MANAGEMENT OF DIABETES IN PREGNANCY

15.



# 15. Management of Diabetes in Pregnancy: *Standards of Care in Diabetes*—2024

Diabetes Care 2024;47(Suppl. 1):S282-S294 | https://doi.org/10.2337/dc24-S015

American Diabetes Association Professional Practice Committee\*

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# **DIABETES IN PREGNANCY**

The prevalence of diabetes in pregnancy has been increasing in the U.S. in parallel with the worldwide epidemic of obesity. Not only is the prevalence of type 1 diabetes and type 2 diabetes increasing in individuals of reproductive age, but there is also a dramatic increase in the reported rates of gestational diabetes mellitus (GDM). Diabetes confers significantly greater maternal and fetal risk largely related to the degree of hyperglycemia but also related to chronic complications and comorbidities of diabetes. In general, specific risks of diabetes in pregnancy include spontaneous abortion, fetal anomalies, preeclampsia, fetal demise, macrosomia, neonatal hyperbilirubinemia, and neonatal respiratory distress syndrome, among others. In addition, diabetes in pregnancy increases the risks of obesity, hypertension, and type 2 diabetes in offspring later in life (1,2).

# **Preconception Counseling**

#### Recommendations

**15.1** Starting at puberty and continuing in all people with diabetes and child-bearing potential, preconception counseling should be incorporated into routine diabetes care. **A** 

**15.2** Family planning should be discussed, and effective contraception (with consideration of long-acting, reversible contraception) should be prescribed and used until an individual's treatment plan and A1C are optimized for pregnancy. **A** 

**15.3** Preconception counseling should address the importance of achieving glucose levels as close to normal as is safely possible, ideally A1C <6.5% (<48 mmol/mol), to reduce the risk of congenital anomalies, preeclampsia, macrosomia, preterm birth, and other complications. **A** 

\*A complete list of members of the American Diabetes Association Professional Practice Committee can be found at https://doi.org/10.2337/dc24-SINT.

Duality of interest information for each author is available at https://doi.org/10.2337/dc24-SDIS.

Suggested citation: American Diabetes Association Professional Practice Committee. 15. Management of diabetes in pregnancy: Standards of Care in Diabetes—2024. Diabetes Care 2024;47(Suppl. 1): 5282–5294

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All individuals with diabetes and childbearing potential should be informed about the importance of achieving and maintaining as near euglycemia as safely possible prior to conception and throughout pregnancy. Observational studies show an increased risk of diabetic embryopathy, especially anencephaly, microcephaly, congenital heart disease, renal anomalies, and caudal regression, directly proportional to elevations in A1C during the first 10 weeks of pregnancy (3). Although observational studies are confounded by the association between elevated periconceptional A1C and other engagement in self-care behaviors, the quantity and consistency of data are convincing and support the recommendation to optimize glycemia prior to conception with an A1C <6.5% (<48 mmol/mol), as this is associated with the lowest risk of congenital anomalies (given that organogenesis occurs primarily at 5-8 weeks of gestation), preeclampsia, and preterm birth (3-7). In a systematic review and meta-analysis of observational studies, preconception care for pregnant individuals with preexisting diabetes was associated with lower A1C and reduced risks of birth defects, preterm delivery, perinatal mortality, small-for-gestational-age births, and neonatal intensive care unit admissions (8).

There are opportunities at any health care visit to educate all adults and adolescents with diabetes and childbearing potential about the risks of unplanned pregnancies and about improved maternal and fetal outcomes with pregnancy planning (9). Education and counseling should be offered, even when individuals already use contraception or do not intend to conceive. Effective preconception counseling could avert substantial health and associated cost (10) burdens in the offspring (11). Family planning should be discussed, including the benefits of long-acting, reversible contraception, and effective contraception should be prescribed and used until the individual is prepared and ready to become pregnant (12-16).

To minimize the occurrence of complications, beginning at the onset of puberty or at diagnosis, all adults and adolescents with diabetes of childbearing potential should receive education about 1) the risks of malformations associated with unplanned pregnancies

and even with mild hyperglycemia and 2) the use of effective contraception at all times when trying to prevent a pregnancy. Preconception counseling using developmentally appropriate educational tools enables adolescent girls to make well-informed decisions (9). Preconception counseling resources tailored for adolescents are available at no cost through the American Diabetes Association (ADA) (17).

# **Preconception Care**

#### Recommendations

**15.4** Individuals with preexisting diabetes who are planning a pregnancy should ideally begin receiving interprofessional care for preconception, which includes an endocrinology health care professional, maternal-fetal medicine specialist, registered dietitian nutritionist, and diabetes care and education specialist, when available. **B** 

**15.5** In addition to focused attention on achieving glycemic targets, **A** standard preconception care should be augmented with extra focus on nutrition, physical activity, diabetes selfcare education, and screening for diabetes comorbidities and complications. **B** 

15.6 Individuals with preexisting type 1 or type 2 diabetes who are planning a pregnancy or who have become pregnant should be counseled on the risk of development and/or progression of diabetic retinopathy. Dilated eye examinations should occur ideally before pregnancy or in the first trimester, and then pregnant individuals should be monitored every trimester and for 1 year postpartum as indicated by the degree of retinopathy and as recommended by the eye care health care professional. B

The importance of preconception care for all pregnant people is highlighted by American College of Obstetricians and Gynecologists (ACOG) Committee Opinion 762, "Prepregnancy Counseling" (10). Preconception counseling for pregnant people with preexisting type 1 or type 2 diabetes is highly effective in reducing the risk of congenital malformations and decreasing the risk of preterm delivery and admission to neonatal intensive

care units. Preconception counseling is also associated with reductions in perinatal mortality and small-for-gestational-age birth weight (18). A key point is the need to incorporate a question about plans for pregnancy into the routine primary and gynecologic care of people with diabetes. Preconception care for people with diabetes should include the standard screening and care recommended for any person planning pregnancy (10). Prescription of prenatal vitamins with at least 400 µg of folic acid (10) and 150 mg of potassium iodide (19) is recommended prior to conception. Review and counseling on the abstinence of use of nicotine products, alcohol, and recreational drugs, including marijuana, is important. Standard care includes screening for sexually transmitted diseases and thyroid disease, recommended vaccinations, routine genetic screening, a careful review of all prescription and nonprescription medications, herbal supplements, and nonherbal supplements used, and a review of travel history and plans with special attention to areas known to have Zika virus, as outlined by ACOG. See Table 15.1 for additional details on elements of preconception care (10,20).

