

GESTATIONAL DIABETES

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ABSTRACT

Gestational Diabetes (GDM) is characterized by glucose intolerance first manifesting during pregnancy and is an important risk factor for abnormal birthweight including large-for-gestational age birth, birth injury, and neonatal metabolic alterations--particularly when persistent maternal hyperglycemia exists. Individuals with GDM face short-term pregnancy complications, such as cesarean section and hypertensive disorders, and long-term complications, including an increased lifetime risk for type 2 diabetes and cardiovascular disease. Many of these complications associated with GDM can be moderated with lifestyle changes and pharmacotherapeutic interventions to reduce maternal hyperglycemia and thereby improve maternal and neonatal health.

PREVALENCE AND PATHOPHYSIOLOGY

Gestational diabetes (GDM) is a major problem in the US with a rapidly rising prevalence ranging from 6 to 20% of pregnancies across the world (1–4). The prevalence is highest in racial and ethnic groups that have a higher incidence of type 2 diabetes mellitus (T2DM): Hispanic, Black, American Indian, and Asian or Pacific Islander individuals (1). In the US, the prevalence of GDM was 7.8 per 100 births in 2020 with a higher annual percent change from 5% annually from 2016-2019 to 13% in 2020 (5). There are significant differences in the rate of GDM also by rural/urban status, age, body mass index (BMI), and state of residence (5,6).

Insulin resistance is paired with increased insulin secretion during pregnancy; however, among individuals with GDM, inadequate β -cell compensation relative to the level of insulin resistance results in failure to maintain euglycemia (7). GDM is caused by

carbohydrate intolerance due to abnormalities in at least 3 aspects of fuel metabolism: insulin resistance, impaired insulin secretion, and increased hepatic glucose production (8,9).

Although insulin resistance is a universal finding in pregnancies with GDM, the cellular mechanisms for insulin resistance are multifactorial. Insulin binding to its receptor is unchanged in pregnant individuals (10). Pregnancy reduces the capacity for insulin-stimulated glucose transport independent of obesity, due in part to a tissue-specific decrease in insulin receptor phosphorylation and decreased expression of Insulin Receptor Substrate-1 (IRS-1), a major docking protein in skeletal muscle (11). In addition to these mechanisms, in muscle specimens from individuals with GDM. IRS-1 is further decreased and there are reciprocal and inverse changes in the degree of serine and tyrosine phosphorylation of the insulin receptor (IR) and IRS-1, further inhibiting insulin signaling (12). Individuals with GDM also have higher circulating free fatty acids (FFA) and reduced peroxisome proliferatoractivated receptor (PPAR) expression in adipose tissue, a target for thiazolidinediones (13). There is evidence for a decrease in the number of glucose transporters (GLUT-4) in adipocytes in individuals with GDM and an abnormal translocation of these transporters that results in the reduced ability of insulin to recruit them to the cell surface, which contributes to the overall insulin resistance with GDM (14). In individuals with GDM, serum adiponectin levels decrease and leptin, IL-6, and TNF α increase (15).

Although dysglycemia usually remits after pregnancy, individuals with a history of GDM have a nearly 10-fold higher risk of progressing to type 2 diabetes than those without GDM and up to 70% of individuals diagnosed with GDM will develop T2DM later in life (16–18). Both GDM and T2DM are further exacerbated by increasing obesity and age. Thus, pregnancy is a "stress test" for the eventual development of glucose intolerance outside of pregnancy, and GDM may represent an unmasking of the predisposition of T2DM induced by the hormonal changes of pregnancy (19,20).

DATA TO SUPPORT THE SCREENING, DIAGNOSIS, AND TREATMENT OF GESTATIONAL DIABETES

As early as the 1940s, glucose intolerance and GDM distinct from pregestational DM were recognized to have adverse maternal and perinatal outcomes (21). Over the course of the following eight decades, candidates for screening or testing as well as the diagnostic criteria of GDM were debated (22,23). Early on, value was placed on recognition of GDM to identify individuals at risk for T2DM (24). More recently, robust studies have demonstrated the more immediate obstetric and perinatal benefits of screening, diagnosing, and treating GDM (1,24,25).

The first was a landmark trial conducted in Austria and New Zealand referred to as the ACHOIS trial (Australian Carbohydrate Intolerance Study in Pregnant Women), which demonstrated reduced serious perinatal outcomes with intervention/treatment of GDM versus no intervention (1% versus 4%) (24). This RCT enrolled 1000 pregnant individuals with either ≥1 risk factor for GDM or positive 1-hour 50 gm glucose challenge test (GCT) (≥140mg/dL) after completion of a blinded 75 gm glucose tolerance test (GTT) at 24-34 weeks gestation and demonstrated no severe glucose impairment. Individuals were randomized to receive dietary advice, self-monitoring of blood glucose (SMBG), and insulin therapy as needed to achieve fasting glucose <99 mg/dL and 2hour postprandial values <126 mg/dL versus routine care. The primary outcome of fetal or neonatal death, shoulder dystocia, bone fracture, and nerve palsy were reduced in the intervention group compared with routine care (1% versus 4%). Although the induction of labor rate was higher in the intervention group, the cesarean delivery rate was not different.

A second landmark randomized controlled trial (RCT), the National Institute of Child Health and Human **Development Maternal- Fetal Medicine Units Network** study (NICHD MFMU Network), demonstrated significant differences in meaningful secondary outcomes (mean birthweight, neonatal fat mass, large for gestational age infants, birthweight >4000 g, shoulder dystocia. cesarean delivery, and hypertensive disorders of pregnancy) by treating mild GDM (25). A total of 958 pregnant individuals who met criteria for mild GDM between 24-31 weeks were randomly assigned to usual prenatal care (control) or dietary interventions, SMBG, and insulin therapy if necessary (treatment group). Although there was no significant difference in groups in the frequency of the composite outcome and no perinatal deaths in this population with very mild GDM, there were significant reductions with treatment in several pre-specified secondary outcomes. Furthermore, treatment of mild GDM was also associated with reduced rates for hypertensive disorders of pregnancy.

There is also compelling data that the risk of adverse maternal and fetal outcomes from maternal carbohydrate intolerance is along a graded continuum (26,27). The Hyperglycemia and Adverse Outcomes (HAPO) trial enrolled 25,505 pregnant individuals at 15 centers in nine countries, with participants completing a 2-hour 75 gm GTT at 24-32 weeks' gestation (27). Data remained blinded if the fasting glucose ≤105 mg/dL and the 2-hour plasma glucose was ≤200 mg/dL. This trial demonstrated that a fasting blood glucose (FBG) ≥92 mg/dl, a 1-hour value ≥180 mg/dl, or a 2-hour value of ≥153 mg/dl increased the risk by 1.75-fold for large for gestational age (LGA or more than 90th percentile for weight of all babies of the same gestational age) and an elevated cord-blood Cpeptide consistent with fetal hyperinsulinemia. Furthermore, the fasting glucose was more strongly predictive of these outcomes than the 1-hour or 2-hour value stressing the importance of fasting glucose levels in predicting poor perinatal outcomes. The results also indicated a strong and continuous association with these outcomes and maternal glucose levels below those considered diagnostic of GDM.

DIAGNOSIS OF GESTATIONAL DIABETES

The implications of diabetes recognized for the first time in pregnancy on both maternal and perinatal outcomes have been known for nearly a century (21,28). Nevertheless, substantial controversy persists when considering which individuals warrant screening or outright diagnostic testing, at which gestational age this should occur, and the laboratory cutoffs which should confirm the diagnosis and prompt possible intervention.

Evaluation for what we currently define as GDM, for "early GDM" or for T2DM first diagnosed in pregnancy may take place in a risk-based or universal manner. In general, the basic tenants of screening as defined by the World Health Organization (WHO) are met: GDM and DM are significant health problems with significant consequences if left untreated, a suitable test exists, with benefits of screening outweighing the risks (29). The lack of consensus generally results from concerns about cost-effectiveness of differing strategies and psychological and public health burdens with increased prevalence of the condition.

Unfortunately, the historical definition of GDM as a glucose-intolerant state with onset or first recognition during pregnancy allows for inclusion of both unrecognized, pregestational, overt diabetes in addition to "true" gestational diabetes resulting from the physiologic and hormonal changes of pregnancy. Since individuals with undiagnosed pregestational diabetes are at increased risk for both maternal and fetal complications, including major malformations if their hemoglobin A1c is $\geq 6.5\%$ in the first trimester, the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) recommends that GDM be only diagnosed if the glucose intolerance was identified in pregnancy and the pregnant individual did not qualify for pre-existing (overt) diabetes (30). The details and nuanced considerations of the current understanding of GDM as well as screening and

testing modalities are described in the literature (31–33).

In the US, the US Preventive Services Task Force (USPSTF) and the American College of Obstetricians and Gynecologists (ACOG) recommend universal screening for all pregnant individuals at 24-28 weeks gestation since prior use of historic factors alone failed to identify 50% of patients with GDM (1). ACOG further supports a two-step process involving a 50 gm,1-hour glucose challenge test (GCT) followed by a 100 gm, 3-hour oral glucose tolerance test (GTT) (1). The diagnosis of GDM is made if two or more abnormal values are seen in the 3-hour GTT. Although elevation

of just one out of four values in the 3-hour GTT is still associated with adverse outcomes, there is not clear evidence that this subset of patients would benefit from treatment (1,34). The one-step International Association of the Diabetes and Pregnancy Study (IADPSG) approach is utilized more frequently internationally and is supported by organizations such as National Institute for Health and Care Excellence (NICE) in UK and Royal Australian and New Zealand College of Obstetricians and **Gynaecologists** (RANZOG) (35,36). The American Diabetes Association (ADA) continues to recognize that there is no clear evidence which supports IADPSG versus traditional ACOG two-step screening approach (37).

Table 1. Gestational Diabetes. Screening and Diagnostic Criteria, performed at 24-							
28 weeks' gestation for individuals without evidence of pregestational							
diabetes ^a							
One-step approach							
Perform a 75 gm GTT, with plasma glucose measurement when patient is fasting, at 1							
and 2 hours. Test should occur in the morning following ≥8 hour fast							
Diagnosis of GDM is made with ≥1 of the following:							
Fasting ≥92mg/dL 1 hour ≥180mg/dL 2 hour ≥153mg/dL							
Benefits: Single diagnostic test							
Disadvantages: Must be fasting, increased prevalence of GDM without clear perinatal or							
long-term differences in outcomes compared to two-step approach, increased							
healthcare costs							
Supported by: IADPSG, ADA, NICE, RANZOG							
Two-step approach							
Perform a non-fasting 50 gm GCT, with plasma glucose measurement at 1 hour							
If glucose level measured 1 hour after the load is \geq 130, 135, or 140 mg/dL ^{β} , proceed to							
a 100 gm GTT.							
Perform a 100 gm GTT, with plasma glucose measurement when patient is fasting, at							
1, 2 & 3 hours. Test should occur in the morning following ≥8 hour fast							
The diagnosis is made when $\geq 2^{\pm}$ of the following (Carpenter/Coustan criteria):							
recommended by ACOG and ADA							
Fasting ≥95mg/dL 1 hour ≥180mg/dL 2 hour ≥155mg/dL 3 hour ≥140mg/dL							
The diagnosis is made when $\geq 2^{4}$ of the following (National Diabetes Data Group							
criteria):							
Fasting ≥105mg/dL 1 hour ≥190mg/dL 2 hour ≥165mg/dL 3 hour ≥145mg/dL							
Benefits: Increased compliance with "milder" initial test, no fasting required on GCT							
Disadvantages: No consensus on cutoffs for GCT							
Supported by: ACOG, ADA							

α: Note that while most international and national guidelines have moved toward universal testing, the United Kingdom's National Institute for Health and Care Excellence continues to recommend risk-based GDM testing (35).

 β : Cutoff of 140mg/dL results in sensitivity of 70–88% and specificity of 69–89% and requires GTT in ~15% patients; cutoff of 130mg/dL results in sensitivity of 88–99% and specificity of 66–77% specific and requires GTT in ~25% patients.

¥: ACOG allows for consideration of diagnosis with \geq 1 criteria met.

The controversy with the diagnosis of GDM relies heavily on the outcomes studied. The IADPSG recommendations are based on the HAPO trial, which showed that a single value on a 75 gm 2-hour GTT resulted in a 1.75-fold increased risk of LGA and thus should be the basis for the diagnosis; however, critics disagree (38,39). Critics contend that a 2.0-fold increase in LGA risk instead of 1.75 could have been chosen which would not have appreciably increased the prevalence of GDM over the ACOG criteria (40,41). Nearly 90% of all individuals who met criteria for GDM using the 75 gm 2-hour GTT were diagnosed based on the fasting blood glucose (FBG) and 1-hour values, raising the question of whether the 2-hour value is worth the extra time and cost (42). Additionally, evaluation of higher glycemic criteria (fasting glucose ≥99 and 2-hour level glucose ≥162 mg/dl) for the diagnosis of gestational diabetes by the Gestational Diabetes Mellitus Trial of Diagnostic Detection Thresholds (GEMS) trial group did not increase the risk for LGA infant (43).

Currently there is no consensus about the adoption of the IADPSG criteria over the ACOG criteria. The NIH held a Consensus Conference in March of 2013 (44). They acknowledged that the HAPO study was the first to demonstrate that glycemic thresholds currently lower than the ACOG diagnostic criteria thresholds correlated with LGA and adopting the 75 gm GTT would be beneficial in standardizing diagnostic criteria internationally. However, they concluded that there were insufficient data from RCTs demonstrating that adopting the lower glucose thresholds would significantly benefit the much larger population of women who make the diagnostic criteria for GDM based on the IADPSG criteria and such adoption could markedly increase cost of treatment. Further, there was a concern that adopting the IADPSG criteria could triple the prevalence of GDM, potentially outstripping the resources to treat it. Recent clinical trials comparing screening strategies confirm that the one-step approach has been associated with an upwards of threefold increase in the prevalence of GDM compared to the two-step approach, but there is no clear evidence that the increased diagnosis is associated with improved maternal or perinatal outcomes (37,39,45,46).

