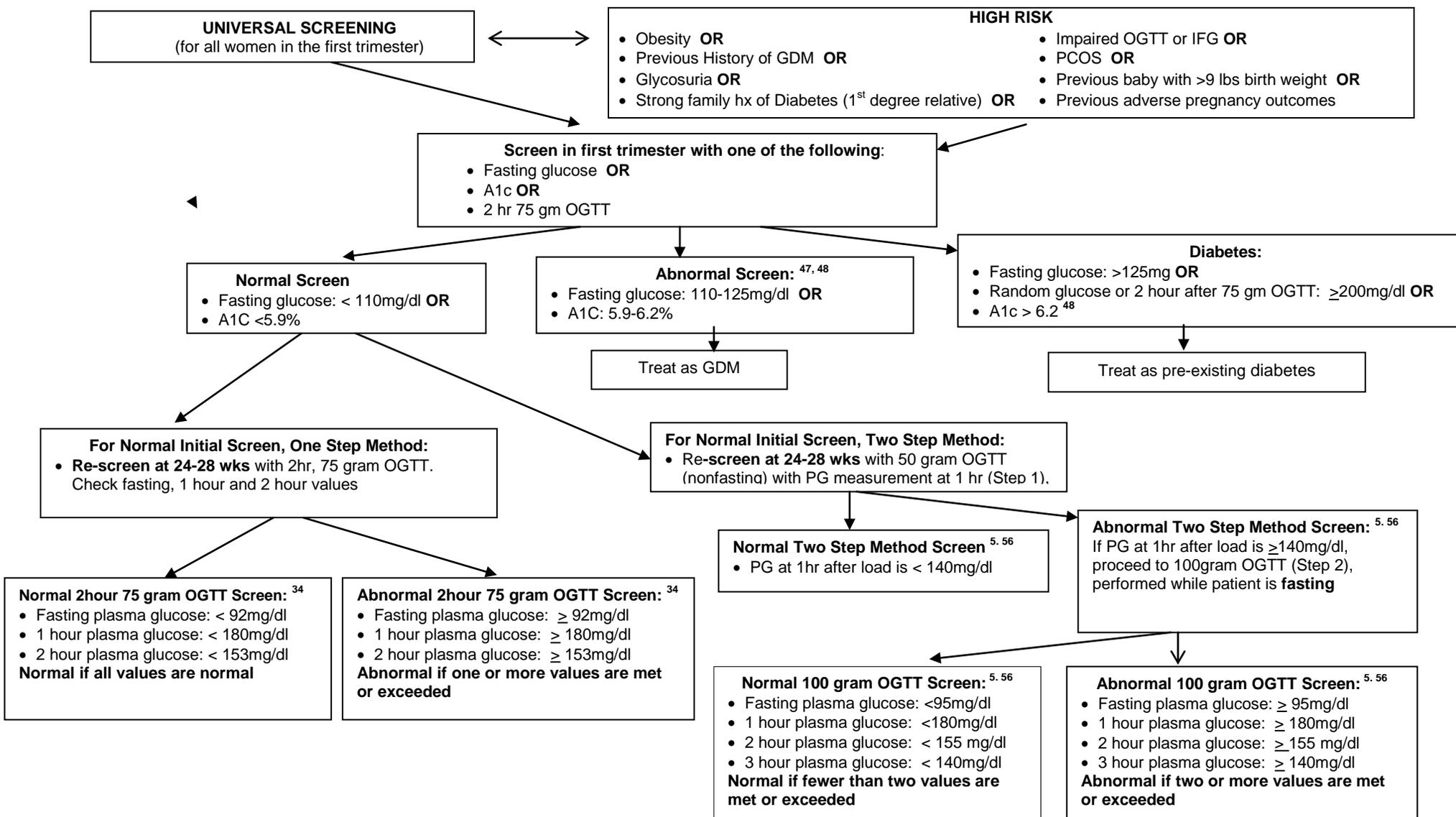
Counseling and Education	<ul style="list-style-type: none"> All pregnant women should receive NT counseling by a registered dietitian (RD), (CDE preferred) All pregnant women should receive SMBG training by a DE (CDE preferred) Daily food records and SMBG records are required to assess effectiveness of NT Carbohydrate counting skills are taught for either a consistent carb 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: <ul style="list-style-type: none"> 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 minute) with RD or RN 1 week after initial visit to assess and modify plan Visit 3 (15 – 45 minute) with RD or RN in 1 – 3 weeks to further assess and modify plan, as needed. Additional visits every 2 – 3 weeks and prn with RD or RN until delivery, and one visit 6 – 8 weeks after delivery 					
Calories	WHO BMI range (kg/m²)	Energy Needs (kcal/kg) °Based on Pregravid kg		Total Weight Gain Range (lbs)		Rates of weight Gain (lb/week) 2nd and 3rd trimesters
		Single	Multiple	Single	Multiples	
	Underweight: <18.5	36-40	42-50	28-40	**	1.0-(1-1.3)
	Normal weight: 18.5-24.9	30	40-45	25-35	37-54	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**		11-20	25-42	0.5 (0.4-0.6)
	<p>*Quick Guide to Calculate Energy Needs: Estimated Energy Requirement's (EER) for Pregnancy EER pregnancy = EER pre-pregnancy + additional energy expended during pregnancy + energy deposition where: First trimester = EER pre-pregnancy + 0 Second trimester = EER pre-pregnancy + 340 singleton Third trimester= EER pre-pregnancy + 452 singleton</p> <p>For 19yrs of age and older: EER pre-pregnancy = 354 –(6.91 X age {Y} + PA X {(9.36 X weight {kg} + 726 X height {m})}) where PA is the physical activity coefficient: PA = 1.0 for sedentary (Physical Activity Level, PAL >= 1.0 < 1.4) PA = 1.12 for low active (PAL >= 1.4 < 1.6) PA = 1.27 for active (PAL >= 1.6 < 1.9) PA = 1.45 for very active (PAL >= 1.9 < 2.5)</p> <p>For twins pregnancy, add an additional 500 kcals to calculated needs after 1st trimester. For multiple pregnancies, add 500 kcal in the 1st trimester</p> <p>* Insufficient information was available to develop a provisional guideline for underweight women with multiple fetuses ** Insufficient information to address energy needs (kcal/kg) in the obese category</p>					
Distribution of Calories	<ul style="list-style-type: none"> Individualize distribution of calories based on usual intake, preferences and medication regimen. <ul style="list-style-type: none"> Consistent timing of 3 meals and 2-4 snacks daily. Smaller frequent meals decrease postprandial hyperglycemia Weight should be monitored at each visit; track patient's weight gain on prenatal weight gain chart 					
Carbohydrate	GDM			Pre-Existing Diabetes		
	40 –55% total calories`			40 – 55% total calories		
	Breakfast	15 – 30 grams +		Consistent carb intake or individualized as per usual intake and BG levels		

