Screening for Gestational Diabetes Mellitus: A Systematic Review for the U.S. Preventive Services Task Force

Teresa A. Hillier, MD, MS; Kimberly K. Vesco, MD, MPH; Kathryn L. Pedula, MS; Tracy L. Beil, MS; Evelyn P. Whitlock, MD, MPH; and David J. Pettitt, MD

Background: In 2003, the U.S. Preventive Services Task Force concluded that evidence was insufficient to advise for or against routinely screening all pregnant women for gestational diabetes mellitus.

Purpose: To review evidence about the benefits and harms of screening for gestational diabetes.

Data Sources: Databases (MEDLINE, Database of Abstracts of Reviews of Effects, Health Technology Assessment Database, National Institute for Health and Clinical Effectiveness, and Cochrane Library) were searched for reports published from January 2000 to 15 November 2007 (and from 1966 to 1999 for additional studies on screening at less than 24 weeks’ gestation), citations in the 2003 evidence report, and studies identified through consultation of experts and searches of bibliographies.

Study Selection: English-language studies that used standard 1- or 2-step testing for gestational diabetes and that evaluated at least 1 of the following outcomes: neonatal mortality; brachial plexus injury; clavicular fracture; admission to a neonatal intensive care unit for hypoglycemia, hyperbilirubinemia, or the respiratory distress syndrome; maternal mortality; and preeclampsia or pregnancy-induced hypertension.

Data Extraction: 2 reviewers evaluated 1607 abstracts, critically appraised 288 articles, and qualitatively synthesized 13 studies.

Gestational diabetes is currently defined as any degree of glucose intolerance with onset or first recognition during pregnancy (1–4). Its prevalence in the United States is 1% to 14%, depending on population characteristics (1, 5). As obesity and diabetes mellitus have become more prevalent in U.S. women of child-bearing age (6), so has gestational diabetes (7, 8).

Although the American Diabetes Association, the American College of Obstetricians and Gynecologists, and the World Health Organization (1, 2, 4, 9) recommend screening most pregnant women for gestational diabetes between 24 and 28 weeks’ gestation and screening high-risk pregnant women (for example, those with a personal history of gestational diabetes or marked obesity) at the first antenatal visit (1, 2, 4, 10), the U.S. Preventive Services Task Force (USPSTF) concluded in 2003 that there was insufficient evidence to advise for or against routinely screening all pregnant women (11). At that time, fair to good evidence showed that screening combined with therapy for gestational diabetes could reduce fetal macrosomia, but insufficient evidence supported other health benefits for mothers or infants (11).

The USPSTF considers the potential benefits and harms of screening, and weighs the net benefit when evaluating the evidence for screening. A potential harm of gestational diabetes screening is unnecessary glucose testing and treatment of many women who would not ultimately develop problems related to gestational diabetes. Potential benefits include reduction in maternal preeclampsia, stillbirth, brachial plexus injuries, and clavicular fractures due to macrosomia (4). A major challenge in evaluating the evidence for the benefits and harms of gestational diabetes screening is the range of adverse maternal and neonatal outcomes associated with untreated gestational diabetes. With the USPSTF, we developed an analytic framework.

Data Synthesis: No randomized, controlled trials that directly evaluated the risks and benefits of gestational diabetes screening were found. One good-quality randomized, controlled trial of treatment of mild gestational diabetes in a screening-detected population supported a reduction in serious neonatal complications and showed that gestational diabetes treatment also reduced the risk for gestational hypertension. Very limited evidence was found to evaluate early screening for gestational diabetes (before 24 weeks’ gestation). Limited evidence suggests that serious maternal hypoglycemia is rare with treatment and that overall quality of life is not worse among women receiving gestational diabetes treatment compared with women not receiving treatment.

Limitation: The literature is limited by lack of a consistent standard for screening or diagnosis of gestational diabetes.

Conclusion: Limited evidence suggests that gestational diabetes treatment after 24 weeks improves some maternal and neonatal outcomes. Evidence is even more sparse for screening before 24 weeks’ gestation.


See also:
Print
Related article.............................759
Summary for Patients.......................I-60
Web-Only
Appendix Tables
CME quiz
Conversion of graphics into slides
Downloadable recommendation summary
(Figure 1) that incorporated 5 key questions to guide the current systematic review:

1. Does screening for gestational diabetes lead to a reduction in perinatal morbidity and mortality for mother or infant? A) After 24 weeks’ gestation? B) During the first trimester and up to 24 weeks’ gestation?

2. What are the sensitivities, specificities, reliabilities, and yields of current screening tests for gestational diabetes? A) After 24 weeks’ gestation? B) During the first trimester and up to 24 weeks’ gestation?