At the consensus conference, it was also argued that it is not clear how much the increased risk of LGA at lower glucose thresholds observed in the HAPO trial on which it was based was due to maternal obesity or mild hyperglycemia. A retrospective review of nearly 10,000 individuals who were diagnosed with GDM using the IADPSG criteria showed an overall GDM prevalence of 24%. After excluding individuals who required treatment for GDM, 75% of GDM individuals were overweight or obese. Although GDM nearly doubled the risk of LGA over obesity alone (22.3% versus 12.7% respectively), in individuals without GDM, 21.6% of LGA was attributable to being overweight and obese. The combination of GDM in addition to being overweight or obese did not add much to the attributable risk for LGA and accounted for 23.3% of LGA infants (47).

The threshold levels for the 3-hour GTT have been debated. The initial diagnostic thresholds for the 3-

hour GTT were initially established by O'Sullivan and Mahan (48). National Diabetes Data Group and Carpenter and Coustan criteria have subsequently been developed since with Carpenter and Coustan criteria suggesting more stringent thresholds (49,50). Further retrospective investigations have shown that the lower Carpenter and Coustan criteria may diagnose more patients that could benefit from treatment of GDM (51–53). Therefore, ACOG and ADA recommend the Carpenter and Coustan criteria (37,54).

Recently, Hillier et al published the results of their pragmatic, randomized trial comparing one-step screening with two-step screening in which nearly 24,000 individuals were randomized (45). The diagnosis of GDM was roughly doubled using the onestep approach versus the two-step approach, at rates of 16.5% and 8.5% respectively (unadjusted relative risk, 1.94; 97.5% confidence interval [CI], 1.79 to 2.11) (40). Importantly, there were no significant differences between diagnostic approaches with the primary (LGA infants. perinatal outcomes composite. gestational hypertension or preeclampsia, and primary cesarean delivery). Potential limitations include a sample size underpowered to detect differences in the groups, treatment of individuals with a single elevated GTT value, and suboptimal adherence to protocols (38). A meta-analysis comparing one-step and twostep screening methods showed a twofold risk of the diagnosis of GDM with the one-step approach without a difference in the risk of LGA infants (39).

Screening Prior to 24 Weeks Gestation- Who, Why, and How?

Several factors have contributed to newer recommendations to consider early screening for diabetes: the rising incidence of T2DM because of the obesity epidemic, in addition to a better understanding of the risks associated with hyperglycemia early in pregnancy, such as congenital anomalies and miscarriage (55). In an obstetric setting, the best time to screen for and diagnose T2DM is as early as possible in the pregnancy, ideally in the first trimester before the placental effects causing insulin resistance have begun. There is not a recognized lower gestational age cutoff at which insulin resistance can be attributed to placental effects, though this likely occurs prior to the GDM screening range of 24-28 weeks.

There is conflicting evidence that screening for GDM prior to 24 weeks gestational age is beneficial. A RCT of 962 individuals examining early screening for GDM in individuals living with obesity compared to standard of care did not show reductions in composite perinatal outcomes (56). Even if an individual is diagnosed with GDM prior to 20 weeks, only modest benefit in composite perinatal outcomes was seen with early treatment (57). As a result, early screening for GDM is not routinely recommended, but screening high-risk individuals for overt diabetes is recommended. The 2024 ADA guidelines recommend screening individuals at the first prenatal visit if BMI >25 kg/m2 (or >23 kg/m2 in Asian Americans) and one or more risk factors (Table 2). Universal screening of pregnant individuals <15 weeks of gestation for undiagnosed pregestational diabetes could also be considered especially in populations with a high prevalence of undiagnosed diabetes. The IADPSG/ADA recommends that individuals diagnosed for the first time in pregnancy prior to 24 weeks should be considered as having overt diabetes following the same criteria for diabetes outside of pregnancy (Table 3) (37,42). ACOG does not recommend screening for GDM prior to 24 weeks, but in line with ADA recommendations it does recommend screening for overt diabetes early in pregnancy (54). The USPSTF concludes there is insufficient evidence to recommend screening for GDM before 24 weeks gestation (58).

The method of screening for diabetes in early pregnancy is also controversial. The ADA recommends screening for abnormal glucose metabolism in early pregnancy may be accomplished with fasting glucose <110 mg/dL or A1c <5.9% (37). ACOG recommends following the same diagnostic criteria for diabetes outside of pregnancy including A1c value \geq 6.5% or higher, fasting plasma glucose value \geq 126 mg/dL, or 2-hour plasma glucose value \geq 200 mg/dL during a 75-g GTT, or random plasma glucose value \geq 200 mg/dL in patients with classic hyperglycemia symptoms (54). Individuals with evidence of impaired glucose tolerance or prediabetes such as A1c value 5.7–6.4% or 2-hour glucose value between 140 and 199 mg/dL on the 75-g GTT, ACOG recommends nutrition counseling when resources are available (54). If overt T2DM is not diagnosed on early screening, then routine screening for GDM between 24-28 weeks is still recommended.

Table 2. Risk Factors for Early Diabetes Screening
ADA and ACOG 2024 (37,54)
Overweight or obesity (BMI >25 kg/m ² or >23 kg/m ² in Asian Americans) who have one or more
of the following risk factors:
First-degree relative with diabetes
High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian
American, Pacific Islander)
History of cardiovascular disease
Hypertension
History of hyperlipidemia (HDL cholesterol level <35 mg/dL and/or a triglyceride level >250
mg/dL)
Women with polycystic ovary syndrome
Physical inactivity
Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis
nigricans)
Age 35 years or greater
Patients with prediabetes (A1C >5.7% IGT, or IFG)
Women who were diagnosed with GDM in prior pregnancy
People with HIV

Table 3. Early Screening: Identification of Prediabetes and Diabetes							
Risk-based testing performed at the first prenatal visit using standard diagnostic criteria							
Diagnostic for diabetes (any one of the following):							
Fasting: ≥126 mg/dL	75 gm GTT with 2- HbA1c ≥6.5 hour value ≥200 mg/dL				Random plasma glucose ≥200 mg/dL in the setting of classic symptoms of hyperglycemia or hyperglycemic crisis		
If diagnostic criteria for diabetes are met, no additional GDM testing required							
Diagnostic for prediabetes or abnormal glucose metabolism (any one of the							
following):							
Fasting:100-125 mg/d	asting:100-125 mg/dL $^{\alpha}$ 75 gm GTT wit		th 2-hour	HbA1c	≥5.7-6.4%		
Fasting: 110-125 mg/dL ^β value 140-199		mg/dL ^α	HbA1c	≥5.9-6.4% ^β			

 α : ACOG recommends the following values for prediabetes.

β: ADA Standards of Care 2024 suggests that using a threshold fasting glucose of 110 or HbA1c of 5.9% can identify individuals who are at higher risk of adverse pregnancy and neonatal outcomes.

RISKS TO THE MOTHER AND INFANT WITH GESTATIONAL DIABETES

The pregnancy-associated risks to the individual with GDM are an increased incidence of cesarean delivery $(\sim 25\%)$, hypertensive disorders of pregnancy $(\sim 20\%)$, and polyhydramnios (~20%) (59-62). The long-term risks are related to recurrent GDM pregnancies and the substantial risk of developing T2DM. Individuals with GDM represent a group with an extremely high risk (~50-70%) of developing T2DM in the subsequent 5-30 years (1,16-18,63,64). Individuals with fasting hyperglycemia, obesity, those belonging to a racial/ethnic group with a high prevalence of T2DM (in particular those who self-identify as Asian and Pacific Islander and Hispanic), or who demonstrate impaired glucose tolerance or fasting glucose at 6 weeks postpartum, have the highest risk of developing T2DM (1,3,63). Counseling about diet, weight loss, and exercise is essential and is likely to improve insulin sensitivity.

Thiazolidinediones, metformin, and lifestyle modifications have all been demonstrated to decrease the risk of developing T2DM in GDM women who have

impaired fasting glucose or glucose intolerance postpartum (65–67).

The potential risks to the infant from GDM are similar to those in pregnancies complicated by T1DM or T2DM with suboptimal control in the second half of pregnancy (stillbirth, macrosomia, shoulder dystocia, premature delivery, neonatal hypoglycemia, hyperbilirubinemia, and NICU admission). Notably congenital malformations and miscarriage risks would not be observed with later-onset insulin resistance with GDM (1,62,68,69). Like pregestational DM, the degree of hyperglycemia correlates with perinatal risk. Among diet-controlled GDM pregnancies the risk of stillbirth is not increased compared to the general population (70). The developmental origin of health and disease suggests that there can be an association with maternal health on the future health of the child (71,72). In addition to immediate postnatal risks, infants of individuals with GDM are themselves at increased risk for childhood and adult-onset obesity and diabetes (73).

MEDICAL NUTRITION MANAGEMENT AND EXERCISE

Individuals with GDM should be taught home glucose monitoring to ensure that their glycemic goals are being met throughout the duration of pregnancy. The same goals are utilized in GDM pregnancies as in pregestational DM: a fasting glucose <95mg/dL, 1hour postprandial <140mg/dL and 2-hour postprandial <120mg/dL (1,37). The best therapy for GDM depends on the severity of the glucose intolerance, the individual's response to non-pharmacologic or pharmacologic treatment, as well as effects on fetal growth. Diet and exercise alone will maintain the fasting and postprandial blood glucose values within the target range in at least 50% of individual with GDM. A 2018 meta-analysis evaluating diet modifications illustrated improvements in fasting and postprandial glucose values and lower need for medical treatment when compared with controls (74). Furthermore, diet modifications were also associated with lower infant birth weight and less macrosomia (74).

Nevertheless, data are limited regarding the optimal GDM diet to achieve euglycemia and avoid perinatal complications of GDM. The current recommended diet for GDM includes consumption of at least 175 gm of carbohydrate, with complex carbohydrates favored over simple carbohydrates, a minimum of 71 gm of protein, and 28 gm of fiber to provide adequate macronutrients and avoid ketosis (75). There is little evidence to support one dietary approach over another, but common practice is three meals and 2-3 snacks daily to distribute carbohydrate intake and reduce postprandial hyperglycemia. The caloric intake and weight gain recommendations are also consistent with what is recommended in individuals with obesity or T2DM. We recommend multidisciplinary care with a dietician or nurse educator familiar with GDM to individualize a dietary plan.

In 2009, the Institute of Medicine (name changed to National Academy of Medicine in 2015), published

recommended gestational weight gain (GWG) based on pre-pregnancy BMI, with less GWG recommended for overweight and obese individuals compared to those with normal BMI (76). Nevertheless, follow up studies demonstrated a large proportion of pregnant individuals worldwide had GWG above (27.8%) and below (39.4%) the IOM guidelines, with highest mean GWG and pre-pregnancy BMI observed in North America (77). Furthermore, a variety of adverse outcomes have been observed in the setting of excess GWG, including LGA and macrosomic infants in the GDM population (78–80). As a result, the question has been raised whether weight gain less than the IOM guidelines in GDM pregnancies could improve outcomes. There are studies suggesting that weight gain less than IOM recommendations for overweight GDM women may decrease insulin requirements, cesarean delivery, and improve pregnancy outcomes without appreciably increasing small for gestational age (SGA) (81-83). Further, a third study suggesting that slight weight loss (mean of 1.4 kg) in overweight GDM women decreased birth weight without increasing SGA (84). Larger meta-analyses confirmed these findings but failed to identify an ideal weight gain range for optimal outcomes (85). These findings have yet to be included in GWG guidelines specific to pregnant individuals living with diabetes.

Since postprandial glucose levels have been strongly associated with the risk of macrosomia it has been suggested that carbohydrate restriction to ~33-40% of total calories may be helpful to blunt the postprandial glucose excursions, in addition to preventing excessive weight gain (86). However, the actual dietary composition that optimizes perinatal outcomes is unknown. There is also growing concern that individuals are substituting fat for carbohydrates which has been associated with adverse fetal programming including oxidative stress as well as an insulin resistant phenotype (87,88). Although a low carbohydrate, higher fat diet has been conventionally recommended to minimize postprandial hyperglycemia, a review of the few randomized controlled trials examining nutritional

management in 250 GDM individuals suggested that a diet higher in complex carbohydrate and fiber, low in simple sugar and lower in saturated fat may be effective in blunting postprandial hyperglycemia, preventing worsened insulin resistance, and excess fetal growth (89). A more recent trial challenged the traditional low-carb/higher-fat diet and demonstrated that a diet with higher complex carbohydrates and lower-fat reduced fasting blood glucose and infant adiposity (90). Given these trials, a diet of complex carbohydrates is recommended over simple carbohydrates primarily due to slower digestion time which prevents rapid increases in blood glucose.

The role of exercise in GDM may be even more important than in individuals with preexisting diabetes given exercise in some individuals may lessen the need for medical therapy. This idea is similar to the evidence in non-pregnant individuals with diabetes which supports weight training due to increases in lean muscle and increased tissue sensitivity to insulin. A 2013 review showed that in individuals with GDM, five of seven (~70%) activitybased interventions showed improvement in glycemic control or limiting insulin use (91). In most successful studies (3 times/week), insulin needs decrease by 2-3-fold, and overweight or obese women benefited the most with a longer delay from diagnosis to initiation of insulin therapy. Moderate exercise is well tolerated and has been shown in several trials in individuals with GDM to lower maternal glucose levels (92-94). Using exercise after a meal in the form of a brisk walk may blunt the postprandial glucose excursions sufficiently in some individuals that medical therapy might be avoided.