Counseling on the specific risks of obesity in pregnancy and lifestyle interventions to prevent and treat obesity, including referral to a registered dietitian nutritionist (RDN), is recommended (21).

Diabetes-specific counseling should include an explanation of the risks to mother and fetus related to pregnancies associated with diabetes and the ways to reduce risks, including glycemic goal setting, lifestyle and behavioral management, and medical nutrition therapy (18). The most important diabetesspecific component of preconception care is the attainment of glycemic goals prior to conception. In addition, the presence of microvascular complications is associated with higher risk of disease progression and adverse pregnancy outcomes (22). Diabetes-specific testing should include A1C, creatinine, and urinary albumin-to-creatinine ratio. Special attention should be paid to the review of the medication list for potentially harmful drugs, i.e., ACE inhibitors (23,24), angiotensin receptor blockers (23), and statins (24,25). A referral for a comprehensive eye exam is recommended. Individuals

with preexisting diabetic retinopathy will need close monitoring during pregnancy to assess stability or progression of retinopathy and provide treatment if indicated (26).

# **GLYCEMIC GOALS IN PREGNANCY**

#### Recommendations

- 15.7 Fasting, preprandial, and postprandial blood glucose monitoring are recommended in individuals with diabetes in pregnancy to achieve optimal glucose levels. Glucose goals are fasting plasma glucose <95 mg/dL (<5.3 mmol/L) and either 1-h postprandial glucose <140 mg/dL (<7.8 mmol/L) or 2-h postprandial glucose <120 mg/dL (<6.7 mmol/L). B
- 15.8 Due to increased red blood cell turnover, A1C is slightly lower during pregnancy in people with and without diabetes. Ideally, the A1C goal in pregnancy is <6% (<42 mmol/mol) if this can be achieved without significant hypoglycemia, but the goal may be relaxed to <7% (<53 mmol/mol) if necessary to prevent hypoglycemia. B 15.9 When used in addition to preand postprandial blood glucose monitoring, continuous glucose monitoring (CGM) can help to achieve the A1C goal in diabetes and pregnancy. B
- 15.10 CGM is recommended in pregnancies associated with type 1 diabetes. A When used in addition to blood glucose monitoring, achieving traditional pre- and postprandial goals, real-time CGM can reduce the risk for large-for-gestational age infants and neonatal hypoglycemia in pregnancy complicated by type 1 diabetes. A
- 15.11 CGM metrics may be used in addition to but should not be used as a substitute for blood glucose monitoring to achieve optimal pre- and postprandial glycemic goals. E
- 15.12 Commonly used estimated A1C and glucose management indicator calculations should not be used in pregnancy as estimates of A1C. C
- 15.13 Nutrition counseling should endorse a balance of macronutrients including nutrient-dense fruits, vegetables, legumes, whole grains, and healthy fats with n-3 fatty acids that include nuts and seeds and fish in the eating pattern. E

# Table 15.1—Checklist for preconception care for people with diabetes Preconception education should include:

- ☐ Comprehensive nutrition assessment and recommendations for:
  - Overweight/obesity or underweight
  - Meal planning
  - · Correction of dietary nutritional deficiencies
  - Caffeine intake
  - Safe food preparation technique
- ☐ Lifestyle recommendations for:
  - Regular moderate exercise
  - Avoidance of hyperthermia (hot tubs)
  - Adequate sleep
- ☐ Comprehensive diabetes self-management education
- $\hfill\Box$  Counseling on diabetes in pregnancy per current standards, including: natural history of insulin resistance in pregnancy and postpartum; preconception glycemic goals; avoidance of DKA/severe hyperglycemia; avoidance of severe hypoglycemia; progression of retinopathy; PCOS (if applicable); fertility in people with diabetes; genetics of diabetes; risks to pregnancy including miscarriage, still birth, congenital malformations, macrosomia, preterm labor and delivery, hypertensive disorders in pregnancy, etc.
- □ Supplementation
  - Folic acid supplement (400 μg routine)
  - Appropriate use of over-the-counter medications and supplements

#### Health assessment and plan should include:

- ☐ General evaluation of overall health
- ☐ Evaluation of diabetes and its comorbidities and complications, including DKA/severe hyperglycemia; severe hypoglycemia/hypoglycemia unawareness; barriers to care; comorbidities such as hyperlipidemia, hypertension, NAFLD, PCOS, and thyroid dysfunction; complications such as macrovascular disease, nephropathy, neuropathy (including autonomic bowel and bladder dysfunction), and retinopathy
- ☐ Evaluation of obstetric/gynecologic history, including a history of cesarean section, congenital malformations or fetal loss, current methods of contraception, hypertensive disorders of pregnancy, postpartum hemorrhage, preterm delivery, previous macrosomia, Rh incompatibility, and thrombotic events (DVT/PE)
- $\hfill\square$  Review of current medications and appropriateness during pregnancy

# Screening should include:

- ☐ Diabetes complications and comorbidities, including comprehensive foot exam; comprehensive ophthalmologic exam; ECG in individuals starting at age 35 years who have cardiac signs/symptoms or risk factors and, if abnormal, further evaluation; lipid panel; serum creatinine; TSH; and urine albumin-to-creatinine ratio
- □ Anemia
- ☐ Genetic carrier status (based on history):
  - Cvstic fibrosis
  - Sickle cell anemia
  - Tay-Sachs disease
  - Thalassemia
- Others if indicated □ Infectious disease
- Neisseria gonorrhoeae/Chlamydia trachomatis
- Hepatitis B and hepatitis C
- HIV
- Pap smear
- Syphilis

#### Immunizations should include:

- □ Inactivated influenza
- ☐ Tdap (tetanus, diphtheria, and pertussis)
- ☐ COVID-19 (certain populations)
- ☐ Hepatitis A and hepatitis B (certain populations)
- □ Others if indicated