3. Does treatment of gestational diabetes lead to reduction in perinatal morbidity and mortality for mother or infant? A) After 24 weeks’ gestation? B) During the first trimester and up to 24 weeks’ gestation?

4. What are the adverse effects associated with screening for gestational diabetes?

5. What are the adverse effects associated with treatment of gestational diabetes?

**METHODS**

We followed the USPSTF’s standard methods for systematic reviews and rating the quality of evidence (12).

**Data Sources and Searches**

For each key question, we searched the following databases for literature published from January 2000 to 15 November 2007: MEDLINE, Cochrane Central Registry of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Health Technology Assessment Database, and National Institute for Health and Clinical Excellence. These searches were supplemented by a search for literature on screening before 24 weeks’ gestation published from 1966 to 1999 (Appendix Table 1, available at www.annals.org). Articles were also obtained from outside experts and through reviewing bibliographies of other relevant articles and systematic reviews. Two authors also reviewed all articles cited in the 2003 USPSTF evidence synthesis (11).

**Study Selection**

We included studies that examined 1 or more of the selected outcomes and used the 1- or 2-step screening method and the diagnostic criteria of the American Diabetes Association, American College of Obstetricians and Gynecologists, or World Health Organization (1, 2, 9, 13, 14). The 1-step method (an oral glucose tolerance test), in which a 75-g or 100-g oral glucose load is administered in a fasting state without previous plasma or serum screening (1), is most commonly used outside the United States. The 2-step method is common in the United States and involves an initial test after administration of 50 g of glucose (1, 2, 14), followed by an oral glucose tolerance test to confirm the diagnosis for patients with an abnormal initial result (glucose level, \( \geq 7.2 \text{ mmol/L} \) \( \geq 130 \text{ mg/dL} \) or \( \geq 7.8 \text{ mmol/L} \) \( \geq 140 \text{ mg/dL} \)).

Using inclusion criteria developed for each key question (described in Appendix Table 2, available at www.annals.org), we first sought randomized trials to assess the potential benefit of gestational diabetes screening and treatment in improving final health outcomes, and then prospective cohort studies if trials were not available. Any study design was considered in the evaluation of potential...
harmful. Inclusion criteria were also less stringent for study harms.

Data Extraction and Quality Assessment

Literature searches were focused for each key question but were reviewed with all key questions in mind. Neonatal outcomes evaluated were mortality (stillbirth or neonatal death); brachial plexus injury; clavicular fracture; and neonatal intensive care for hypoglycemia, hyperbilirubinemia, or the respiratory distress syndrome. Maternal outcomes were mortality and preeclampsia or pregnancy-induced hypertension.

For all included studies, 1 primary reviewer abstracted relevant information into standardized evidence tables (full evidence review available at www.ahrq.gov/clinic/uspsf.htm). A second reviewer checked the abstracted data for accuracy. Two investigators critically appraised and rated the quality of all included articles by using USPSTF quality criteria (12). If the investigators disagreed on study content or quality, a third investigator reviewed the study and disagreements were resolved by consensus.

Data Synthesis

Studies were synthesized qualitatively rather than quantitatively because of heterogeneity and were categorized according to whether diagnosis and treatment occurred before or after 24 weeks’ gestation and whether the comparison was against no treatment or a comparison treatment. Because this was a qualitative synthesis, we reported the statistics as published in the original studies; when reported, we used the 95% CI. If the 95% CI was not available, we reported a P value. Studies evaluating the harms of screening were evaluated individually because of the variety of instruments used to measure the psychological effect of screening.

Role of the Funding Source

The Agency for Healthcare Research and Quality funded this work, provided project oversight, and assisted with internal and external review of the draft evidence synthesis. The authors worked with 4 USPSTF members to develop the analytic framework and resolve issues involving the scope of the review.

Results

We reviewed 1607 English-language abstracts and 288 full-text articles. Figure 2 summarizes the search and selection process, which resulted in the inclusion of the following articles: 7 randomized, controlled trials reported in 8 publications that tested interventions that alter glycemic control and reported specified health outcomes in women receiving a diagnosis at 24 weeks’ gestation or later (key question 3A) (15–22); 1 prospective study addressing treatment of women in whom gestational diabetes was diagnosed before 24 weeks’ gestation (key question 3B) (23); and 3 studies reporting harms of screening for gestational diabetes (key question 4) (24–26). One additional article, along with 6 of the 8 articles related to key question 3, reported adverse effects of treatment (key question 5) (15–19, 21, 27). The details of each included study are available in the full evidence tables (available at www.ahrq.gov/clinic/uspsf.htm). Appendix Table 3 (available at www.annals.org) summarizes the excluded studies. The Table displays study-level summaries of the data.