Establishing a regular routine of modest exercise during pregnancy, per ACOG of 30 minutes of moderate-intensity aerobic activity at least 5 days/week, may also have long lasting benefits for the individual with GDM who clearly has an appreciable risk of developing T2DM in the future (1).

MEDICAL TREATMENT OPTIONS

Once the diagnosis of gestational diabetes is confirmed and glycemic control exceeds target ranges despite dietary education and lifestyle changes, pharmacotherapy must be considered. Prior to the 21st century, insulin was the sole medical option for GDM. After the introduction of oral agents such as glyburide and metformin, initiation of these agents increased, with addition or transition to insulin therapy if alvcemic control remained suboptimal. In 2018. ACOG joined the ADA in endorsing insulin as first-line therapy and this was reaffirmed in the 2024 ADA Standards of Care. In contrast, the Society of Maternal-Fetal Medicine (SMFM) released а statement recommending metformin as a reasonable first-choice therapy in addition to insulin (1,75,95). The optimal use of oral agents for the management of GDM is an area of ongoing investigation (96,97).

Although there are few data from randomized controlled trials to determine the optimal therapeutic glycemic targets, the standard of care is that individuals who have fasting blood glucose levels >95 mg/dl, 1-hour postprandial glucose levels >140 mg/dl or 2-hour postprandial glucose levels >120 mg/dl be started on medical therapy. In 5 randomized trials it was demonstrated that if insulin therapy is started in individuals with GDM whose maternal glucose values are at target levels on diet alone but whose fetuses demonstrate excessive growth by an increased abdominal circumference (AC) relative to the biparietal diameter (BPD) i.e. body to head disproportion, the rate of fetal macrosomia can be decreased (81). This fetal based strategy using ultrasound at 29-33 weeks to measure the AC in order dictate the aggressiveness of maternal glycemic control has been recommended by the Fifth International Workshop-Conference on Gestational Diabetes and the IADPSG (30,98,99). Evidence also suggests that higher glycemic targets may have similar outcomes to lower glycemic targets (100). The threshold to initiate pharmacologic therapy by maternal fetal medicine specialists can differ, but most providers recommend initiation of pharmacologic therapy if 30-50% of blood glucose values are elevated (101).

Continuous glucose monitoring (CGM) has also been proposed as an adjunct to traditional glucose monitoring. CGM use has proven beneficial in type 1 diabetes in pregnancy, and its use is recommended by ADA and ACOG (75,102,103). However, there is no clear evidence of its benefit in the setting of GDM. One meta-analysis including 6 trials of 482 individuals with GDM showed that CGM use may achieve lower average blood glucose levels, lower maternal weight gain and infant birth weight, but the studies were limited by overall small sample sizes (104). The specific metrics of CGM data, including pregnancyspecific time-in-range, has not been clearly established and further research should be done before widespread implementation of CGM in GDM.

GDM can often be treated with twice daily injections of intermediate or long-acting insulin (i.e., NPH, glargine, detemir) and mealtime injections of lispro or aspart as necessary for postprandial hyperglycemia. Short acting insulin (i.e., lispro or aspart) is preferred over regular insulin due to time of onset and duration to better control postprandial glycemic excursions. See Endotext chapter "Pregestational Diabetes" for details regarding antepartum, intrapartum, and postpartum insulin dosing regimens (105).

Metformin

One of the largest experiences with metformin in the setting of GDM was with metformin initiated later in pregnancy (106). In this randomized, controlled Metformin in Gestation (MIG) trial, 751 individuals with GDM were randomized to metformin versus insulin. Individuals that did not get adequate glycemic control on metformin received insulin. There was no

difference in both groups concerning the primary composite outcome (neonatal hypoglycemia, respiratory distress, need for phototherapy, birth trauma, 5- minute APGAR <7), or premature birth. As such, metformin did not appear to increase any adverse outcomes, although it was associated with a slight increase in preterm birth; however, this did not appear to be clinically relevant.

Importantly, 46% of the individuals in the metformin group required supplemental insulin to achieve adequate glycemic control. This study demonstrated interesting metformin benefits including reduced maternal weight gain, improved patient satisfaction, and reduced incidence of gestational hypertension. In a smaller RCT, Ijas et al demonstrated metformin had a 32% rate of requiring supplemental insulin (107). They also noted individuals needing supplemental insulin added to metformin were more likely to be obese, have higher fasting blood glucose levels, and initiated pharmacotherapy earlier. Spaulonci et al randomized 47 individuals with GDM to metformin or insulin and demonstrated significant metformin benefits including: less gestational weight gain, lower mean glucose levels, and lower rates of neonatal hypoglycemia (108). Overall, meta-analyses have demonstrated largely reassuring outcomes for metformin compared to insulin and glyburide (109-112). Early initiation of metformin after diagnosis of GDM did not show benefit in fasting BGs over standard of care (113).

Metformin should be avoided in individuals with renal insufficiency. It is typically prescribed in divided doses starting with 500 mg once or twice daily for 1 week and then increasing to a maximum dose of 2500 mg daily in divided doses with meals. Common side effects include gastrointestinal complaints (occurring in 2.5-45.7% of pregnant individuals in studies) (109). These randomized trials have shown short-term efficacy and safety of metformin use in pregnancy for GDM treatment.

Until recently, long-term safety data of in-utero metformin exposure has been lacking, though several studies have been published commenting on infant and childhood weight, BMI, cardiovascular health, and neurodevelopmental outcomes. The earliest follow-up studies in metformin-exposed infants suggested they had larger measures of subcutaneous fat when compared to those exposed to insulin (110). Another study in PCOS women comparing metformin to placebo showed that although women randomized to metformin gained less weight during pregnancy, at 1 year postpartum the women who used metformin in pregnancy lost less weight and their infants were heavier than those in the placebo group (112). These fetal and neonatal results are likely because metformin is concentrated in the fetal compartment with umbilical artery and vein levels being up to twice those seen in the maternal serum (114,115). Hypothetically if metformin increases insulin sensitivity in the fetus, it might be possible for excess nutrient flux across the placenta to result in increased fetal adipogenesis. More recent studies also identified slight increased weight in metformin-exposed infants, a relationship that may no longer be present after 4 years of age (116,117). Long-term follow up of BMI is conflicting (112,117). A very large study in New Zealand evaluated outcomes at 4 years of age in nearly 4000 individuals, with no differences in growth and development assessments compared to insulinexposed children (118). The metabolic and weight differences warrant further investigation since similar patterns of low birth weight followed by accelerated growth are associated with adverse long-term outcomes (119). At least one study has failed to demonstrate such a relationship in this population (120). A study of 211 individuals with GDM randomized to insulin versus metformin during pregnancy found similar developmental outcomes by 2 years of age (111).

In review, the ADA and ACOG note that insulin is the first-line agent for treatment of GDM if lifestyle changes have not achieved glycemic targets (1,75). The ADA notes that although individual RCTs have

shown short-term benefits and safety of metformin and glyburide, long- term safety data are lacking (75). Both organizations acknowledge that 20-45% of women fail metformin monotherapy necessitating that insulin be added (1). Counseling is necessary to explain to women that although current data do not demonstrate any adverse short-term outcomes, there are concerns about placental transfer of metformin, potential increased preterm birth, and lack of data on long term outcomes of fetuses exposed to metformin inutero, metformin's effect on fetal insulin sensitivity, hepatic gluconeogenesis, and the long-term fetal programming implications are unknown. SMFM suggests that metformin is a reasonable and safe alternate first line pharmacologic treatment (95). The UK NICE guidelines also suggest that metformin as a first-line medication for patients with GDM who require pharmacologic therapy (121).

Glyburide and Other Agents

Glyburide is the only sulfonylurea that has been studied in a large, randomized trial in individuals with GDM. It was approved by the 5th International Workshop and IADPSG as a possible alternative to insulin in individuals with GDM due to several RCTs (122). The dose ranges from 2.5-20 mg daily in divided doses.

Glyburide exposure in most RCTs is limited to the second and third trimesters, so the effect on embryogenesis was not studied, but there are no convincing reports that it is a teratogen. Due to its peak at 3-4 hours, many individuals have inadequate control of their 1- or 2-hour postprandial glucoses and then become hypoglycemic 3-4 hours later and data suggest that serum concentrations with usual doses are lower in pregnant individuals. If used, it should be given 30 mins-1-hour before breakfast and dinner and should not be given before bedtime due to the risk of nocturnal or early morning hypoglycemia considering its 3–4-hour peak (similar to regular insulin). For individuals unwilling to

administer multiple daily insulin injections who have postprandial glucoses well controlled by glyburide but have fasting hyperglycemia, adding intermediate or long-acting insulin before bedtime to the glyburide can sometimes be useful. If both postprandial and fasting glucoses remain elevated, the individual should be switched to insulin.

The earliest RCTs offered glyburide as a safe alternative to insulin, without significant differences in perinatal outcomes (123). In the last 20 years, growing evidence has suggested there is increased risk of both maternal and neonatal hypoglycemia with glyburide use (109,124-127). In some trials, maternal glycemic control, macrosomia, neonatal hypoglycemia, and neonatal outcomes were not different between groups although in others, there was a significantly greater rate of macrosomic infants in the glyburide group ((123,128,129)). In a metaanalysis examining metformin versus insulin versus glibenclamide (glyburide) treatment for individuals with GDM, there were higher rates of macrosomia (risk ratio 2.62) and neonatal hypoglycemia (risk ratio 2.04) among those treated with glibenclamide compared with insulin (109). This is the same publication reviewed above that showed the increased risk of preterm birth in individuals treated with metformin compared with insulin. This metaanalysis in addition to a second meta-analysis showed significantly worse neonatal outcomes among offspring of individuals with GDM treated with glyburide compared to insulin (109,128). There were higher rates of neonatal hypoglycemia, respiratory distress syndrome, macrosomia, and birth injury without significant differences in glycemic control (124,128).

A RCT compared the efficacy of metformin with glyburide for glycemic control in GDM (124). In the individuals who achieved adequate glycemic control, the mean glucose levels were not statistically different between the two groups. However, 26 individuals in the metformin group (34.7%) and 12

individuals in the glyburide group (16.2%) did not achieve adequate glycemic control and required insulin therapy (p=0.01). Thus, in this study, the need for insulin supplementation with metformin was twice as high as the failure rate of glyburide when used in the management of GDM (124). These findings are consistent with the general finding that approximately, 15% of individuals will fail maximum dose glyburide therapy and need supplemental insulin, especially if dietary restriction is not carefully followed. Although it was initially thought not to appreciably cross the placenta or significantly affect fetal insulin levels, examination using HPLC mass spectrometry suggested a modest amount of glyburide does cross (114).

There is not sufficient information available on thiazolidinediones, meglitinides, dipeptidyl peptidase IV (DPP-4) inhibitors, glucagon like peptide 1 (GLP-1) agonists, sodium-glucose transport protein 2 (SGLT-2) inhibitors, and such agents should only be used in the setting of approved clinical trials as their teratogenic potential is unknown. Acarbose was studied in two very small studies in individuals with GDM and given its minimal GI absorption is likely to be safe, but GI side effects are often prohibitive (130). Safety studies of GLP-1 agonists and SGLT2 inhibitors have shown potential teratogenicity and adverse pregnancy outcomes mostly derived from animal studies (131). Limited observational studies in humans have not shown significant adverse outcomes with periconceptional use of GLP-1 agonists (132,133). The effect of use in later pregnancy and for gestational diabetes is unknown. Additional information about the use of these medications outside of pregnancy can be found in the chapter entitled "Oral and Injectable (Non-Insulin) Pharmacological Agents for the Treatment of Type 2 Diabetes" in the Diabetes Mellitus and Carbohydrate Metabolism section of Endotext (134).

FETAL SURVEILLANCE AND DELIVERY OPTIONS IN GESTATIONAL DIABETES

Individuals with GDM who require pharmacotherapy but do not have other comorbidities should initiate once or twice weekly antenatal fetal surveillance at 32 weeks gestation

(135). There is no consensus regarding antepartum testing in individuals with diet-controlled GDM (1). For those individuals with diet-controlled GDM extending pregnancy beyond 40 weeks gestation, consideration could be made to initiate antenatal testing (135).

An ultrasound for growth to look for head to body disproportion (large abdominal circumference compared to the biparietal diameter) and evidence of LGA should be considered at ~29-32 weeks (1). The documented risks associated with attempted vaginal delivery with a fetal estimated weight >4500 gm in the setting of pregestational diabetes have resulted in a reasonable practice of offering cesarean delivery (136). This recommendation is extended to those with GDM and a fetal estimated weight >4500 gm (1). Nevertheless, a Cochrane review found insufficient evidence in using fetal biometry to assist in guiding the medical management of GDM to improve either perinatal or maternal health outcomes (137).

When GDM is well-controlled with either diet or medications, delivery <39 weeks gestation is not warranted. Delivery is usually recommended by 40 6/7 weeks for uncomplicated diet-controlled GDM and by 39 6/7 weeks for well-controlled GDM on medication(138). Earlier delivery should be considered with suboptimal glucose control or other complicating factors such as hypertension (138). The framework of evaluating the risks and benefits of induction of labor to expectant management in both high-risk and low-risk individuals has shifted from a historical lens of induction of labor compared to spontaneous labor; multiple studies have demonstrated no increased risk of cesarean delivery

with induction of labor <40 weeks gestation (139–141).