# Preconception plan should include:

- □ Nutrition and medication plan to achieve glycemic goals prior to conception, including appropriate implementation of monitoring, continuous glucose monitoring, and pump technology
- ☐ Contraceptive plan to prevent pregnancy until glycemic goals are achieved
- ☐ Management plan for general health, gynecologic concerns, comorbid conditions, or complications, if present, including hypertension, nephropathy, retinopathy; Rh incompatibility; and thyroid dysfunction

Created using information from American College of Obstetricians and Gynecologists (10) and Ramos (20). COVID-19, coronavirus disease 2019; DKA, diabetic ketoacidosis; DVT/PE, deep vein thrombosis/pulmonary embolism; ECG, electrocardiogram; NAFLD, nonalcoholic fatty liver disease; PCOS, polycystic ovary syndrome; TSH, thyroid-stimulating hormone.

Pregnancy in people with normal glucose metabolism is characterized by fasting levels of blood glucose that are lower than in the nonpregnant state due to insulin-independent glucose uptake by the fetus and placenta and by mild postprandial hyperglycemia and carbohydrate intolerance as a result of diabetogenic placental factors. In people with preexisting diabetes, glycemic goals are usually achieved through a combination of insulin administration and medical nutrition therapy. Because glycemic goals in pregnancy are stricter than in nonpregnant individuals, it is important that pregnant people with diabetes eat consistent amounts of carbohydrates to match with insulin dosage and to avoid hyperglycemia or hypoglycemia. Referral to an RDN is important to establish a food plan and insulin-tocarbohydrate ratio and determine weight gain goals. The quality of the carbohydrates should be evaluated. A subgroup analysis of the Continuous Glucose Monitoring in Pregnant Women With Type 1 Diabetes Trial (CONCEPTT) study demonstrated that the diets of individuals planning pregnancy and currently pregnant assessed during the run-in phase prior to randomization were characterized by high-fat, low-fiber, and poor-quality carbohydrate intakes. Fruit and vegetable consumption was inadequate, with one in four participants at risk for micronutrient deficiencies, highlighting the importance of medical nutrition therapy (27). An expert panel on nutrition in pregnancy recommends a balance of macronutrients. A diet that severely restricts any macronutrient class should be avoided, specifically the ketogenic diet that lacks carbohydrates, the Paleo diet because of dairy restriction, and any diet characterized by excess saturated fats. Nutrient-dense, whole foods are recommended, including fruits, vegetables, legumes, whole grains, and healthy fats with n-3 fatty acids that include nuts and seeds and fish, which are less likely to promote excessive weight gain. Processed foods, fatty red meat, and sweetened foods and beverages should be limited (28).

#### Insulin Physiology

Given that early pregnancy may be a time of enhanced insulin sensitivity and lower glucose levels, many people with type 1 diabetes will have lower insulin requirements and an increased risk for hypoglycemia (29). At around 16 weeks, insulin resistance begins to increase, and total daily insulin doses increase linearly  $\sim$ 5% per week through week 36. This usually results in a doubling of daily insulin dose compared with the prepregnancy requirement. While there is an increase in both basal and bolus insulin requirements, bolus insulin requirements take up a larger proportion of overall total daily insulin needs in individuals with preexisting diabetes as pregnancy progresses (30,31). The insulin requirement levels off toward the end of the third trimester. A rapid reduction in insulin requirements can indicate the development of placental insufficiency (32). In people with normal pancreatic function, insulin production is sufficient to meet the challenge of this physiological insulin resistance and to maintain normal glucose levels. However, in people with diabetes, hyperglycemia occurs if treatment is not adjusted appropriately.

#### **Glucose Monitoring**

Reflecting this physiology, fasting and postprandial blood glucose monitoring is recommended to achieve metabolic control in pregnant people with diabetes. Preprandial testing is also recommended when using insulin pumps or basal-bolus therapy so that premeal rapid-acting insulin dosage can be adjusted. Postprandial monitoring is associated with better glycemic outcomes and a lower risk of preeclampsia (32–34). There are no adequately powered randomized trials comparing different fasting and postmeal glycemic goals for preexisting diabetes in pregnancy.

Similar to the targets recommended by ACOG (upper limits are the same as for GDM, described below) (35), the ADA-recommended targets for pregnant people with type 1 or type 2 diabetes are as follows:

- Fasting glucose 70–95 mg/dL (3.9–5.3 mmol/L) and either
- One-hour postprandial glucose 110–140 mg/dL (6.1–7.8 mmol/L) or
- Two-hour postprandial glucose 100–120 mg/dL (5.6–6.7 mmol/L)

Lower limits are based on the mean of normal blood glucose in pregnancy (36). Lower limits do not apply to individuals with type 2 diabetes treated with nutrition alone. Hypoglycemia in

pregnancy is as defined and treated in Recommendations 6.11-6.17 (see Section 6, "Glycemic Goals and Hypoglycemia"). The most appropriate hypoglycemia threshold level in pregnancy has not been validated but has ranged from <60 to <70 mg/dL (<3.3 to <3.9 mmol/L) in the past. Current recommendations for hypoglycemia thresholds include blood glucose <70 mg/dL (<3.9 mmol/L) and sensor glucose <63 mg/dL (<3.5 mmol/L) (36,37). These fasting/premeal and postprandial glucose values represent optimal levels if they can be achieved safely. In practice, it may be challenging for a person with type 1 diabetes to achieve these goals without hypoglycemia, particularly those with a history of recurrent hypoglycemia or hypoglycemia unawareness. If an individual cannot achieve these goals without significant hypoglycemia, the ADA suggests less stringent goals based on clinical experience and individualization of care.