Key Question 1

Does screening for gestational diabetes lead to a reduction in perinatal morbidity and mortality for mother or infant? A) After 24 weeks’ gestation? B) During the first trimester and up to 24 weeks’ gestation?

We identified no randomized, controlled trials of screening and subsequent treatment.

Key Question 2

What are the sensitivities, specificities, reliabilities, and yields of current screening tests for gestational diabetes? A) After 24 weeks’ gestation? B) During the first trimester and up to 24 weeks’ gestation?

No articles met our inclusion criteria for this key question. Although 2 studies reported the sensitivity or specificity of gestational diabetes screening for at least 1 of the specified health outcomes (28, 29), both were limited by using a mixture of treated and untreated women to evaluate sensitivity and specificity and by lack of blinding of treating providers to screening results. The pending Hyperglycemia and Adverse Pregnancy Outcome prospective cohort study of 25,000 pregnant women will probably address these limitations (30). In sum, there was little available evidence on sensitivity and specificity for our primary health outcomes; evidence was available only for macrosomia, which was not an outcome of primary interest to us.

Key Question 3

Does treatment of gestational diabetes lead to reduction in perinatal morbidity and mortality for mother or infant? A) After 24 weeks’ gestation? B) During the first trimester and up to 24 weeks’ gestation?

Seven randomized, controlled trials of gestational diabetes treatment after 24 weeks’ gestation (15–22) and 1 prospective cohort study (23) compared outcomes of women given a diagnosis at the first prenatal visit with outcomes of women given a diagnosis after 24 weeks’ gestation. Appendix Tables 4 and 5 (available at www.annals.org) summarize these studies, and details are available in the full evidence review (www.ahrq.gov/clinic/uspsf.htm).

Diagnosis and Treatment at More Than 24 Weeks’ Gestation

Treatment versus No Treatment of Gestational Diabetes.

We found 2 eligible randomized, controlled trials that tested treatment versus no treatment of gestational diabetes detected in universal screening programs. We judged 1 to be good quality (16) and the other to be fair quality (22).

The good-quality ACHOIS (Australian Carbohydrate Intolerance Study in Pregnant Women) study was a multicenter, blinded, randomized, controlled trial that in-
included 1000 women and was conducted at 14 sites in Australia and 4 sites in the United Kingdom (16). It was designed to determine whether the treatment of mild gestational diabetes would reduce perinatal complications and to assess the effects of treatment on maternal outcomes, mood, and quality of life. Inclusion criteria were a singleton or twin pregnancy at 16 to 30 weeks’ gestation and positive result on 2-step screening for mild gestational diabetes by current World Health Organization criteria with a 75-g oral glucose tolerance test (2-hour glucose level, 7.8 to 11.0 mmol/L [140 to 200 mg/dL] and fasting plasma glucose level <7.8 mmol/L [<140 mg/dL]). At the time of the study, these glucose criteria were defined by the World Health Organization as glucose intolerance of pregnancy (that is, intermediate between normal and gestational diabetes), and thus it was considered ethical to randomly assign and evaluate treatment compared with a blinded untreated group. The intervention group received both individualized dietary advice and instructions to self-monitor glucose levels 4 times daily until glucose values were at the normoglycemic goal (fasting glucose level of 3.5 to 5.0 mmol/L [63 to 99 mg/dL]) for 2 weeks. Insulin treatment was initiated and the dosage titrated as needed to achieve glycemic goals (20% of women in the intervention group required insulin). The treated group gained statistically significantly less weight during pregnancy than the untreated group (8.1 vs. 9.8 kg; adjusted mean difference, −1.4 kg [95% CI, −2.3 to −0.4 kg]), but the study did not collect data on glucose values (Crowther CA. Personal communication. 25 July 2006.) and therefore does not allow estimation of the relative effect of glycemic control compared with weight control on outcomes.