POSTPARTUM ISSUES IN WOMEN WITH GESTATIONAL DIABETES

Re-Evaluating Glucose Tolerance Postpartum and Future Risk of Diabetes

Identification of poor glycemic control in pregnancy to predict risk for T2DM was present in the earliest screening and diagnostic strategies. Up to 70% of individuals with GDM are estimated to ultimately develop T2DM within 20-30 years after delivery. Differentiation of GDM from previously undiagnosed T2DM should be performed via a 75-gram 2-hour GTT 4-12 within weeks postpartum as recommended by the ADA, Canadian Diabetes Association (CDA), Fifth International Workshop, and ACOG since most individuals with impaired glucose intolerance will be missed if only a FBG is checked (142). A 2-hour value of at least 200 mg/dl establishes a diagnosis of diabetes and a 2-hour value of at least 140 mg/dl but less than 200 mg/dl makes the diagnosis of impaired glucose tolerance. Additionally, individuals who have been diagnosed with GDM should be screened at least every 3 years for overt diabetes (37).

An alternative approach that is endorsed by ACOG in a 2024 Clinical Practice Update is to perform the 75-gram GTT on postpartum day 2 prior to hospital discharge, since completion of postpartum screening is historically low (54). A large series of ~23,000 individuals who received lab testing through Quest diagnostics suggested that only 19% of individuals receive postpartum diabetes testing within a 6-month period (143). Waters et al. demonstrated a negative GTT prior to hospital discharge excluded T2DM diagnosis at 4-12 weeks postpartum (144). Werner et al. showed similar diagnostic value of 2-day postpartum GTT to the standard 4-12 weeks postpartum GTT (145) A weight loss program consisting of diet and exercise should be instituted for individuals with GDM to improve their insulin sensitivity and hopefully to prevent the development of T2DM (146). Hyperglycemia generally resolves in most individuals during this interval but up to 10% of patients will fulfill criteria for T2DM. At the minimum, a fasting blood glucose should be done to determine if the woman has persistent diabetes (glucose >125 mg/dl) or impaired fasting glucose (glucose \geq 100 mg/dl). Of note, breastfeeding has been shown to improve insulin resistance and glucose values in postpartum individuals with GDM (147,148).

Utility of using the A1c postpartum to predict the subsequent occurrence of T2DM in individuals with a history of GDM has not been studied extensively and may be affected by glycemic control during pregnancy if done before 3 months postpartum (149). A study looking at utility of using A1c vs 2h GTT vs FPG for screening of individuals with recent GDM showed that A1c and A1c plus FPG did not have the sensitivity and specificity to diagnose impaired carbohydrate metabolism postpartum (150,151). The importance of diagnosing impaired glucose intolerance lies in its value in predicting the future development of T2DM. In one series which mainly studied Hispanic individuals, a diagnosis of impaired glucose tolerance was the most potent predictor of the development of T2DM in individuals with a history of GDM; 80% of such women developed diabetes in the subsequent 5-7 years (152). Intensified efforts promoting diet, exercise and weight loss should be instituted in these individuals.

Other studies have shown other risk factors for development of prediabetes and/or T2DM after GDM including earlier diagnosis of GDM in pregnancy, insulin therapy during pregnancy, and BMI (64,153,154). A study in Italy showed pre-pregnancy BMI and PCOS as strong predictors of postpartum impaired glucose tolerance (155,156). A1c within 12 months postpartum may be useful in addition to GTT to diagnose some women with history of GDM and normal glucose tolerance. A study of 141 individuals in Spain with recent GDM found that 10% had normal glucose tolerance, normal FPG, and isolated A1c 5.7-6.4% suggesting that A1c is a useful tool to diagnose prediabetes in individuals with a history of GDM with normal glucose tolerance postpartum (156). Interestingly, in this study the group of individuals with isolated A1c 5.7-6.4% with normal glucose tolerance and normal FPG were more likely to be non-Hispanic White and more likely had higher LDL-C values. A1c is a sensitive test in detecting prediabetes and overt diabetes in postpartum individuals with history of GDM (157).

The TRIPOD study demonstrated that the use of a thiazolidinedione postpartum in individuals with a history of GDM and persistent impaired glucose intolerance decreased the development of T2DM (158). The rate of T2DM in the 133 individuals randomized to troglitazone was 5.4% versus 12.1% in the 133 individuals randomized to placebo at a median follow-up of 30 months (159). The protection from diabetes was closely related to the degree of reduction of insulin secretion three months after randomization and persisted 8 months after the medication was stopped. In the PIPOD study, use of Pioglitazone to the same high-risk patient group stabilized previously falling β-cell function and revealed a close association between reduced insulin requirements and low risk of diabetes (7,67). However, using thiazolidinediones for the purpose of preventing the development of T2DM in individuals with a history of GDM has not been recommended. The Diabetes Prevention Program (DPP) Trial analyzed their data in individuals with a history of GDM (66). A total of 349 individuals had a history of GDM, and such a history conferred a 74% increased risk for the development of T2DM compared with individuals without a history of GDM. In the placebo arm, individuals developed T2DM at an alarming rate of 17% per year but this rate was cut in half by either use of metformin or diet and exercise.

The DPP, TRIPOD, and PIPOD studies support clinical management that focuses on identifying individuals who meet criteria for metabolic syndrome, achieving postpartum weight loss, and instituting aggressive interventions beginning with lifestyle changes to decrease insulin resistance for the primary prevention of T2DM. Individuals with a history of GDM who display normal testing postpartum should undergo lifestyle interventions for postpartum weight reduction and receive repeat testing at least every 3 years (37). For individuals who may have subsequent pregnancies, screening more frequently has the advantage of detecting abnormal glucose metabolism before the next pregnancy to ensure preconception glucose control (1).

Breastfeeding

Breastfeeding should be encouraged in all individuals with a history of GDM for improving maternal and offspring health outcomes. Lactation completes the reproductive cycle and is associated with significant short- and long-term cardiometabolic benefits for both mother and infant, with most demonstrating a dose-dependent relationship (160). Professional society recommendations recommend exclusive breastfeeding for the first 6 months of life, then ongoing breastfeeding with complementary foods through the second year or as long as desired by both mother and child (160–162).

Initially the correlation between breastfeeding and reduced incidence of T2DM were based on selfreported lactation status and diabetes diagnoses. Subsequent larger studies have confirmed this relationship. Over 1200 individuals who had at least 1 live birth and reported lactation duration were followed in a community-based prospective study over 30 years, with diabetes screening performed up to 7 times (CARDIA study) (163). Not only was there a three-fold increased incidence of T2DM in those breastfeeding with no compared to anv

breastfeeding, but the relative hazard was also graded based on duration of breastfeeding (163). These findings were also reported in the most recent meta-analysis evaluating the relationship between lactation and maternal risk of T2DM (164).

For children, breastmilk intake also appears to decrease the risk of developing obesity and impaired glucose tolerance (165). In the large EPOCH study (Exploring Perinatal Outcomes Among Children Study), offspring of individuals with diabetes (primarily GDM) who were breastfed for at least 6 months had a slower BMI growth trajectory during childhood and a lower childhood BMI than those who were not breastfed (166). There is a growing literature suggesting that some of the protective benefits on childhood obesity and programming the infant immune system from breast milk may be influenced by appetite regulatory hormones, biomarkers of oxidative stress and inflammation, and the milk microbiome (167–170).

Contraception

Discussing contraception and family planning during pregnancy is an effective way to promote safe pregnancy interval, with optimal outcomes observed when delivery and conception are at least 18 months apart (171). For individuals with GDM, the postpartum and inter-pregnancy periods offer a tremendous opportunity to employ diet, lifestyle, and other therapeutic changes to reduce the risk of subsequent GDM or T2DM (171). All pharmacologic options for contraception are considered safe in the setting of recent or remote GDM, though estrogencontaining methods should be delayed until ≥21 days postpartum to reduce the risk of thromboembolism (172). Estrogen may negatively impact breast milk production, so consideration of infant feeding method should also be weighed against initiation. We recommend a patient-centered approach to counseling and selecting a contraceptive method.

There is limited data on the influence of various contraceptive methods on long-term risk of T2DM, insulin sensitivity, glycemic control, weight gain, and hypercholesterolemia (173). Extensive research evaluating these relationships concludes the adverse outcomes observed with methods such as Depo-Provera in the GDM population are more closely associated with initial BMI and pregnancy weight gain than with GDM.

CONCLUSION

Different organizations recommend different screening and diagnostic strategies for GDM settings. reflectina variations in geographic Treatment with lifestyle or medication to achieve glycemic targets improves obstetric and perinatal outcomes. Due to the obesity epidemic, the incidence of GDM is only expected to rise, with

REFERENCES

- 1. Caughey AB, Turrentine M. ACOG Practice Bulletin No. 190: Gestational Diabetes Mellitus. Obstetrics and [Internet]. [cited gynecology 2018 2024 Jun 1];131(2):E49-64. Available from: https://pubmed.ncbi.nlm.nih.gov/29370047/
- 2. Eades CE, Burrows KA, Andreeva R, Stansfield DR, Evans JMM. Prevalence of gestational diabetes in the United States and Canada: a systematic review and meta-analysis. BMC Pregnancy Childbirth [Internet]. 2024 Dec 1 [cited 2024 Jun 2];24(1):1-15. Available from:

https://bmcpregnancychildbirth.biomedcentral.com/articl es/10.1186/s12884-024-06378-2

- Deputy NP, Kim SY, Conrey EJ, Bullard KM. Prevalence 3. and Changes in Preexisting Diabetes and Gestational Diabetes Among Women Who Had a Live Birth - United States, 2012-2016. MMWR Morb Mortal Wkly Rep [Internet]. 2018 Nov 2 [cited 2024 Jun 2];67(43):1201-7. Available from: https://pubmed.ncbi.nlm.nih.gov/30383743/
- 4. Bardenheier BH, Imperatore G, Gilboa SM, Geiss LS, Saydah SH, Devlin HM, et al. Trends in Gestational Diabetes Among Hospital Deliveries in 19 U.S. States, 2000-2010. Am J Prev Med [Internet]. 2015 Jul 1 [cited

subsequent or eventual T2DM diagnosis increasing accordingly. Further investigation on the benefits of specific pharmacologic therapies and glucose monitoring strategies with CGM are ongoing.

The development of T2DM in individuals with a history of GDM as well as obesity and glucose intolerance in the offspring of those with preexisting DM or GDM set the stage for a perpetuating metabolic cycle that must be aggressively addressed with effective primary prevention strategies that begin in-utero. Pregnancy is a unique opportunity to implement strategies to improve the mother's lifetime risk for adverse cardiometabolic health outcomes in addition to that of her offspring and offers the potential to decrease the intergenerational risk of diabetes. and other adverse obesity, cardiometabolic outcomes.

> 2024 Jun 1];49(1):12-9. Available from: https://pubmed.ncbi.nlm.nih.gov/26094225/

- 5. Gregory ECW, Ely DM. National Vital Statistics Reports Volume 71, Number 3 July 19, 2022. National Vital Statistics Reports. 2016;71(3).
- 6. Venkatesh KK, Huang X, Cameron NA, Petito LC, Joseph J, Landon MB, et al. Rural-urban disparities in pregestational and gestational diabetes in pregnancy: Serial, cross-sectional analysis of over 12 million pregnancies. 2023 [cited 2024 Jun 2]; Available from: https://obgyn.onlinelibrary.wiley.com/doi/10.1111/1471-0528.17587,
- 7. Buchanan TA, Xiang A, Kjos SL, Watanabe R. What is gestational diabetes? Diabetes Care [Internet]. 2007 Jul [cited 2024 Jun 2];30 Suppl 2(SUPPL. 2). Available from: https://pubmed.ncbi.nlm.nih.gov/17596457/
- 8. Catalano PM, Drago NM, Amini SB. Longitudinal changes in pancreatic beta-cell function and metabolic clearance rate of insulin in pregnant women with normal and abnormal glucose tolerance. Diabetes Care [Internet]. 1998 Mar [cited 2024 Jun 1];21(3):403-8. Available from:

https://pubmed.ncbi.nlm.nih.gov/9540023/

- Catalano PM, Huston L, Amini SB, Kalhan SC. Longitudinal changes in glucose metabolism during pregnancy in obese women with normal glucose tolerance and gestational diabetes mellitus. Am J Obstet Gynecol [Internet]. 1999 [cited 2024 Jun 1];180(4):903– 16. Available from: https://pubmed.ncbi.nlm.nih.gov/10203659/
- ANDERSEN O, KUHL C. Insulin receptor binding to monocytes and erythrocytes during normal human pregnancy. Eur J Clin Invest [Internet]. 1986 Jun 1 [cited 2024 Jun 1];16(3):226–32. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/j.1365-2362.1986.tb01333.x
- Fallucca F, Dalfrà MG, Sciullo E, Masin M, Buongiorno AM, Napoli A, et al. Polymorphisms of insulin receptor substrate 1 and beta3-adrenergic receptor genes in gestational diabetes and normal pregnancy. Metabolism [Internet]. 2006 Nov [cited 2024 Jun 1];55(11):1451–6. Available from: https://pubmed.ncbi.nlm.nih.gov/17046546/
- Barbour LA, McCurdy CE, Hernandez TL, Kirwan JP, Catalano PM, Friedman JE. Cellular mechanisms for insulin resistance in normal pregnancy and gestational diabetes. Diabetes Care [Internet]. 2007 Jul [cited 2024 Jun 1];30 Suppl 2(SUPPL. 2). Available from: https://pubmed.ncbi.nlm.nih.gov/17596458/
- 13. Lain KY, Catalano PM. Metabolic changes in pregnancy. Clin Obstet Gynecol [Internet]. 2007 Dec [cited 2024 Jun 1];50(4):938–48. Available from: https://pubmed.ncbi.nlm.nih.gov/17982337/
- Garvey WT, Maianu L, Zhu JH, Hancock JA, Golichowski AM. Multiple defects in the adipocyte glucose transport system cause cellular insulin resistance in gestational diabetes. Heterogeneity in the number and a novel abnormality in subcellular localization of GLUT4 glucose transporters. Diabetes [Internet]. 1993 [cited 2024 Jun 1];42(12):1773–85. Available from: https://pubmed.ncbi.nlm.nih.gov/8243823/
- Atègbo JM, Grissa O, Yessoufou A, Hichami A, Dramane KL, Moutairou K, et al. Modulation of adipokines and cytokines in gestational diabetes and macrosomia. J Clin Endocrinol Metab [Internet]. 2006 [cited 2024 Jun 1];91(10):4137–43. Available from: https://pubmed.ncbi.nlm.nih.gov/16849405/
- Zhu Y, Zhang C. Prevalence of Gestational Diabetes and Risk of Progression to Type 2 Diabetes: a Global Perspective. Curr Diab Rep [Internet]. 2016 Jan 1 [cited 2024 Jun 1];16(1):1–11. Available from: https://pubmed.ncbi.nlm.nih.gov/26742932/
- Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet [Internet]. 2009 [cited