#### A1C in Pregnancy

In studies of individuals without preexisting diabetes, increasing A1C levels within the normal range are associated with adverse outcomes (38). In the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, increasing levels of glycemia were also associated with worsening outcomes (39). Observational studies in preexisting diabetes and pregnancy show the lowest rates of adverse fetal outcomes in association with A1C <6-6.5% (<42-48 mmol/mol) early in gestation (4-6,40). Clinical trials have not evaluated the risks and benefits of achieving these goals, and treatment goals should account for the risk of maternal hypoglycemia in setting an individualized goal of <6% (<42 mmol/mol) to <7% (<53 mmol/mol). Due to physiological increases in red blood cell turnover, A1C levels fall during normal pregnancy (41,42). Additionally, as A1C represents an integrated measure of glucose, it may not fully capture postprandial hyperglycemia, which drives macrosomia. Thus, although A1C may be useful, it should be used as a secondary measure of glycemic outcomes in pregnancy, after blood glucose monitoring.

In the second and third trimesters, A1C <6% (<42 mmol/mol) has the lowest risk of large-for-gestational-age infants (40,43,44), preterm delivery (45), and

preeclampsia (1,46). Taking all of this into account, a goal of <6% (<42 mmol/mol) is optimal during pregnancy if it can be achieved without significant hypoglycemia. The A1C goal in a given individual should be achieved without hypoglycemia, which, in addition to the usual adverse sequelae, may increase the risk of low birth weight (47,48). Given the alteration in red blood cell kinetics during pregnancy and physiological changes in glycemic parameters, A1C levels may need to be monitored more frequently than usual (e.g., monthly).

# Continuous Glucose Monitoring in Pregnancy

CONCEPTT was a randomized controlled trial (RCT) of real-time continuous glucose monitoring (CGM) in addition to standard care, including optimization of pre- and postprandial glucose goals versus standard care for pregnant people with type 1 diabetes. It demonstrated the value of real-time CGM in pregnancy complicated by type 1 diabetes by showing a mild improvement in A1C and a significant improvement in the maternal glucose time in range (TIR), without an increase in hypoglycemia, and reductions in large-for-gestational-age births, length of infant hospital stays, and severe neonatal hypoglycemia (49). An observational cohort study that evaluated the glycemic variables reported using CGM systems found that lower mean glucose, lower standard deviation, and a higher percentage of time in range were associated with lower risks of large-forgestational-age births and other adverse neonatal outcomes (50). Data from one study suggest that the use of the CGMreported mean glucose is superior to the use of estimated A1C, glucose management indicator, and other calculations to estimate A1C, given the changes to A1C that occur in pregnancy (51). CGM TIR can be used for assessment of glycemic outcomes in people with type 1 diabetes, but it does not provide actionable data to address fasting and postprandial hypoglycemia or hyperglycemia. The cost of CGM in pregnancies complicated by type 1 diabetes is offset by improved maternal and neonatal outcomes (52).

There are insufficient data to support the use of CGM in all people with type 2 diabetes or GDM (53,54). The decision of whether to use CGM in pregnant individuals with type 2 diabetes or GDM should be individualized based on treatment regimen, circumstances, preferences, and needs.

The international consensus on TIR (37) endorses pregnancy target ranges and goals for TIR for people with type 1 diabetes using CGM as reported on the ambulatory glucose profile; however, it does not specify the type or accuracy of the device or need for alarms and alerts. A prospective, observational study including 20 pregnant people with type 1 diabetes simultaneously monitored with intermittently scanning CGM (isCGM) and real-time CGM (rtCGM) for 7 days in early pregnancy demonstrated a higher percentage of time-below-range in the isCGM group. Asymptomatic hypoglycemia measured by isCGM should therefore not necessarily lead to a reduction of insulin dose and/or increased carbohydrate intake at bedtime unless these episodes are confirmed by blood glucose meter measurements (55). Selection of CGM device should be based on an individual's circumstances, preferences, and needs.

- Target sensor glucose range 63–140 mg/dL (3.5-7.8 mmol/L): TIR, goal > 70%
- Time below range (<63 mg/dL [<3.5</li> mmol/L]): level 1 TBR, goal <4%
- Time below range (<54 mg/dL [<3.0 mmol/L]): level 2 TBR, goal <1%
- Time above range (>140 mg/dL [>7.8 mmol/L]): TAR, goal <25%

The international consensus on TIR (37) endorsed the same sensor glucose target ranges for individuals with type 2 diabetes in pregnancy and GDM but could not quantify the goal of amount of time spent within each category because of insufficient data.

# MANAGEMENT OF GESTATIONAL DIABETES MELLITUS

#### Recommendations

15.14 Lifestyle behavior change is an essential component of management of gestational diabetes mellitus (GDM) and may suffice as treatment for many individuals. Insulin should be added if needed to achieve glycemic goals. A 15.15 Insulin is the preferred medication for treating hyperglycemia in GDM. Metformin and glyburide, individually or in combination, should not be used as first-line agents, as both

cross the placenta to the fetus. A Other oral and noninsulin injectable glucose-lowering medications lack longterm safety data. E

15.16 Metformin, when used to treat polycystic ovary syndrome and induce ovulation, should be discontinued by the end of the first trimester. A

15.17 Telehealth visits used in combination with in-person visits for pregnant people with GDM can improve outcomes compared with standard inperson care alone. A

GDM is characterized by an increased risk of large-for-gestational-age birth weight and neonatal and pregnancy complications and an increased risk of long-term maternal type 2 diabetes and abnormal glucose metabolism of offspring in childhood. These associations with maternal oral glucose tolerance test (OGTT) results are continuous with no clear inflection points (39.56). Offspring with exposure to untreated GDM have reduced insulin sensitivity and B-cell compensation and are more likely to have impaired glucose tolerance in childhood (57). In other words, short-term and long-term risks increase with progressive maternal hyperglycemia. Therefore, all pregnant people should be screened as outlined in Section 2, "Diagnosis and Classification of Diabetes." Although there is some heterogeneity, many RCTs and a Cochrane review suggest that the risk of GDM may be reduced by diet, exercise, and lifestyle counseling, particularly when interventions are started during the first or early in the second trimester (58-60). There are no intervention trials in offspring of mothers with GDM. A meta-analysis of 11 RCTs demonstrated that metformin treatment in pregnancy does not reduce the risk of GDM in highrisk individuals with obesity, polycystic ovary syndrome, or preexisting insulin resistance (61). A meta-analysis of 32 RCTs evaluating the effectiveness of telemedicine interventions, which ranged from telemedicine visits to the use of health apps, used in combination with in-person visits for GDM demonstrated reduced incidences of cesarean delivery, premature rupture of membranes, pregnancy-induced hypertension or preeclampsia, preterm birth, neonatal asphyxia, and polyhydramnios compared with standard in-person care alone (62).