Carbohydrates (continued)	Other meals	45 grams lunch and dinner	Consistent carb intake or individualized as per usual intake and BG levels
	HS snack	15 – 30 grams carbohydrate	15 – 30 grams carbohydrate
	Pregnant women should consume a minimum of 175 grams of carbohydrate per day + May be increased if insulin is added Diet mainly containing low glycemic index carbohydrates Carbohydrate counting at each meal and snack		
Fiber	<ul style="list-style-type: none"> Calculate 14 grams of fiber per 1000 kcals per day (25-30 grams/day) based on provider assessment 		
Protein	<ul style="list-style-type: none"> Calculate 1.1 grams of protein per kg per day, based on provider assessment Multiple pregnancies: An additional 50 gram of protein per day, above the non-pregnant DRI for protein during 2nd and 3rd trimester 		
Fat	<ul style="list-style-type: none"> <u>Pre-existing diabetes</u>: 30 – 40% of total calories, with <10% total calories from saturated fat <u>GDM</u>: 30-40% total calories with <10% total calories from saturated fat Encourage use of monounsaturated and polyunsaturated fats instead of saturated fats (e.g., olive oil, canola oil, soybean oil, nuts/seeds, avocado and fish, particularly those high in omega-3 fatty acids) instead of saturated fats. Limit fish low in mercury to 12 ounces per week. (e.g. salmon, herring, trout, sardines as a source of omega-3 fatty acids). Avoid high mercury fish such as shark, swordfish, king mackerel, tile fish. 		
Nutritive and Non-nutritive Sweeteners	<ul style="list-style-type: none"> The safety of non-nutritive sweeteners has not been established. 		
Vitamin/ Mineral Supplement	<ul style="list-style-type: none"> Prenatal multivitamin and mineral supplement including: <ul style="list-style-type: none"> Iron (30 mg/day) Folic acid 400 mcg to supplement average daily dietary intake of 400 mcg for a total daily intake of 800 mcg to 1 mg daily to decrease risk of neural tube defects (begin 400 mcg prior to conception) Additional calcium supplementation may be needed to meet daily requirement of 1000 mg per day (1300 mg per day if under age 19yrs). Begin prior to conception. Vitamin D 600 IUs/day. <ul style="list-style-type: none"> Tolerable Upper Intake (UL): 4,000 IU/day for 12 weeks 		
Caffeine/ Fluid intake	<ul style="list-style-type: none"> Limit caffeine to <200 mg per day (equivalent to 1 cup). Excess caffeine consumption during pregnancy may increase the risk of miscarriage 3 liters of water per day for adequate hydration or about 10 cups a day in total beverage intake 		
Physical Activity	<ul style="list-style-type: none"> Regular physical activity is recommended after clearance by provider. Engage in 30 minutes of moderate exercise on most days of the week or at least 150 minutes of moderate physical activity per week. Unless contraindications are present, previously inactive and active women should be encouraged to be physically active <ul style="list-style-type: none"> Benefits include reducing insulin resistance, postprandial hyperglycemia and excessive weight gain Hypoglycemia is more likely with prolonged exercise (>60 minutes) Encourage activity after meals to reduce postprandial hyperglycemia 		
Alcohol and Tobacco Use	<ul style="list-style-type: none"> Alcohol and tobacco use should be avoided during pregnancy. 		