2024 Jun 1];373(9677):1773–9. Available from: https://pubmed.ncbi.nlm.nih.gov/19465232/

- Vounzoulaki E, Khunti K, Abner SC, Tan BK, Davies MJ, Gillies CL. Progression to type 2 diabetes in women with a known history of gestational diabetes: systematic review and meta-analysis. BMJ [Internet]. 2020 May 13 [cited 2024 Jun 2];369. Available from: https://pubmed.ncbi.nlm.nih.gov/32404325/
- Arabin B, Baschat AA. Pregnancy: An Underutilized Window of Opportunity to Improve Long-term Maternal and Infant Health-An Appeal for Continuous Family Care and Interdisciplinary Communication. Front Pediatr [Internet]. 2017 Apr 13 [cited 2024 Jun 1];5. Available from: https://pubmed.ncbi.nlm.nih.gov/28451583/
- Gilmore LA, Klempel-Donchenko M, Redman LM. Pregnancy as a window to future health: Excessive gestational weight gain and obesity. Semin Perinatol [Internet]. 2015 Jun 1 [cited 2024 Jun 1];39(4):296–303. Available from: https://pubmed.ncbi.nlm.nih.gov/26096078/
- 21. Miller HC. The effect of diabetic and prediabetic pregnancies on the fetus and newborn infant. J Pediatr [Internet]. 1946 [cited 2024 Jun 1];29(4):455–61. Available from: https://pubmed.ncbi.nlm.nih.gov/21002159/
- 22. Mestman JH. Historical Notes on Diabetes and Pregnancy. Endocrinologist. 2002;12(3):224–42.
- 23. Kim C, Ferrara Assiamira. Gestational diabetes during and after pregnancy. 2010;394.
- Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med [Internet]. 2005 Jun 16 [cited 2024 Jun 1];352(24):2477–86. Available from: https://pubmed.ncbi.nlm.nih.gov/15951574/
- Landon MB, Spong CY, Thom E, Carpenter MW, Ramin SM, Casey B, et al. A multicenter, randomized trial of treatment for mild gestational diabetes. N Engl J Med [Internet]. 2009 Oct [cited 2024 Jun 1];361(14):1339–48. Available from: https://pubmed.ncbi.nlm.nih.gov/19797280/
- Metzger BE, Lowe LP, Dyer AR, Trimble ER, Sheridan B, Hod M, et al. Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study: associations with neonatal anthropometrics. Diabetes [Internet]. 2009 Feb [cited 2024 Jun 1];58(2):453–9. Available from: https://pubmed.ncbi.nlm.nih.gov/19011170/
- BE M, LP L, AR D, ER T, U C, DR C, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med [Internet]. 2008 May 8 [cited 2024 Jun 1];358(19):1991– 2002. Available from: https://pubmed.ncbi.nlm.nih.gov/18463375/

- Lambie CG. Diabetes and Pregnancy. BJOG [Internet]. 1926 Dec 1 [cited 2024 Jun 1];33(4):563–606. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/j.1471-0528.1926.tb12131.x
- Wilson JMG, Jungner G. Principles and practice of screening for disease [Internet]. Geneva: World Health Organization; 1968 [cited 2024 Jun 1]. Available from: https://iris.who.int/handle/10665/37650
- BE M, SG G, B P, TA B, PA C, P D, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care [Internet].
 2010 Mar [cited 2024 Jun 1];33(3):676–82. Available from: https://pubmed.ncbi.nlm.nih.gov/20190296/
- Mishra S, Rao CR, Shetty A. Trends in the Diagnosis of Gestational Diabetes Mellitus. Scientifica (Cairo) [Internet]. 2016 [cited 2024 Jun 1];2016. Available from: https://pubmed.ncbi.nlm.nih.gov/27190681/
- Meek CL. Natural selection? The evolution of diagnostic criteria for gestational diabetes. Ann Clin Biochem [Internet]. 2017 Jan 1 [cited 2024 Jun 1];54(1):33–42. Available from: https://pubmed.ncbi.nlm.nih.gov/27687080/
- Coustan DR, Dyer AR, Metzger BE. One-step or 2-step testing for gestational diabetes: which is better? Am J
- Obstet Gynecol [Internet]. 2021 Dec 1 [cited 2024 Jun 1];225(6):634–44. Available from: http://www.ajog.org/article/S0002937821005561/fulltext
- 34. Roeckner JT, Sanchez-Ramos L, Jijon-Knupp R, Kaunitz AM. Single abnormal value on 3-hour oral glucose tolerance test during pregnancy is associated with adverse maternal and neonatal outcomes: a systematic review and metaanalysis. Am J Obstet Gynecol [Internet]. 2016 Sep 1 [cited 2024 Jun 3];215(3):287–97. Available from: https://pubmed.ncbi.nlm.nih.gov/27133007/
- 35. Recommendations | Diabetes in pregnancy: management from preconception to the postnatal period | Guidance | NICE.
- Ranzcog. Diagnosis of Gestational Diabetes Mellitus (GDM). [cited 2024 Jun 3]; Available from: https://www.ranzcog.edu.au/news/Diagnosis-GDM-Australia
- Committee ADAPP, ElSayed NA, Aleppo G, Bannuru RR, Bruemmer D, Collins BS, et al. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2024. Diabetes Care [Internet]. 2024 Jan 1 [cited 2024 Jun 3];47(Supplement_1):S20–42. Available from: https://dx.doi.org/10.2337/dc24-S002

- Coustan DR, Dyer AR, Metzger BE. One-step or 2-step testing for gestational diabetes: which is better? Am J Obstet Gynecol. 2021 Dec 1;225(6):634–44.
- Brady M, Hensel DM, Paul R, Doering MM, Kelly JC, Frolova AI, et al. One-Step Compared With Two-Step Gestational Diabetes Screening and Pregnancy Outcomes: A Systematic Review and Meta-analysis. Obstetrics and Gynecology [Internet]. 2022 Nov 1 [cited 2024 Jun 3];140(5):712–23. Available from: https://journals.lww.com/greenjournal/fulltext/2022/1100 0/one_step_compared_with_two_step_gestational.3.as px
- 40. Ryan EA. Diagnosing gestational diabetes. Diabetologia [Internet]. 2011 Mar [cited 2024 Jun 3];54(3):480–6. Available from: https://pubmed.ncbi.nlm.nih.gov/21203743/
- Manzoor N, Moses RG. Diagnosis of gestational diabetes mellitus: a different paradigm to consider. Diabetes Care [Internet]. 2013 Nov [cited 2024 Jun 3];36(11). Available from: https://pubmed.ncbi.nlm.nih.gov/24159183/
- 42. Sacks DA, Coustan DR, Hadden DR, Hod M, Maresh M, Oats JJN, et al. Frequency of gestational diabetes mellitus at collaborating centers based on IADPSG consensus panel-recommended criteria: The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study. Diabetes Care. 2012 Mar;35(3):526–8.
- Crowther CA, Samuel D, McCowan LME, Edlin R, Tran T, McKinlay CJ. Lower versus Higher Glycemic Criteria for Diagnosis of Gestational Diabetes. New England Journal of Medicine [Internet]. 2022 Aug 18 [cited 2024 Jun 5];387(7):587–98. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa2204091
- 44. National Institutes of Health Consensus Development Conference Statement. Obstetrics & Gynecology [Internet]. 2013 Aug [cited 2024 Jun 1];122(2):358–69. Available from: https://journals.lww.com/greenjournal/fulltext/2013/0800 0/national_institutes_of_health_consensus.25.aspx
- Hillier TA, Pedula KL, Ogasawara KK, Vesco KK, Oshiro CES, Lubarsky SL, et al. A Pragmatic, Randomized Clinical Trial of Gestational Diabetes Screening. N Engl J Med [Internet]. 2021 Mar 11 [cited 2024 Jun 3];384(10):895–904. Available from: https://pubmed.ncbi.nlm.nih.gov/33704936/
- Davis EM, Abebe KZ, Simhan HN, Catalano P, Costacou T, Comer D, et al. Perinatal Outcomes of Two Screening Strategies for Gestational Diabetes Mellitus: A Randomized Controlled Trial. Obstetrics and gynecology [Internet]. 2021 Jul 1 [cited 2024 Jun 3];138(1):6–15. Available from: https://pubmed.ncbi.nlm.nih.gov/34259458/

- Black MH, Sacks DA, Xiang AH, Lawrence JM. The relative contribution of prepregnancy overweight and obesity, gestational weight gain, and IADPSG-defined gestational diabetes mellitus to fetal overgrowth. Diabetes Care [Internet]. 2013 Jan [cited 2024 Jun 3];36(1):56–62. Available from: https://pubmed.ncbi.nlm.nih.gov/22891256/
- O'Sullivan JB, Mahan CM, Charles D, Dandrow R V. Screening criteria for high-risk gestational diabetic patients. Am J Obstet Gynecol [Internet]. 1973 [cited 2024 Jun 5];116(7):895–900. Available from: https://pubmed.ncbi.nlm.nih.gov/4718216/
- Carpenter MW, Coustan DR. Criteria for screening tests for gestational diabetes. Am J Obstet Gynecol [Internet].
 1982 Dec 1 [cited 2024 Jun 5];144(7):768–73. Available from: https://pubmed.ncbi.nlm.nih.gov/7148898/
- 50. Group NDD. Classification and Diagnosis of Diabetes Mellitus and Other Categories of Glucose Intolerance. Diabetes [Internet]. 1979 Dec 1 [cited 2024 Jun 5];28(12):1039–57. Available from: https://dx.doi.org/10.2337/diab.28.12.1039
- Harper LM, Mele L, Landon MB, Carpenter MW, Ramin SM, Reddy UM, et al. Carpenter-Coustan Compared With National Diabetes Data Group Criteria for Diagnosing Gestational Diabetes. Obstetrics and gynecology [Internet]. 2016 Apr 4 [cited 2024 Jun 5];127(5):893. Available from: /pmc/articles/PMC4840065/
- Berggren EK, Boggess KA, Stuebe AM, Jonsson Funk M. National Diabetes Data Group versus Carpenter-Coustan Criteria to Diagnose Gestational Diabetes. Am J Obstet Gynecol [Internet]. 2011 [cited 2024 Jun 5];205(3):253.e1. Available from: /pmc/articles/PMC3670957/
- 53. Cheng YW, Block-Kurbisch I, Caughey AB. Carpentercoustan criteria compared with the national diabetes data group thresholds for gestational diabetes mellitus. Obstetrics and Gynecology [Internet]. 2009 [cited 2024 Jun 5];114(2):326–32. Available from: https://journals.lww.com/greenjournal/fulltext/2009/0800 0/carpenter_coustan_criteria_compared_with_the.19.as px
- Screening for Gestational and Pregestational Diabetes in Pregnancy and Postpartum. Obstetrics & Gynecology [Internet]. 2024 May 21 [cited 2024 Jun 4]; Available from: https://journals.lww.com/greenjournal/fulltext/9900/scre ening for gestational and pregestational.1074.aspx
- 55. Starikov R, Bohrer J, Goh W, Kuwahara M, Chien EK, Lopes V, et al. Hemoglobin A1c in pregestational diabetic gravidas and the risk of congenital heart disease in the fetus. Pediatr Cardiol [Internet]. 2013 Oct 26 [cited 2024

Jun 1];34(7):1716–22. Available from: https://link.springer.com/article/10.1007/s00246-013-0704-6