#### Lifestyle and Behavioral Management

After diagnosis, treatment starts with medical nutrition therapy, physical activity, and weight management, depending on pregestational weight, as outlined in the section below on preexisting type 2 diabetes, as well as glucose monitoring aiming for the goals recommended by the Fifth International Workshop-Conference on Gestational Diabetes Mellitus (63):

- Fasting glucose <95 mg/dL (<5.3 mmol/L) and either
- One-hour postprandial glucose <140 mg/dL (<7.8 mmol/L) or</li>
- Two-hour postprandial glucose <120 mg/dL (<6.7 mmol/L)</li>

The glycemic goal lower limits defined above for preexisting diabetes apply for GDM treated with insulin. Depending on the population, studies suggest that 70–85% of people diagnosed with GDM under Carpenter-Coustan criteria can manage GDM with lifestyle modification alone; it is anticipated that this proportion will be even higher if the lower International Association of the Diabetes and Pregnancy Study Groups (64) diagnostic thresholds are used.

#### **Medical Nutrition Therapy**

Medical nutrition therapy for GDM is an individualized nutrition plan developed between the pregnant person and an RDN familiar with the management of GDM (65,66). The food plan should provide adequate calorie intake to promote fetal/neonatal and maternal health, achieve glycemic goals, and promote appropriate weight gain, according to the 2009 National Academy of Medicine recommendations (67). There is no definitive research that identifies a specific optimal calorie intake for people with GDM or suggests that their calorie needs are different from those of pregnant individuals without GDM. The food plan should be based on a nutrition assessment with dietary reference intake guidance from the National Academy of Medicine. The recommended dietary reference intake for all pregnant people is a minimum of 175 g of carbohydrate ( $\sim$ 35% of a 2,000-calorie diet), a minimum of 71 g of protein, and 28 g of fiber (68). The nutrition plan should emphasize monounsaturated and polyunsaturated fats while limiting saturated fats and avoiding trans fats. As is true for all nutrition therapy in

people with diabetes, the amount and type of carbohydrate will impact glucose levels. Promoting higher-quality, nutrient-dense carbohydrates results in controlled fasting/postprandial glucose, lower free fatty acids, improved insulin action, and vascular benefits and may reduce excess infant adiposity. Individuals who substitute fat for carbohydrates may unintentionally enhance lipolysis, promote elevated free fatty acids, and worsen maternal insulin resistance (69,70). Fasting urine ketone testing may be useful to identify those who are severely restricting carbohydrates to manage blood glucose. Simple carbohydrates will result in higher postmeal excursions.

#### Physical Activity

A systematic review demonstrated improvements in glucose outcomes and reductions in need to start insulin or insulin dose requirements with an exercise intervention. There was heterogeneity in the types of effective exercise (aerobic, resistance, or both) and duration of exercise (20–50 min/day, 2–7 days/week of moderate intensity) (71).

# Pharmacologic Therapy

Treatment of GDM with lifestyle and insulin has been demonstrated to improve perinatal outcomes in two large randomized studies, as summarized in a U.S. Preventive Services Task Force review (72). Insulin is the first-line agent recommended for the treatment of GDM in the U.S. While individual RCTs support limited efficacy of metformin (73,74) and glyburide (75) in reducing glucose levels for the treatment of GDM, these agents are not recommended as the first-line treatment for GDM because they are known to cross the placenta and data on long-term safety for offspring is of some concern (35). Furthermore, in separate RCTs, glyburide and metformin failed to provide adequate glycemic outcomes in 23% and 25-28% of participants with GDM, respectively (76,77).

# Sulfonylureas

Sulfonylureas are known to cross the placenta and have been associated with increased neonatal hypoglycemia. Concentrations of glyburide in umbilical cord plasma are approximately 50–70% of maternal levels (76,77). In meta-analyses

and systematic reviews, glyburide was associated with a higher rate of neonatal hypoglycemia, macrosomia, and increased neonatal abdominal circumference than insulin or metformin (78,79).

Glyburide failed to be found noninferior to insulin based on a composite outcome of neonatal hypoglycemia, macrosomia, and hyperbilirubinemia (80). Long-term safety data for offspring exposed to glyburide are not available (80).

#### Metformin

Metformin was associated with a lower risk of neonatal hypoglycemia and less maternal weight gain than insulin in systematic reviews and RCTs (78,81-83). However, metformin readily crosses the placenta, resulting in umbilical cord blood levels of metformin as high or higher than simultaneous maternal levels (84,85). In the Metformin in Gestational Diabetes: The Offspring Follow-Up (MiG TOFU) study's analyses of 7- to 9-year-old offspring, the 9-year-old offspring exposed to metformin for the treatment of GDM in the Auckland cohort were heavier and had a higher waist-to-height ratio and waist circumference than those exposed to insulin (86). This difference was not found in the Adelaide cohort. In one RCT of metformin use in pregnancy for polycystic ovary syndrome, follow-up of 4-year-old offspring demonstrated higher BMI and increased obesity in the offspring exposed to metformin (87). A follow-up study at 5-10 years showed that the offspring had higher BMI, weight-toheight ratios, waist circumferences, and a borderline increase in fat mass (88,89). A meta-analysis demonstrated that metformin exposure resulted in smaller neonates with an acceleration of postnatal growth, resulting in higher BMI in childhood (88). Follow-up of offspring from the Metformin in Women with Type 2 Diabetes in Pregnancy (MiTy Kids) trial showed no differences in anthropometrics of children at 24 months (90).

Randomized, double-blind, controlled trials comparing metformin with other therapies for ovulation induction in individuals with polycystic ovary syndrome have not demonstrated benefit in preventing spontaneous abortion or GDM (91), and there is no evidence-based need to continue metformin in these individuals (92–94).