POST-PARTUM CARE

- Breastfeeding is encouraged in patients with pre-existing 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 6-8 weeks post-partum: ophthalmology, RD or RN and endocrinology.
- For women who develop GDM:
 - A 2-hour 75 g OGTT should be checked at 6 weeks to evaluate for persistent diabetes
 - Normal: fasting glucose level <100mg/dl
 - Impaired fasting glucose: fasting glucose level 100-125mg/dl
 - Diabetes: fasting glucose level \geq 126mg/dl
 - Normal glucose tolerance: 2 hour OGTT value <140 mg/dl
 - Impaired glucose tolerance: 2 hour OGTT value 140-199mg/dl
 - Diabetes: 2 hr OGTT value \geq 200mg/dl
 - Counsel women with GDM on the role of lifestyle management and weight loss to reduce the risk of future type 2 DM (of note: approximately 50% of women with GDM will develop overt type 2 diabetes 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 5-7% weight loss from the preconception weight.
- Discuss family planning/contraceptive issues. Depo-provera and progestin-only oral contraceptives are less preferred in patients who have had gestational diabetes, as they can accelerate the development of type 2 diabetes. In patients with pre-existing diabetes, depo-provera may worsen glycemic control. The intrauterine device (IUD) is preferred in monogamous partnerships because it is a metabolically neutral and highly effective form of contraception.
- Assist women with gestational diabetes with the transfer of care back to the primary care physician for longer term diabetes screening (including yearly fasting glucose, 1 year post partum and every 3 years afterwards 75 gram 2hour OGTT), risk reduction and for lifestyle management.

Gestational Diabetes Mellitus
 Screening Strategy to Detect GDM
 Risk assessment should be done at first prenatal visit



Glossary

A1C: glycosylated hemoglobin	Kcals/kg: kilocalories per kilogram
ACE: angiotensin converting enzyme inhibitor	Kg/m²: kilogram per meter
Age (y): age in years	mcg: microgram
ARB: angiotensin receptor blocker	MDI: multiple daily injection
BMI: body mass index	mg: milligrams
CAD: coronary artery disease	mg/dl: milligrams per deciliter
CDE: certified diabetes educator, a healthcare provider with advanced education in diabetes management	mmol/L: millimoles per liter
DE: diabetes educator	NT: nutrition therapy
DPP-4 inhibitor: dipeptidyl-4 inhibitor	OGTT: oral glucose tolerance test
DRI: Dietary Reference Intake	PA: physical activity co-efficient
EER: estimated energy requirement	PAL: physical activity level
EKG: electrocardiogram	PCOS: polycystic ovarian syndrome
ETT: exercise tolerance test	PG: plasma glucose
GDM: gestational diabetes mellitus	RD: registered dietitian
Hadlock AC: formula to identify macrosomia established by Hadlock et al	SGLT2 inhibitor: sodium-glucose cotransporter-2 inhibitor
lb : pounds	SMBG: self monitoring of blood glucose
IGF receptor: insulin-like growth factor receptor	TSH: thyroid stimulating hormone
IUD: intrauterine device	MNT: medical nutrition therapy
	UL: upper limit

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Elizabeth Blair, MSN, ANP-BC, CDE	Sylvia Rosas, MD
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Lori Laffel, MD, MPH	John Zrebiec, LICSW, CDE
Melinda Maryniuk, MEd, RD, CDE	Robert Gabbay,MD (<i>ex officio</i>)

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