The rate of serious perinatal complications (stillbirth or neonatal death, shoulder dystocia, bone fracture, or nerve palsy) was lower in the treated group than in the untreated group after adjustment for maternal age, race, and parity (relative risk, 0.33 [CI, 0.14 to 0.75]). The relative risk for these individual perinatal outcomes was not calculated between groups because no patients in the treatment group died or developed bone fracture or nerve palsy. Overall, 7 infants in the treatment group had serious perinatal complications (all shoulder dystocia) compared with 23 infants in the untreated group (5 who died, 1 with a fractured humerus, 3 with nerve palsy, and 16 with shoulder dystocia). Shoulder dystocia was not a specified health outcome for this evidence review, and critics of ACHOIS believe that the composite outcome was misleading because shoulder dystocia accounted for most adverse outcomes (31). The ACHOIS investigators did not specifically report the rate of admission to the neonatal intensive care unit.
### Table. Summary of Evidence*

<table>
<thead>
<tr>
<th>Studies, n (Reference)</th>
<th>Design</th>
<th>Limitation</th>
<th>Consistency</th>
<th>Applicability</th>
<th>Overall Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>KQ1: Does screening for gestational diabetes lead to a reduction in perinatal morbidity and mortality for mother or infant?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>A. After 24 weeks’ gestation?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No evidence</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td><strong>B. During the first trimester and up to 24 weeks’ gestation?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No evidence</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td><strong>KQ2: What are the sensitivities, specificities, reliabilities, and yields of current screening tests for gestational diabetes?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>A. After 24 weeks’ gestation?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No evidence</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td><strong>B. During the first trimester and up to 24 weeks’ gestation?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No evidence</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td><strong>KQ3: Does treatment of gestational diabetes lead to a reduction in perinatal morbidity and/or mortality for mother or infant?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>A. After 24 weeks’ gestation?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated vs. untreated</td>
<td>2 (16, 22)</td>
<td>RCT</td>
<td>No serious limitations. 1 of 2 RCTs occurred 40 y ago, when ability to achieve tight glucose control was limited.</td>
<td>No inconsistencies</td>
<td>Studies conducted in inner-city Boston (race/ethnicity not reported) and Australia (75% white).</td>
</tr>
<tr>
<td><strong>Trials of treatment comparisons</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 (15, 17–21)</td>
<td>RCT</td>
<td>3 of the 6 studies evaluated &lt;75 women.</td>
<td>Studies varied in treatment tested, but none had serious inconsistencies with other trials regarding outcomes.</td>
<td>4 of 6 trials included predominantly Hispanic women and limited numbers of other ethnic groups.</td>
<td>Fair</td>
</tr>
<tr>
<td><strong>B. During the first trimester and up to 24 weeks’ gestation?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (23)</td>
<td>Prospective cohort</td>
<td>Hypertension categories were not defined.</td>
<td>Not applicable</td>
<td>Conducted in Spain.</td>
<td>Fair</td>
</tr>
<tr>
<td><strong>KQ4: What are the adverse effects associated with screening for gestational diabetes?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 (24–26)</td>
<td>2 prospective cohort; 1 cross-sectional</td>
<td>No serious limitations. Studies did not attempt to isolate the psychological effect of antenatal surveillance, such as the modified biophysical profile. Antenatal surveillance is presumed to be more common among women with gestational diabetes and thus represented by the diagnosis itself.</td>
<td>No serious inconsistencies</td>
<td>2 Australian studies and 1 U.S. study; all included primarily white women.</td>
<td>Fair</td>
</tr>
<tr>
<td><strong>KQ5: What are the adverse effects associated with treatment of gestational diabetes?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 (15–19, 21, 27)</td>
<td>RCT, 1 prospective cohort</td>
<td>Limited data available; only 2 of the studies included &gt;100 women with gestational diabetes.</td>
<td>No serious inconsistencies</td>
<td>1 RCT is Australian, but reasonably representative of U.S. primary care practice; the RCT included 75% white women; the remaining studies included primarily Hispanic women.</td>
<td>Fair</td>
</tr>
</tbody>
</table>

* FPG = fasting plasma glucose; GCT = glucose challenge test; KQ = key question; OGTT = oral glucose tolerance test; RCT = randomized, controlled trial; RR = relative risk.
### Table—Continued