There are some people with GDM requiring medical therapy who may not be able to use insulin safely or effectively during pregnancy due to cost, language barriers, comprehension, or cultural influences. Oral agents may be an alternative for these individuals after discussing the known risks and the need for more long-term safety data in offspring. However, due to the potential for growth restriction or acidosis in the setting of placental insufficiency, metformin should not be used in pregnant people with hypertension or preeclampsia or those at risk for intrauterine growth restriction (90,95,96).

#### Insulin

Insulin use should follow the guidelines below. Both multiple daily insulin injections and continuous subcutaneous insulin infusion are reasonable delivery strategies, and neither has been shown to be superior to the other during pregnancy (97).

# MANAGEMENT OF PREEXISTING TYPE 1 DIABETES AND TYPE 2 DIABETES IN PREGNANCY

#### Recommendations

15.18 Insulin should be used to manage type 1 diabetes in pregnancy. A Insulin is the preferred agent for the management of type 2 diabetes in pregnancy. B

15.19 Either multiple daily injections or insulin pump technology can be used in pregnancy complicated by type 1 diabetes. C

The physiology of pregnancy necessitates frequent titration of insulin to match changing requirements and underscores the importance of daily and frequent blood glucose monitoring. Due to the complexity of insulin management in pregnancy, referral to a specialized center offering team-based care (with team members including a maternal-fetal medicine specialist, endocrinologist or other health care professional experienced in managing pregnancy and preexisting diabetes, RDN, diabetes care and education specialist, and social worker, as needed) is recommended if this resource is available. When a single specialized center is not available, providing a interprofessional team approach through interprofessional

team members at different centers may still be beneficial.

None of the currently available human insulin preparations have been demonstrated to cross the placenta (93-98). Insulins studied in RCTs are preferred (97,99-103) over those studied in cohort studies (104), which are preferred over those studied in case reports only.

While many health care professionals prefer insulin pumps in pregnancy, it is not clear that they are superior to multiple daily injections (105,106). None of the current automated insulin delivery (AID) systems approved by the U.S. Food and Drug Administration (FDA) have algorithms set to achieve pregnancy goals. It may be appropriate to continue or initiate AID therapy in carefully selected pregnant individuals with type 1 diabetes in the setting of using assistive techniques with expert guidance (107). Assessments of potential candidates for AID wear in pregnancy should include relevant parameters such as glycemic levels, presence or absence of severe hypoglycemic or hyperglycemic events, ability or comfort in engaging with diabetes technology, psychosocial determinants, cost, individual preference, and other factors as relevant. In addition, individuals who use AID systems that do not have pregnancyspecific glucose targets often benefit from assistive techniques for pump management as determined by expert guidance from an experienced interprofessional team (107). Partial closed-loop therapy, such as predictive low-glucose suspend (PLGS) technology, has been shown in nonpregnant people to be better than sensoraugmented insulin pumps (SAP) for reducing low glucose values (108). It may be suited for pregnancy because the predictive low-glucose threshold for suspending insulin is in the range of premeal and overnight glucose value targets in pregnancy and may allow for more aggressive prandial dosing. See SENSOR-AUGMENTED PUMPS and AUTO-MATED INSULIN DELIVERY SYSTEMS In Section 7, "Diabetes Technology," for more information on these systems.

#### Type 1 Diabetes

Pregnant individuals with type 1 diabetes have an increased risk of hypoglycemia in the first trimester and, like all pregnant people, have altered counter-regulatory response in pregnancy that may decrease hypoglycemia awareness. Education for

people with diabetes and family members about the prevention, recognition, and treatment of hypoglycemia is important before, during, and after pregnancy to help prevent and manage hypoglycemia risk. Insulin resistance drops rapidly with the delivery of the placenta.

Pregnancy is a ketogenic state, and people with type 1 diabetes, and to a lesser extent those with type 2 diabetes, are at risk for diabetic ketoacidosis (DKA) at lower blood glucose levels than in the nonpregnant state. Pregnant people with type 1 diabetes should be advised to obtain ketone test strips and receive education on DKA prevention and detection. DKA carries a high risk of stillbirth. Those in DKA who are unable to eat often require 10% dextrose with an insulin drip to adequately meet the higher carbohydrate demands of the placenta and fetus in the third trimester in order to resolve their ketosis.

Retinopathy is a special concern in pregnancy. The necessary rapid implementation of euglycemia in the setting of retinopathy is associated with worsening of retinopathy (109). Meta-analyses have also demonstrated a high risk of newonset retinopathy and progression of existing retinopathy in pregnant individuals with type 1 or type 2 diabetes (110,111).

# Type 2 Diabetes

Type 2 diabetes is often associated with obesity. Recommended weight gain during pregnancy for people with overweight is 15-25 lb (6.8-11.3 kg) and for those with obesity is 10-20 lb (4.5-9.1 kg) (67). There are no adequate data on optimal weight gain versus weight maintenance in pregnant people with BMI >35 kg/m<sup>2</sup>; however, losing weight is not recommended because of the increased risk of small-for-gestational age infants (21).

Optimal glycemic goals are often easier to achieve during pregnancy with type 2 diabetes than with type 1 diabetes but can require much higher doses of insulin, sometimes necessitating concentrated insulin formulations. Insulin is the preferred treatment for type 2 diabetes in pregnancy. An RCT of metformin added to insulin for the treatment of type 2 diabetes found less maternal weight gain and fewer cesarean births. There were fewer macrosomic neonates, but there was a doubling of small-for-gestational-age neonates (112). As in type 1 diabetes, insulin requirements drop dramatically after delivery.

The risk for associated hypertension and other comorbidities may be as high or higher with type 2 diabetes compared with type 1 diabetes, even if diabetes is better managed and of shorter apparent duration, with pregnancy loss appearing to be more prevalent in the third trimester in those with type 2 diabetes, compared with the first trimester in those with type 1 diabetes (113,114).

#### PREECLAMPSIA AND ASPIRIN

#### Recommendation

**15.20** Pregnant individuals with type 1 or type 2 diabetes should be prescribed low-dose aspirin 100–150 mg/day starting at 12 to 16 weeks of gestation to lower the risk of preeclampsia. **E** A dosage of 162 mg/day may be acceptable; **E** currently, in the U.S., low-dose aspirin is available in 81-mg tablets.