- Harper LM, Jauk V, Longo S, Biggio JR, Szychowski JM, Tita AT. Early gestational diabetes screening in obese women: a randomized controlled trial. Am J Obstet Gynecol [Internet]. 2020 May 1 [cited 2024 Jun 3];222(5):495.e1-495.e8. Available from: https://pubmed.ncbi.nlm.nih.gov/31926951/
- 57. Simmons D, Immanuel J, Hague WM, Teede H, Nolan CJ, Peek MJ, et al. Treatment of Gestational Diabetes Mellitus Diagnosed Early in Pregnancy. N Engl J Med [Internet]. 2023 Jun 8 [cited 2024 Jun 3];388(23):2132–44. Available from: https://pubmed.ncbi.nlm.nih.gov/37144983/
- Davidson KW, Barry MJ, Mangione CM, Cabana M, Caughey AB, Davis EM, et al. Screening for Gestational Diabetes: US Preventive Services Task Force Recommendation Statement. JAMA [Internet]. 2021 Aug 10 [cited 2024 Jun 3];326(6):531–8. Available from: https://jamanetwork.com/journals/jama/fullarticle/27828 58
- 59. Landon MB. Obstetric management of pregnancies complicated by diabetes mellitus. Clin Obstet Gynecol [Internet]. 2000 Mar [cited 2024 Jun 1];43(1):65–74. Available from: https://pubmed.ncbi.nlm.nih.gov/10694989/
- Scifres CM, Feghali M, Dumont T, Althouse AD, Speer P, Caritis SN, et al. Large-for-Gestational-Age Ultrasound Diagnosis and Risk for Cesarean Delivery in Women With Gestational Diabetes Mellitus. Obstetrics and gynecology [Internet]. 2015 Oct 20 [cited 2024 Jun 1];126(5):978–86. Available from: https://pubmed.ncbi.nlm.nih.gov/26444129/
- Crimmins S, Mo C, Nassar Y, Kopelman JN, Turan OM. Polyhydramnios or Excessive Fetal Growth Are Markers for Abnormal Perinatal Outcome in Euglycemic Pregnancies. Am J Perinatol [Internet]. 2018 Jan 1 [cited 2024 Jun 1];35(2):140–5. Available from: https://pubmed.ncbi.nlm.nih.gov/28838004/
- 62. Wang J, Pan L, Liu E, Liu H, Liu J, Wang S, et al. Gestational diabetes and offspring's growth from birth to 6 years old. Int J Obes (Lond) [Internet]. 2019 Apr 1 [cited 2024 Jun 1];43(4):663–72. Available from: https://pubmed.ncbi.nlm.nih.gov/30181654/
- 63. Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. Diabetes Care [Internet]. 2002 [cited 2024 Jun 3];25(10):1862–8. Available from: https://pubmed.ncbi.nlm.nih.gov/12351492/
- 64. Moses RG, Goluza I, Borchard JP, Harman A, Dunning A, Milosavljevic M. The prevalence of diabetes after

gestational diabetes - An Australian perspective. Aust N Z J Obstet Gynaecol [Internet]. 2017 Apr 1 [cited 2024 Jun 2];57(2):157–61. Available from: https://pubmed.ncbi.nlm.nih.gov/28272746/

- Versace VL, Beks H, Wesley H, McNamara K, Hague W, Anjana RM, et al. Metformin for Preventing Type 2 Diabetes Mellitus in Women with a Previous Diagnosis of Gestational Diabetes: A Narrative Review. Semin Reprod Med [Internet]. 2020 Nov 1 [cited 2024 Jun 1];38(6):366–76. Available from: http://www.thiemeconnect.com/products/ejournals/html/10.1055/s-0041-1727203
- Ratner RE, Christophi CA, Metzger BE, Dabelea D, Bennett PH, Pi-Sunyer X, et al. Prevention of Diabetes in Women with a History of Gestational Diabetes: Effects of Metformin and Lifestyle Interventions. J Clin Endocrinol Metab [Internet]. 2008 [cited 2024 Jun 3];93(12):4774. Available from: /pmc/articles/PMC2626441/
- Xiang AH, Peters RK, Kjos SL, Marroquin A, Goico J, Ochoa C, et al. Effect of pioglitazone on pancreatic betacell function and diabetes risk in Hispanic women with prior gestational diabetes. Diabetes [Internet]. 2006 Feb [cited 2024 Jun 1];55(2):517–22. Available from: https://pubmed.ncbi.nlm.nih.gov/16443789/
- Starikov R, Dudley D, Reddy UM. Stillbirth in the pregnancy complicated by diabetes. Curr Diab Rep [Internet]. 2015 Mar 1 [cited 2024 Jun 1];15(3). Available from: https://pubmed.ncbi.nlm.nih.gov/25667005/
- Mitanchez D, Burguet A, Simeoni U. Infants born to mothers with gestational diabetes mellitus: mild neonatal effects, a long-term threat to global health. J Pediatr [Internet]. 2014 Mar [cited 2024 Jun 1];164(3):445–50. Available from: https://pubmed.ncbi.nlm.nih.gov/24331686/
- Karmon A, Levy A, Holcberg G, Wiznitzer A, Mazor M, Sheiner E. Decreased perinatal mortality among women with diet-controlled gestational diabetes mellitus. Int J Gynaecol Obstet [Internet]. 2009 [cited 2024 Jun 1];104(3):199–202. Available from: https://pubmed.ncbi.nlm.nih.gov/19189868/
- 71. Sharma A, Mishra M, Sharan K. Editorial: Developmental origin of diseases: a special focus on the parental contribution towards offspring's adult health. Front Endocrinol (Lausanne) [Internet]. 2023 [cited 2024 Jun 3];14. Available from: /pmc/articles/PMC10225984/
- 72. Sugino KY, Hernandez TL, Barbour LA, Kofonow JM, Frank DN, Friedman JE. A maternal higher-complex carbohydrate diet increases bifidobacteria and alters early life acquisition of the infant microbiome in women with gestational diabetes mellitus. Front Endocrinol (Lausanne) [Internet]. 2022 Jul 28 [cited 2024 Jun

3];13:921464. Available http://www.clinicaltrials.gov

from:

- 73. Mantzorou M, Papandreou D, Pavlidou E, Papadopoulou SK, Tolia M, Mentzelou M, et al. Maternal Gestational Diabetes Is Associated with High Risk of Childhood Overweight and Obesity: A Cross-Sectional Study in Pre-School Children Aged 2–5 Years. Medicina (B Aires) [Internet]. 2023 Mar 1 [cited 2024 Jun 3];59(3). Available from: /pmc/articles/PMC10051905/
- 74. Yamamoto JM, Kellett JE, Balsells M, García-Patterson A, Hadar E, Solà I, et al. Gestational Diabetes Mellitus and Diet: A Systematic Review and Meta-analysis of Randomized Controlled Trials Examining the Impact of Modified Dietary Interventions on Maternal Glucose Control and Neonatal Birth Weight. Diabetes Care [Internet]. 2018 Jul 1 [cited 2024 Jun 1];41(7):1346–61. Available from: https://pubmed.ncbi.nlm.nih.gov/29934478/
- Committee ADAPP, ElSayed NA, Aleppo G, Bannuru RR, Bruemmer D, Collins BS, et al. 15. Management of Diabetes in Pregnancy: Standards of Care in Diabetes— 2024. Diabetes Care [Internet]. 2024 Jan 1 [cited 2024 Jun 5];47(Supplement_1):S282–94. Available from: https://dx.doi.org/10.2337/dc24-S015
- 76. KM R, AL Y. Weight Gain During Pregnancy: Reexamining the Guidelines. 2009 Dec 14 [cited 2024 Jun 1]; Available from: https://pubmed.ncbi.nlm.nih.gov/20669500/
- 77. Martínez-Hortelano JA, Cavero-Redondo I, Álvarez-Bueno C, Garrido-Miguel M, Soriano-Cano A, Martínez-Vizcaíno V. Monitoring gestational weight gain and prepregnancy BMI using the 2009 IOM guidelines in the global population: a systematic review and metaanalysis. BMC Pregnancy Childbirth [Internet]. 2020 Dec 1 [cited 2024 Jun 1];20(1). Available from: https://pubmed.ncbi.nlm.nih.gov/33109112/
- Harper LM, Tita A, Biggio JR. The institute of medicine guidelines for gestational weight gain after a diagnosis of gestational diabetes and pregnancy outcomes. Am J Perinatol [Internet]. 2015 [cited 2024 Jun 1];32(3):239– 46. Available from: https://pubmed.ncbi.nlm.nih.gov/24971568/
- 79. Berggren EK, Stuebe AM, Boggess KA. Excess Maternal Weight Gain and Large for Gestational Age Risk among Women with Gestational Diabetes. Am J Perinatol [Internet]. 2015 [cited 2024 Jun 5];32(3):251–6. Available from: https://pubmed.ncbi.nlm.nih.gov/24971567/
- Wong T, Barnes RA, Ross GP, Cheung NW, Flack JR. Are the Institute of Medicine weight gain targets applicable in women with gestational diabetes mellitus? Diabetologia [Internet]. 2017 Mar 1 [cited 2024 Jun

1];60(3):416–23. Available from: https://pubmed.ncbi.nlm.nih.gov/27942798/

- Park JE, Park S, Daily JW, Kim SH. Low gestational weight gain improves infant and maternal pregnancy outcomes in overweight and obese Korean women with gestational diabetes mellitus. Gynecol Endocrinol [Internet]. 2011 Oct [cited 2024 Jun 1];27(10):775–81. Available from: https://pubmed.ncbi.nlm.nih.gov/21190417/
- Cheng YW, Chung JH, Kurbisch-Block I, Inturrisi M, Shafer S, Caughey AB. Gestational weight gain and gestational diabetes mellitus: perinatal outcomes. Obstetrics and gynecology [Internet]. 2008 Nov [cited 2024 Jun 1];112(5):1015–22. Available from: https://pubmed.ncbi.nlm.nih.gov/18978100/
- Kurtzhals LL, Nørgaard SK, Secher AL, Nichum VL, Ronneby H, Tabor A, et al. The impact of restricted gestational weight gain by dietary intervention on fetal growth in women with gestational diabetes mellitus. Diabetologia [Internet]. 2018 Dec 1 [cited 2024 Jun 1];61(12):2528–38. Available from: https://pubmed.ncbi.nlm.nih.gov/30255376/
- Katon J, Reiber G, Williams MA, Yanez D, Miller E. Weight loss after diagnosis with gestational diabetes and birth weight among overweight and obese women. Matern Child Health J [Internet]. 2013 [cited 2024 Jun 1];17(2):374–83. Available from: https://pubmed.ncbi.nlm.nih.gov/22692470/
- Viecceli C, Remonti LR, Hirakata VN, Mastella LS, Gnielka V, Oppermann MLR, et al. Weight gain adequacy and pregnancy outcomes in gestational diabetes: a meta-analysis. Obes Rev [Internet]. 2017 May 1 [cited 2024 Jun 1];18(5):567–80. Available from: https://pubmed.ncbi.nlm.nih.gov/28273690/
- 86. de Veciana M, Major CA, Morgan MA, Asrat T, Toohey JS, Lien JM, et al. Postprandial versus preprandial blood glucose monitoring in women with gestational diabetes mellitus requiring insulin therapy. N Engl J Med [Internet]. 1995 Nov 9 [cited 2024 Jun 1];333(19):1237–41. Available from: https://pubmed.pcbi.plm.pib.gov/7565999/

https://pubmed.ncbi.nlm.nih.gov/7565999/

- 87. Simeoni U, Barker DJ. Offspring of diabetic pregnancy: long-term outcomes. Semin Fetal Neonatal Med [Internet]. 2009 Apr [cited 2024 Jun 1];14(2):119–24. Available from: https://pubmed.ncbi.nlm.nih.gov/19208505/
- Uplinger N. The controversy continues: nutritional management of the pregnancy complicated by diabetes. Curr Diab Rep [Internet]. 2009 [cited 2024 Jun 1];9(4):291–5. Available from: https://pubmed.ncbi.nlm.nih.gov/19640342/

- Hernandez TL, Anderson MA, Chartier-Logan C, Friedman JE, Barbour LA. Strategies in the nutritional management of gestational diabetes. Clin Obstet Gynecol [Internet]. 2013 Dec [cited 2024 Jun 1];56(4):803–15. Available from: https://pubmed.ncbi.nlm.nih.gov/24047934/
- 90. Hernandez TL, Pelt RVE, Anderson MA, Reece MS, Reynolds RM, De La Houssaye BA, et al. Women With Gestational Diabetes Mellitus Randomized to a Higher-Complex Carbohydrate/Low-Fat Diet Manifest Lower Adipose Tissue Insulin Resistance, Inflammation, Glucose, and Free Fatty Acids: A Pilot Study. Diabetes Care [Internet]. 2016 Jan 1 [cited 2024 Jun 1];39(1):39– 42. Available from: https://pubmed.ncbi.nlm.nih.gov/26223240/
- Ruchat SM, Mottola MF. The important role of physical activity in the prevention and management of gestational diabetes mellitus. Diabetes Metab Res Rev [Internet].
 2013 Jul [cited 2024 Jun 1];29(5):334–46. Available from: https://pubmed.ncbi.nlm.nih.gov/23436340/
- Carpenter MW. The role of exercise in pregnant women with diabetes mellitus. Clin Obstet Gynecol [Internet].
 2000 Mar [cited 2024 Jun 1];43(1):56–64. Available from: https://pubmed.ncbi.nlm.nih.gov/10694988/
- 93. Demaio M, Magann EF. Exercise and pregnancy. J Am Acad Orthop Surg [Internet]. 2009 [cited 2024 Jun 1];17(8):504–14. Available from: https://pubmed.ncbi.nlm.nih.gov/19652032/
- 94. Anjana RM, Sudha V, Lakshmipriya N, Anitha C, Unnikrishnan R, Bhavadharini B, et al. Physical activity patterns and gestational diabetes outcomes - The wings project. Diabetes Res Clin Pract [Internet]. 2016 Jun 1 [cited 2024 Jun 1];116:253–62. Available from: https://pubmed.ncbi.nlm.nih.gov/27321343/
- of Maternal-Fetal Medicine Publications Committee S. SMFM Statement: Pharmacological treatment of gestational diabetes. 2018 [cited 2024 Jun 5]; Available from: https://doi.org/10.1016/j.ajog.2018.01.041
- 96. Venkatesh KK, Chiang CW, Castillo WC, Battarbee AN, Donneyong M, Harper LM, et al. Changing patterns in medication prescription for gestational diabetes during a time of guideline change in the USA: a cross-sectional study. BJOG [Internet]. 2022 Feb 1 [cited 2024 Aug 27];129(3):473–83. Available from: https://pubmed.ncbi.nlm.nih.gov/34605130/
- 97. Venkatesh KK, Wu J, Trinh A, Cross S, Rice D, Powe CE, et al. Patient Priorities, Decisional Comfort, and Satisfaction with Metformin versus Insulin for the Treatment of Gestational Diabetes Mellitus. Am J Perinatol [Internet]. 2024 Jun 4 [cited 2024 Aug 27];41(S 01):E3170–82. Available from: https://pubmed.ncbi.nlm.nih.gov/38049101/