Diabetes in pregnancy is associated with an increased risk of preeclampsia (115). The U.S. Preventive Services Task Force recommends using low-dose aspirin (81 mg/day) as a preventive medication at 12 weeks of gestation in individuals at high risk for preeclampsia, such as those with type 1 or type 2 diabetes (116). However, a meta-analysis and an additional trial demonstrate that low-dose aspirin <100 mg is not effective in reducing preeclampsia. Low-dose aspirin >100 mg is required (117-119). A costbenefit analysis has concluded that this approach would reduce morbidity, save lives, and lower health care costs (120). There are insufficient data about whether the use of aspirin specifically in pregnant people with preexisting diabetes ultimately reduces the incidence of preeclampsia (121,122), although a meta-analysis showed that preeclampsia reductions occurred with aspirin administration in high-risk groups overall (115). Individuals with GDM may be candidates for aspirin therapy for preeclampsia prevention if they have a single high risk factor, such as chronic hypertension or an autoimmune disease, or multiple moderate risk factors, such as being nulliparous, having obesity, being age ≥35 years, or other factors per the U.S. Preventive

Services Task Force (116). More studies are needed to assess the long-term effects of prenatal aspirin exposure on offspring (121).

# PREGNANCY AND DRUG CONSIDERATIONS

#### Recommendations

15.21 In pregnant individuals with diabetes and chronic hypertension, a blood pressure threshold of 140/90 mmHg for initiation or titration of therapy is associated with better pregnancy outcomes than reserving treatment for severe hypertension, with no increase in risk of small-forgestational-age birth weight. A There are limited data on the optimal lower limit, but therapy should be deintensified for blood pressure <90/60 mmHg. E A blood pressure target of 110-135/ 85 mmHg is suggested in the interest of reducing the risk for accelerated maternal hypertension. A

**15.22** Potentially harmful medications in pregnancy (i.e., ACE inhibitors, angiotensin receptor blockers, statins) should be stopped prior to conception and avoided in sexually active individuals of childbearing potential who are not using reliable contraception. **B** 

In normal pregnancy, blood pressure is lower than in the nonpregnant state. The Chronic Hypertension and Pregnancy (CHAP) Trial Consortium's RCT on treatment for mild chronic hypertension during pregnancy demonstrated that a blood pressure of 140/90 mmHg, as the threshold for initiation or titration of treatment, reduces the incidence of adverse pregnancy outcomes without compromising fetal growth (123). The CHAP Consortium's study mitigates concerns about small-for-gestational-age birth weight. Attained mean ± SD blood pressure measurements in the treated versus untreated groups were systolic 129.5 ± 10.0 vs. 132.6 ± 10.1 mmHg (betweengroup difference -3.11 [95% CI -3.95 to 2.28]) and diastolic 79.1  $\pm$  7.4 vs. 81.5  $\pm$ 8.0 mmHg (-2.33 [95% CI -2.97 to 0.04]) (123). Individuals with diabetes had an even better composite outcome score than those without diabetes (123).

As a result of the CHAP study, ACOG issued a Practice Advisory recommending a blood pressure of 140/90 mmHg

as the threshold for initiation or titration of medical therapy for chronic hypertension in pregnancy (124) rather than their previously recommended threshold of 160/110 mmHg (125).

The CHAP study provides additional guidance for the management of hypertension in pregnancy. Data from the previously published Control of Hypertension in Pregnancy Study (CHIPS) supports a target blood pressure goal of 110-135/85 mmHg to reduce the risk of uncontrolled maternal hypertension and minimize impaired fetal growth (125-127). The 2015 study (126) excluded pregnancies complicated by preexisting diabetes, and only 6% of participants had GDM at enrollment. There was no difference in pregnancy loss, neonatal care, or other neonatal outcomes between the groups with tighter versus less tight control of hypertension (126).

During pregnancy, treatment with ACE inhibitors and angiotensin receptor blockers is contraindicated because they may cause fetal renal dysplasia, oligohydramnios, pulmonary hypoplasia, and intrauterine growth restriction (23).

A large study found that after adjusting for confounders, first trimester ACE inhibitor exposure does not appear to be associated with congenital malformations (128). However, ACE inhibitors and angiotensin receptor blockers should be stopped as soon as possible in the first trimester to avoid second and third trimester fetopathy (128). Antihypertensive drugs known to be effective and safe in pregnancy include methyldopa, nifedipine, labetalol, diltiazem, clonidine, and prazosin. Atenolol is not recommended, but other β-blockers may be used, if necessary. Chronic diuretic use during pregnancy is not recommended as it has been associated with restricted maternal plasma volume, which may reduce uteroplacental perfusion (129). On the basis of available evidence, statins should also be avoided in pregnancy (130).

See pregnancy and antihypertensive medications in Section 10, "Cardiovascular Disease and Risk Management," for more information on managing blood pressure in pregnancy.

#### POSTPARTUM CARE

#### Recommendations

**15.23** Insulin resistance decreases dramatically immediately postpartum,

and insulin requirements need to be evaluated and adjusted as they are often roughly half the prepregnancy requirements for the initial few days postpartum. C

15.24 A contraceptive plan should be discussed and implemented with all people with diabetes of childbearing potential. A

15.25 Screen individuals with a recent history of GDM at 4-12 weeks postpartum, using the 75-g oral glucose tolerance test and clinically appropriate nonpregnancy diagnostic criteria. B 15.26 Individuals with overweight/ obesity and a history of GDM found to have prediabetes should receive intensive lifestyle interventions and/or metformin to prevent diabetes. A

15.27 Breastfeeding efforts are recommended for all individuals with diabetes. A Breastfeeding is recommended for individuals with a history of GDM for multiple benefits, A including a reduced risk for type 2 diabetes later in life. B

15.28 Individuals with a history of GDM should have lifelong screening for the development of type 2 diabetes or prediabetes every 1-3 years. B 15.29 Individuals with a history of GDM should seek preconception screening for diabetes and preconception care to identify and treat hyperglycemia and prevent congenital malformations. E

15.30 Postpartum care should include psychosocial assessment and support for self-care. E

# Gestational Diabetes Mellitus **Postpartum Care**

Because GDM often represents previously undiagnosed prediabetes, type 2 diabetes, maturity-onset diabetes of the young, or even developing type 1 diabetes, individuals with GDM should be tested for persistent diabetes or prediabetes at 4-12 weeks postpartum with a fasting 75-g OGTT using nonpregnancy criteria as outlined in Section 2, "Diagnosis and Classification of Diabetes," specifically Tables 2.1 and 2.2. The OGTT is recommended over A1C at 4-12 weeks postpartum because A1C may be persistently impacted (lowered) by the increased red blood cell turnover related to pregnancy, by blood loss at delivery, or by

the preceding 3-month glucose profile. The OGTT is more sensitive at detecting glucose intolerance, including both prediabetes and diabetes. In the absence of unequivocal hyperglycemia, a positive screen for diabetes requires two abnormal values. If both the fasting plasma glucose (≥126 mg/dL [≥7.0 mmol/L]) and 2-h plasma glucose (≥200 mg/dL [≥11.1 mmol/L]) are abnormal in a single screening test, then the diagnosis of diabetes is made. If only one abnormal value in the OGTT meets diabetes criteria, the test should be repeated to confirm that the abnormality persists. OGTT testing immediately postpartum, while still hospitalized, has demonstrated improved engagement in testing but also variably reduced sensitivity to the diagnosis of impaired fasting glucose, impaired glucose tolerance, and type 2 diabetes (131,132).

Individuals with a history of GDM should have ongoing screening for prediabetes or type 2 diabetes every 1-3 years, even if the results of the initial 4-12 week postpartum 75-g OGTT are normal. Ongoing evaluation may be performed with any recommended glycemic test (e.g., annual A1C, annual fasting plasma glucose, or triennial 75-g OGTT using thresholds for nonpregnant individuals).

Individuals with a history of GDM have an increased lifetime maternal risk for diabetes estimated at 50-60% (133,134), and those with GDM have a 10-fold increased risk of developing type 2 diabetes compared with those without GDM (133). Absolute risk of developing type 2 diabetes after GDM increases linearly through a person's lifetime, being approximately 20% at 10 years, 30% at 20 years, 40% at 30 years, 50% at 40 years, and 60% at 50 years (134). In the prospective Nurses' Health Study II (NHS II), subsequent diabetes risk after a history of GDM was significantly lower in those who followed healthy eating patterns (135). Adjusting for BMI attenuated this association moderately, but not completely. Interpregnancy weight gain is associated with increased risk of adverse pregnancy outcomes (136) and higher risk of GDM, while in people with BMI >25 kg/m<sup>2</sup>, weight loss is associated with lower risk of developing GDM in the subsequent pregnancy (137). Development of type 2 diabetes is 18% higher per unit of BMI increase from prepregnancy BMI at follow-up, highlighting the importance of

effective weight management after GDM (138). In addition, postdelivery lifestyle interventions are effective in reducing risk of type 2 diabetes (139).

Both metformin and intensive lifestyle intervention prevent or delay progression to diabetes in individuals with prediabetes and a history of GDM. Only five to six individuals with prediabetes and a history of GDM need to be treated with either intervention to prevent one case of diabetes over 3 years (140). In these individuals, lifestyle intervention and metformin reduced progression to diabetes by 35% and 40%, respectively, over 10 years compared with placebo (141). If the pregnancy has motivated the adoption of healthy nutrition, building on these gains to support weight loss is recommended in the postpartum period. (See Section 3, "Prevention or Delay of Diabetes and Associated Comorbidities.")

Individuals with prediabetes or a history of GDM will need preconception evaluation for as long as they have childbearing potential.

# Preexisting Type 1 and Type 2 **Diabetes Postpartum Care**

Insulin sensitivity increases dramatically with the delivery of the placenta. In one study, insulin requirements in the immediate postpartum period are roughly 34% lower than prepregnancy insulin requirements (142). Insulin sensitivity then returns to prepregnancy levels over the following 1-2 weeks. For individuals taking insulin, particular attention should be directed to hypoglycemia prevention in the setting of breastfeeding and erratic sleep and eating schedules (143).

#### Lactation

Considering the immediate nutritional and immunological benefits of breastfeeding for the baby, all mothers, including those with diabetes, should be supported in attempts to breastfeed. An analysis of 28 systematic reviews and meta-analyses of associations between breastfeeding and outcomes in children found that breastfeeding was associated with numerous health benefits for children such as reduced infant mortality due to infectious diseases at <6 months of age (odds ratio [OR] 0.22-0.59 across studies), reduced respiratory infections in children aged <2 years, and reduced asthma or wheezing in children aged 5-18 years (OR 0.91, 0.85-0.98) (144). The same analysis found that breastfeeding was associated with improved maternal health outcomes including reduced risks of breast cancer (OR 0.81 [95% CI 0.77-0.86]), ovarian cancer (OR 0.70 [95% CI 0.64-0.75]), and type 2 diabetes (OR 0.68 [95% CI 0.57-0.82]). Breastfeeding may also confer longer-term metabolic benefits to both mother (145) and offspring (146). Breastfeeding reduces the risk of developing type 2 diabetes in mothers with previous GDM (145). It may improve the metabolic risk factors of offspring, but more studies are needed (147). However, lactation can increase the risk of overnight hypoglycemia, and insulin dosing may need to be adjusted.

#### Contraception

A major barrier to effective preconception care is the fact that the majority of pregnancies are unplanned. Planning pregnancy is critical in individuals with preexisting diabetes to achieve the optimal glycemic goals necessary to prevent congenital malformations and reduce the risk of other complications. Therefore, all individuals with diabetes of childbearing potential should have family planning options reviewed at regular intervals to make sure that effective contraception is implemented and maintained. This applies to individuals in the immediate postpartum period. Individuals with diabetes have the same contraception options and recommendations as those without diabetes. Long-acting, reversible contraception may be ideal for individuals with diabetes and childbearing potential. The risk of an unplanned pregnancy outweighs the risk of any currently available contraception option.

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