- Kjos SL, Schaefer-Graf UM. Modified therapy for gestational diabetes using high-risk and low-risk fetal abdominal circumference growth to select strict versus relaxed maternal glycemic targets. Diabetes Care [Internet]. 2007 Jul [cited 2024 Jun 2];30 Suppl 2(SUPPL. 2). Available from: https://pubmed.ncbi.nlm.nih.gov/17596472/
- Bonomo M, Cetin I, Pisoni MP, Faden D, Mion E, Taricco E, et al. Flexible treatment of gestational diabetes modulated on ultrasound evaluation of intrauterine growth: a controlled randomized clinical trial. Diabetes Metab [Internet]. 2004 [cited 2024 Jun 2];30(3):237–43. Available from: https://pubmed.ncbi.nlm.nih.gov/15223975/
- Crowther CA, Samuel D, Hughes R, Tran T, Brown J, Alsweiler JM. Tighter or less tight glycaemic targets for women with gestational diabetes mellitus for reducing maternal and perinatal morbidity: A stepped-wedge, cluster-randomised trial. PLoS Med [Internet]. 2022 Sep 1 [cited 2024 Jun 5];19(9):e1004087. Available from: https://journals.plos.org/plosmedicine/article?id=10.137 1/journal.pmed.1004087
- 101. Davitt C, Flynn KE, Harrison RK, Pan A, Palatnik A. Current practices in gestational diabetes mellitus diagnosis and management in the United States: survey of maternal-fetal medicine specialists. Am J Obstet Gynecol [Internet]. 2021 Aug 1 [cited 2024 Jun 5];225(2):203–4. Available from: http://www.ajog.org/article/S0002937821005524/fulltext
- 102. ACOG Practice Bulletin No. 201: Pregestational Diabetes Mellitus. Obstetrics and Gynecology [Internet].
 2018 Dec 1 [cited 2024 Jun 5];132(6):E228–48. Available from: https://pubmed.ncbi.nlm.nih.gov/30461693/
- 103. Liang X, Fu Y, Lu S, Shuai M, Miao Z, Gou W, et al. Continuous glucose monitoring-derived glycemic metrics and adverse pregnancy outcomes among women with gestational diabetes: a prospective cohort study. Lancet Reg Health West Pac [Internet]. 2023 Oct 1 [cited 2024 Jun 5];39:100823. Available from: http://www.thelancet.com/article/S2666606523001414/f ulltext
- 104. García-Moreno RM, Benítez-Valderrama P, Barquiel B, González Pérez-de-Villar N, Hillman N, Lora Pablos D, et al. Efficacy of continuous glucose monitoring on maternal and neonatal outcomes in gestational diabetes mellitus: a systematic review and meta-analysis of randomized clinical trials. Diabetic Medicine [Internet]. 2022 Jan 1 [cited 2024 Jun 5];39(1):e14703. Available from:

https://onlinelibrary.wiley.com/doi/full/10.1111/dme.147 03

- 105. Cleary EM, Thung SF, Buschur EO. Pregestational Diabetes Mellitus. Endotext [Internet]. 2021 Jul 26 [cited 2024 Aug 27]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK572754/
- 106. Rowan JA, Hague WM, Gao W, Battin MR, Peter Moore M. Metformin versus Insulin for the Treatment of Gestational Diabetes A bs t r ac t. N Engl J Med [Internet]. 2008 [cited 2023 Apr 8];358:2003–18. Available from: www.nejm.org
- 107. Ijäs H, Vääräsmäki M, Morin-Papunen L, Keravuo R, Ebeling T, Saarela T, et al. Metformin should be considered in the treatment of gestational diabetes: a prospective randomised study. BJOG [Internet]. 2011 Jun [cited 2024 Jun 2];118(7):880–5. Available from: https://pubmed.ncbi.nlm.nih.gov/21083860/
- 108. Spaulonci CP, Bernardes LS, Trindade TC, Zugaib M, Francisco RPV. Randomized trial of metformin vs insulin in the management of gestational diabetes. Am J Obstet Gynecol [Internet]. 2013 [cited 2024 Jun 2];209(1):34.e1-34.e7. Available from: https://pubmed.ncbi.nlm.nih.gov/23524173/
- 109. Balsells M, García-Patterson A, Solà I, Roqué M, Gich I, Corcoy R. Glibenclamide, metformin, and insulin for the treatment of gestational diabetes: a systematic review and meta-analysis. BMJ [Internet]. 2015 Jan 21 [cited 2024 Jun 2];350. Available from: https://pubmed.ncbi.nlm.nih.gov/25609400/
- 110. Rowan JA, Rush EC, Obolonkin V, Battin M, Wouldes T, Hague WM. Metformin in gestational diabetes: the offspring follow-up (MiG TOFU): body composition at 2 years of age. Diabetes Care [Internet]. 2011 Oct [cited 2024 Jun 2];34(10):2279–84. Available from: https://pubmed.ncbi.nlm.nih.gov/21949222/
- 111. Wouldes TA, Battin M, Coat S, Rush EC, Hague WM, Rowan JA. Neurodevelopmental outcome at 2 years in offspring of women randomised to metformin or insulin treatment for gestational diabetes. Arch Dis Child Fetal Neonatal Ed [Internet]. 2016 Nov 1 [cited 2024 Jun 2];101(6):F488–93. Available from: https://pubmed.ncbi.nlm.nih.gov/26912348/
- 112. Carlsen SM, Martinussen MP, Vanky E. Metformin's effect on first-year weight gain: a follow-up study. Pediatrics [Internet]. 2012 [cited 2024 Jun 5];130(5). Available from: https://pubmed.ncbi.nlm.nih.gov/23071212/
- Dunne F, Newman C, Alvarez-Iglesias A, Ferguson J, Smyth A, Browne M, et al. Early Metformin in Gestational Diabetes: A Randomized Clinical Trial. JAMA [Internet]. 2023 Oct 24 [cited 2024 Jun 5];330(16):1547–56. Available from: https://jamanetwork.com/journals/jama/fullarticle/28103 87

114. Paglia MJ, Coustan DR. The use of oral antidiabetic medications in gestational diabetes mellitus. Curr Diab Rep [Internet]. 2009 [cited 2024 Jun 2];9(4):287–90. Available from:

https://pubmed.ncbi.nlm.nih.gov/19640341/

- 115. Vanky E, Zahlsen K, Spigset O, Carlsen SM. Placental passage of metformin in women with polycystic ovary syndrome. Fertil Steril [Internet]. 2005 [cited 2024 Jun 2];83(5):1575–8. Available from: https://pubmed.ncbi.nlm.nih.gov/15866611/
- 116. van Weelden W, Wekker V, de Wit L, Limpens J, Ijäs H, van Wassenaer-Leemhuis AG, et al. Long-Term Effects of Oral Antidiabetic Drugs During Pregnancy on Offspring: A Systematic Review and Meta-analysis of Follow-up Studies of RCTs. Diabetes Ther [Internet]. 2018 Oct 1 [cited 2024 Jun 2];9(5):1811–29. Available from: https://pubmed.ncbi.nlm.nih.gov/30168045/
- 117. Xu Q, Xie Q. Long-term effects of prenatal exposure to metformin on the health of children based on follow-up studies of randomized controlled trials: a systematic review and meta-analysis. Arch Gynecol Obstet [Internet]. 2019 May 1 [cited 2024 Jun 5];299(5):1295– 303. Available from: https://pubmed.ncbi.nlm.nih.gov/30953188/

https://publied.ncbi.nini.nin.gov/50955186/

- 118. Landi SN, Radke S, Engel SM, Boggess K, Stürmer T, Howe AS, et al. Association of Long-term Child Growth and Developmental Outcomes With Metformin vs Insulin Treatment for Gestational Diabetes. JAMA Pediatr [Internet]. 2019 Feb 1 [cited 2024 Jun 2];173(2):160–8. Available from: https://pubmed.ncbi.nlm.nih.gov/30508164/
- 119. Tarry-Adkins JL, Aiken CE, Ozanne SE. Neonatal, infant, and childhood growth following metformin versus insulin treatment for gestational diabetes: A systematic review and meta-analysis. PLoS Med [Internet]. 2019 [cited 2024 Jun 2];16(8). Available from: https://pubmed.ncbi.nlm.nih.gov/31386659/
- 120. Yang L, Lacey L, Whyte S, Quenby S, Denison FC, Dhaun N, et al. Metformin in obese pregnancy has no adverse effects on cardiovascular risk in early childhood. J Dev Orig Health Dis [Internet]. 2022 Jun 17 [cited 2024 Jun 2];13(3):390–4. Available from: https://pubmed.ncbi.nlm.nih.gov/34134812/
- 121. Recommendations | Diabetes in pregnancy: management from preconception to the postnatal period | Guidance | NICE.
- 122. Metzger BE, Buchanan TA, Coustan DR, De Leiva A, Dunger DB, Hadden DR, et al. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. Diabetes Care [Internet]. 2007 Jul [cited 2024 Jun 2];30 Suppl

2(SUPPL. 2). Available from: https://pubmed.ncbi.nlm.nih.gov/17596481/

- Langer O, Conway DL, Berkus MD, Xenakis EMJ, Gonzales O. A comparison of glyburide and insulin in women with gestational diabetes mellitus. N Engl J Med [Internet]. 2000 Oct 19 [cited 2024 Jun 2];343(16):1134– 8. Available from: https://pubmed.ncbi.nlm.nih.gov/11036118/
- 124. Moore LE, Clokey D, Rappaport VJ, Curet LB. Metformin compared with glyburide in gestational diabetes: a randomized controlled trial. Obstetrics and gynecology [Internet]. 2010 Jan [cited 2024 Jun 2];115(1):55–9. Available from: https://pubmed.ncbi.nlm.nih.gov/20027034/
- 125. Helal KF, Badr MS, Rafeek MES, Elnagar WM, Lashin MEB. Can glyburide be advocated over subcutaneous insulin for perinatal outcomes of women with gestational diabetes? A systematic review and meta-analysis. Arch Gynecol Obstet [Internet]. 2020 Jan 1 [cited 2024 Jun 2];301(1):19–32. Available from: https://pubmed.ncbi.nlm.nih.gov/31989292/
- 126. Song R, Chen L, Chen Y, Si X, Liu Y, Liu Y, et al. Comparison of glyburide and insulin in the management of gestational diabetes: A meta-analysis. PLoS One [Internet]. 2017 Aug 1 [cited 2024 Jun 2];12(8). Available from: https://pubmed.ncbi.nlm.nih.gov/28771572/
- 127. Sénat MV, Affres H, Letourneau A, Coustols-Valat M, Cazaubiel M, Legardeur H, et al. Effect of Glyburide vs Subcutaneous Insulin on Perinatal Complications Among Women With Gestational Diabetes: A Randomized Clinical Trial. JAMA [Internet]. 2018 May 1 [cited 2024 Jun 2];319(17):1773–80. Available from: https://pubmed.ncbi.nlm.nih.gov/29715355/
- 128. Poolsup N, Suksomboon N, Amin M. Efficacy and safety of oral antidiabetic drugs in comparison to insulin in treating gestational diabetes mellitus: a meta-analysis. PLoS One [Internet]. 2014 Oct 10 [cited 2024 Jun 5];9(10). Available from: https://pubmed.ncbi.nlm.nih.gov/25302493/
- 129. Lain KY, Garabedian MJ, Daftary A, Jeyabalan A. Neonatal adiposity following maternal treatment of gestational diabetes with glyburide compared with insulin. Am J Obstet Gynecol [Internet]. 2009 [cited 2024 Jun 2];200(5):501.e1-501.e6. Available from: https://pubmed.ncbi.nlm.nih.gov/19375570/
- Bertini AM, Silva JC, Taborda W, Becker F, Lemos Bebber FR, Zucco Viesi JM, et al. Perinatal outcomes and the use of oral hypoglycemic agents. J Perinat Med [Internet]. 2005 Dec [cited 2024 Jun 2];33(6):519–23. Available from: https://pubmed.ncbi.nlm.nih.gov/16318615/

- 131. Muller DRP, Stenvers DJ, Malekzadeh A, Holleman F, Painter RC, Siegelaar SE. Effects of GLP-1 agonists and SGLT2 inhibitors during pregnancy and lactation on offspring outcomes: a systematic review of the evidence. Vol. 14, Frontiers in Endocrinology. 2023.
- 132. Dao K, Shechtman S, Weber-Schoendorfer C, Diav-Citrin O, Murad RH, Berlin M, et al. Use of GLP1 receptor agonists in early pregnancy and reproductive safety: a multicentre, observational, prospective cohort study based on the databases of six Teratology Information Services. BMJ Open [Internet]. 2024 Apr 24 [cited 2024 Jun 30];14(4). Available from: https://pubmed.ncbi.nlm.nih.gov/38663923/
- 133. Cesta CE, Rotem R, Bateman BT, Chodick G, Cohen JM, Furu K, et al. Safety of GLP-1 Receptor Agonists and Other Second-Line Antidiabetics in Early Pregnancy. JAMA Intern Med [Internet]. 2024 Feb 1 [cited 2024 Jun 30];184(2):144–52. Available from: https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2812743
- 134. Feingold KR. Oral and Injectable (Non-Insulin) Pharmacological Agents for the Treatment of Type 2 Diabetes. Endotext [Internet]. 2022 Aug 26 [cited 2024 Jun 30]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK279141/
- 135. Indications for Outpatient Antenatal Fetal Surveillance: ACOG Committee Opinion, Number 828. Obstetrics and gynecology [Internet]. 2021 Jun 1 [cited 2024 Jun 2];137(6):E177–97. Available from: https://pubmed.ncbi.nlm.nih.gov/34011892/
- 136. Abdelwahab M, Frey HA, Lynch CD, Klebanoff MA, Thung SF, Costantine MM, et al. Association between Diabetes in Pregnancy and Shoulder Dystocia by Infant Birth Weight in an Era of Cesarean Delivery for Suspected Macrosomia. Am J Perinatol [Internet]. 2023 Mar 25 [cited 2024 Aug 1];40(9):929–36. Available from: https://pubmed.ncbi.nlm.nih.gov/36848935/
- Rao U, de Vries B, Ross GP, Gordon A. Fetal biometry for guiding the medical management of women with gestational diabetes mellitus for improving maternal and perinatal health. Cochrane Database Syst Rev [Internet].
 2019 Sep 3 [cited 2024 Jun 2];9(9). Available from: https://pubmed.ncbi.nlm.nih.gov/31476798/
- Medically Indicated Late-Preterm and Early-Term Deliveries: ACOG Committee Opinion, Number 818.
 Obstetrics and gynecology [Internet]. 2021 Feb 1 [cited 2024 Jun 2];137(2):e29–33. Available from: https://pubmed.ncbi.nlm.nih.gov/33481529/
- Grobman WA, Rice MM, Reddy UM, Tita ATN, Silver RM, Mallett G, et al. Labor Induction versus Expectant Management in Low-Risk Nulliparous Women. N Engl J Med [Internet]. 2018 Aug 9 [cited 2024 Jun

2];379(6):513–23. Available from: https://pubmed.ncbi.nlm.nih.gov/30089070/

- Feghali MN, Caritis SN, Catov JM, Scifres CM. Timing of delivery and pregnancy outcomes in women with gestational diabetes. Am J Obstet Gynecol [Internet].
 2016 Aug 1 [cited 2024 Jun 2];215(2):243.e1-243.e7. Available from: https://pubmed.ncbi.nlm.nih.gov/26976558/
- 141. Sutton AL, Mele L, Landon MB, Ramin SM, Varner MW, Thorp JM, et al. Delivery timing and cesarean delivery risk in women with mild gestational diabetes mellitus. Am J Obstet Gynecol [Internet]. 2014 [cited 2024 Jun 2];211(3):244.e1-244.e7. Available from: https://pubmed.ncbi.nlm.nih.gov/24607755/
- 142. Kitzmiller JL, Dang-Kilduff L, Taslimi MM. Gestational diabetes after delivery. Short-term management and long-term risks. Diabetes Care [Internet]. 2007 Jul [cited 2024 Jun 2];30 Suppl 2(SUPPL. 2). Available from: https://pubmed.ncbi.nlm.nih.gov/17596477/
- 143. Blatt AJ, Nakamoto JM, Kaufman HW. Gaps in diabetes screening during pregnancy and postpartum. Obstetrics and gynecology [Internet]. 2011 Jan [cited 2024 Jun 2];117(1):61–8. Available from: https://pubmed.ncbi.nlm.nih.gov/21173645/
- 144. Waters TP, Kim SY, Werner E, Dinglas C, Carter EB, Patel R, et al. Should women with gestational diabetes be screened at delivery hospitalization for type 2 diabetes? Am J Obstet Gynecol [Internet]. 2020 Jan 1 [cited 2024 Jun 2];222(1):73.e1-73.e11. Available from: https://pubmed.ncbi.nlm.nih.gov/31351065/
- 145. Werner EF, Has P, Rouse D, Clark MA. Two-day postpartum compared with 4- to 12-week postpartum glucose tolerance testing for women with gestational diabetes. Am J Obstet Gynecol [Internet]. 2020 Sep 1 [cited 2024 Jun 5];223(3):439.e1-439.e7. Available from: https://pubmed.ncbi.nlm.nih.gov/32470456/
- 146. Gabbe SG, Landon MB, Warren-Boulton E, Fradkin J. Promoting Health After Gestational Diabetes: A National Diabetes Education Program Call to Action. Obstetrics and gynecology [Internet]. 2012 Jan [cited 2024 Jun 5];119(1):171. Available from: /pmc/articles/PMC3244679/
- 147. Gunderson EP, Crites Y, Chiang V, Walton D, Azevedo RA, Fox G, et al. Influence of breastfeeding during the postpartum oral glucose tolerance test on plasma glucose and insulin. Obstetrics and gynecology [Internet]. 2012 [cited 2024 Jun 2];120(1):136–43. Available from: https://pubmed.pabi.plm.pib.gov/22011402/

https://pubmed.ncbi.nlm.nih.gov/22914402/

148. Martorell R, Stein AD, Schroeder DG. Early nutrition and later adiposity. J Nutr [Internet]. 2001 [cited 2024 Jun

5];131(3). Available from: https://pubmed.ncbi.nlm.nih.gov/11238778/

- Kim C, Herman WH, Cheung NW, Gunderson EP, 149. Richardson C. Comparison of hemoglobin A1c with fasting plasma glucose and 2-h postchallenge glucose for risk stratification among women with recent gestational diabetes mellitus. Diabetes Care [Internet]. 2011 Sep [cited 2024 Jun 5];34(9):1949-51. Available from: https://pubmed.ncbi.nlm.nih.gov/21750276/
- Picón MJ, Murri M, Muñoz A, Fernández-García JC, 150. Gomez-Huelgas R, Tinahones FJ. Hemoglobin A1c versus oral glucose tolerance test in postpartum diabetes screening. Diabetes Care [Internet]. 2012 Aug [cited 2024 Jun 2];35(8):1648-53. Available from: https://pubmed.ncbi.nlm.nih.gov/22688550/
- 151. Su X, Zhang Z, Qu X, Tian Y, Zhang G. Hemoglobin A1c for diagnosis of postpartum abnormal glucose tolerance among women with gestational diabetes mellitus: diagnostic meta-analysis. PLoS One [Internet]. 2014 Jul 11 [cited 2024 Jun 2];9(7). Available from: https://pubmed.ncbi.nlm.nih.gov/25014072/
- Kjos SL, Peters RK, Xiang A, Henry OA, Montoro M, 152. Buchanan TA. Predicting future diabetes in Latino women with gestational diabetes. Utility of early postpartum glucose tolerance testing. Diabetes [Internet]. 1995 [cited 2024 Jun 2];44(5):586-91. Available from: https://pubmed.ncbi.nlm.nih.gov/7729620/

- 153. Alves JM, Stollmeier A, Leite IG, Pilger CG, Detsch JCM, Radominski RB, et al. Postpartum Reclassification of Glycemic Status in Women with Gestational Diabetes Mellitus and Associated Risk Factors. Rev Bras Ginecol Obstet [Internet]. 2016 Aug 1 [cited 2024 Jun Available 2];38(8):381-90. from: https://pubmed.ncbi.nlm.nih.gov/27541185/
- 154. Kugishima Y, Yasuhi I, Yamashita H, Fukuda M, Kuzume A, Sugimi S, et al. Risk factors associated with abnormal glucose tolerance in the early postpartum period among Japanese women with gestational diabetes. Int J Gynaecol Obstet [Internet]. 2015 Apr 1 [cited 2024 Jun 21:129(1):42-5. Available from: https://pubmed.ncbi.nlm.nih.gov/25497883/
- 155. Capula C, Chiefari E, Vero A, Foti DP, Brunetti A, Vero R. Prevalence and predictors of postpartum glucose intolerance in Italian women with gestational diabetes mellitus. Diabetes Res Clin Pract [Internet]. 2014 [cited 2024 Jun 2];105(2):223-30. Available from: https://pubmed.ncbi.nlm.nih.gov/24931701/
- Benaiges D, Chillaron JJ, Pedro-Botet J, Mas A, Puig De 156. Dou J. Sagarra E. et al. Role of A1c in the postpartum screening of women with gestational diabetes. Gynecol Endocrinol [Internet]. 2013 Jul [cited 2024 Jun

2];29(7):687-90. Available from: https://pubmed.ncbi.nlm.nih.gov/23638620/

- Kim KS, Kim SK, Cho YW, Park SW. Diagnostic value of 157. haemoglobin A1c in post-partum screening of women with gestational diabetes mellitus. Diabet Med [Internet]. 2016 Dec 1 [cited 2024 Jun 2];33(12):1668–72. Available from: https://pubmed.ncbi.nlm.nih.gov/26996814/
- Azen SP, Peters RK, Berkowitz K, Kjos S, Xiang A, 158. Buchanan TA. TRIPOD (TRoglitazone In the Prevention Of Diabetes): A randomized, placebo-controlled trial of troglitazone in women with prior gestational diabetes mellitus. Control Clin Trials [Internet]. 1998 Apr [cited 2024 Jun 5];19(2):217-31. Available from: https://pubmed.ncbi.nlm.nih.gov/9551285/
- 159. Buchanan TA, Xiang AH, Peters RK, Kjos SL, Marroquin A, Goico J, et al. Preservation of pancreatic beta-cell function and prevention of type 2 diabetes by pharmacological treatment of insulin resistance in highrisk hispanic women. Diabetes [Internet]. 2002 [cited 2024 Jun 51:51(9):2796-803. Available from: https://pubmed.ncbi.nlm.nih.gov/12196473/
- ACOG Committee Opinion No. 756: Optimizing Support 160. for Breastfeeding as Part of Obstetric Practice. Obstetrics and gynecology [Internet]. 2018 Oct 1 [cited 2024 Jun 5];132(4):e187–96. Available from: https://pubmed.ncbi.nlm.nih.gov/30247365/
- 161. Infant and young child feeding [Internet]. [cited 2024 Jun Available 2]. from: https://www.who.int/data/nutrition/nlis/info/infant-andvouna-child-feedina
- Eidelman AI, Schanler RJ. Breastfeeding and the use of 162. human milk. Pediatrics. 2012 Mar;129(3).
- Gunderson EP, Lewis CE, Lin Y, Sorel M, Gross M, 163. Sidney S, et al. Lactation Duration and Progression to Diabetes in Women Across the Childbearing Years: The 30-Year CARDIA Study. JAMA Intern Med [Internet]. 2018 Mar 1 [cited 2024 Jun 2];178(3):328-37. Available from: https://pubmed.ncbi.nlm.nih.gov/29340577/
- Pinho-Gomes AC, Morelli G, Jones A, Woodward M. 164. Association of lactation with maternal risk of type 2 diabetes: A systematic review and meta-analysis of observational studies. Diabetes Obes Metab. 2021 Aug 1;23(8):1902-16.
- 165. Zheng X, Wang H, Wu H. Association between diet quality scores and risk of overweight and obesity in children and adolescents. BMC Pediatr [Internet]. 2023 Apr 13 [cited 2023 Apr 23];23(1):169. Available from: https://pubmed.ncbi.nlm.nih.gov/37046233/
- 166. Crume TL, Ogden LG, Mayer-Davis EJ, Hamman RF, Norris JM, Bischoff KJ, et al. The impact of neonatal breast-feeding on growth trajectories of youth exposed and unexposed to diabetes in utero: the EPOCH Study.

Int J Obes (Lond) [Internet]. 2012 Apr [cited 2024 Jun5];36(4):529–34.Availablehttps://pubmed.ncbi.nlm.nih.gov/22290537/

- 167. Fields DA, Demerath EW. Relationship of insulin, glucose, leptin, IL-6 and TNF-α in human breast milk with infant growth and body composition. Pediatr Obes [Internet]. 2012 Aug [cited 2024 Jun 2];7(4):304–12. Available from: https://pubmed.ncbi.nlm.nih.gov/22577092/
- 168. Soderborg TK, Borengasser SJ, Barbour LA, Friedman JE. Microbial transmission from mothers with obesity or diabetes to infants: an innovative opportunity to interrupt a vicious cycle. Diabetologia [Internet]. 2016 May 1 [cited 2024 Jun 2];59(5):895–906. Available from: https://pubmed.ncbi.nlm.nih.gov/26843076/
- 169. Chan D, Goruk S, Becker AB, Subbarao P, Mandhane PJ, Turvey SE, et al. Adiponectin, leptin and insulin in breast milk: associations with maternal characteristics and infant body composition in the first year of life. Int J Obes (Lond) [Internet]. 2018 Jan 1 [cited 2024 Jun 5];42(1):36–43. Available from: https://pubmed.ncbi.nlm.nih.gov/28925410/

- 170. Kugananthan S, Gridneva Z, Lai CT, Hepworth AR, Mark PJ, Kakulas F, et al. Associations between Maternal Body Composition and Appetite Hormones and Macronutrients in Human Milk. Nutrients [Internet]. 2017 Mar 9 [cited 2024 Jun 5];9(3). Available from: https://pubmed.ncbi.nlm.nih.gov/28282925/
- Louis JM, Bryant A, Ramos D, Stuebe A, Blackwell SC. Interpregnancy Care. Am J Obstet Gynecol [Internet].
 2019 Jan 1 [cited 2024 Jun 5];220(1):B2–18. Available from: https://pubmed.ncbi.nlm.nih.gov/30579872/
- 172. Curtis KM, Tepper NK, Jatlaoui TC, Berry-Bibee E, Horton LG, Zapata LB, et al. U.S. Medical Eligibility Criteria for Contraceptive Use, 2016. MMWR Recomm Rep [Internet]. 2016 [cited 2024 Jun 2];65(3):1–104. Available from: https://pubmed.ncbi.nlm.nih.gov/27467196/
- 173. Turner AM, Donelan EA, Kiley JW. Contraceptive Options Following Gestational Diabetes: Current Perspectives. Open Access J Contracept [Internet]. 2019 Oct [cited 2024 Jun 5];10:41–53. Available from: https://pubmed.ncbi.nlm.nih.gov/31749639/