<table>
<thead>
<tr>
<th>Summary of Findings</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal: Reported in only 1 study; gestational hypertension reduced with treatment compared with no treatment (adjusted RR, 0.70 [95% CI, 0.51–0.95]).</td>
<td>Both used 50-g GCT; recent study used 75-g diagnostic OGTT and included only women with mild gestational diabetes (FPG level &lt; 7.8 mmol/L [&lt;140 mg/dL] and 2-h OGTT level 7.8–11.0 mmol/L [140–198 mg/dL]).</td>
</tr>
<tr>
<td>Neonatal: Composite outcome (stillbirth, neonatal death, shoulder dystocia, bone fracture, and nerve palsy) reduced with treatment of mild gestational diabetes compared with no treatment (adjusted RR, 0.33 [CI, 0.14–0.75]); 0 vs. 5 stillbirths/neonatal deaths with treatment vs. no treatment. Older study did not find a significant difference in perinatal mortality (only macrosomia improved with treatment).</td>
<td></td>
</tr>
<tr>
<td>Maternal: None reported maternal death or found significant differences in gestational hypertension with treatment.</td>
<td>No evidence available for metformin. The Metformin in Gestational Diabetes trial is in progress.</td>
</tr>
<tr>
<td>Neonatal: Outcomes did not differ with treatment or improved if treatment improved glycemic control (e.g., neonatal hyperbilirubinemia and hypoglycemia).</td>
<td></td>
</tr>
<tr>
<td>Maternal: Women with early-onset gestational diabetes (first antenatal visit) were significantly more likely to have preexisting chronic hypertension, hypertension, combined preeclampsia (preeclampsia and superimposed preeclampsia) than those diagnosed before 24 weeks.</td>
<td></td>
</tr>
<tr>
<td>Neonatal: Neonates of women with early-onset gestational diabetes were more likely to have perinatal death and hypoglycemia.</td>
<td></td>
</tr>
<tr>
<td>Maternal: Limited data are mixed on whether anxiety/quality of life is worsened in the first several weeks after screening. The RCT found no differences between women who screened positive vs. those who screened negative in measures of anxiety, depression, or concern for baby’s health immediately after screening or later in pregnancy. The prospective cohort study found that health perceptions (in a minority of self-reported health domains) were worse at 30 weeks’ gestation among screening-positive women but did not differ at 36 weeks’ gestation or 6 weeks’ postpartum. The cross-sectional study found no differences in anxiety or depression at 35 weeks.</td>
<td></td>
</tr>
<tr>
<td>Neonatal: No adverse effects identified in the literature.</td>
<td></td>
</tr>
<tr>
<td>Maternal: No maternal deaths were reported. Clinically significant maternal hypoglycemia was rarely reported, regardless of type of treatment. No evidence supported psychological harm with treatment. On the contrary, 1 RCT found a statistically significant reduction in postpartum depression (based on the Edinburgh Postnatal Depression Scale questionnaire) among women treated for gestational diabetes compared with those not treated (adjusted RR, 0.46 [CI, 0.29–0.73]).</td>
<td>No data are available for metformin.</td>
</tr>
<tr>
<td>Neonatal: Limited data in small studies found no harm to the fetus; we found no good-quality data on other potential harms to the offspring associated with maternal treatment of gestational diabetes.</td>
<td></td>
</tr>
</tbody>
</table>
but identified no statistically significant differences by treatment group in infants who required intravenous therapy for hypoglycemia, phototherapy for jaundice, or supplemental oxygen more than 4 hours after birth (Appendix Table 5, available at www.annals.org). Women in the treatment group had a 30% lower risk for preeclampsia or gestational hypertension compared with untreated patients (12% vs. 18%; adjusted relative risk, 0.70 [CI, 0.51 to 0.95]).

A fair-quality randomized, controlled trial reported in 1966 (22) found that treatment in a screened population of women at high risk for gestational diabetes reduced macrosomia but not perinatal death. Initial treatment was a small daily dose of insulin (10 units per day). Of note, this trial occurred when home glucose monitoring was unavailable; thus, the ability to achieve tight glycemic control was limited.

Treatment Comparisons for Gestational Diabetes. Five randomized, controlled trials (reported in 6 publications) compared different treatment strategies for gestational diabetes. One was good quality and the other fair quality, and none blinded participants to treatment. Heterogeneity of treatment precluded quantitative synthesis.

The best comparative evidence came from a trial of 404 predominantly Latina women with gestational diabetes in whom diet therapy had failed and were randomly assigned to receive glyburide or insulin (glyburide is not currently Food and Drug Administration–approved for gestational diabetes). The investigators found excellent and similar control in both groups (mean glycosylated hemoglobin level, 5.7% in the glyburide group and 5.6% in the insulin group) and no differences in maternal weight gain or neonatal outcomes (20).

A fair-quality trial (n = 68) compared women who had mild gestational diabetes treated with diet and home glucose monitoring to women treated with diet and no monitoring (15). Compared with the unmonitored group, the glucose-monitored group achieved statistically significantly lower glycosylated hemoglobin levels at 32 weeks, with no significant difference in hypoglycemia frequency and no neonatal deaths in either group.

Another trial compared insulin given 4 versus 2 times per day and found mean hemoglobin A1c values of 5.5% and 5.8%, respectively (mean difference, −0.3% [CI, −0.4% to −0.2%]) (21). The only perinatal death occurred with a mother in the twice-daily insulin (less intensive) treatment group. The relative risks for neonatal hypoglycemia (0.12 [CI, 0.02 to 0.97]) and hyperbilirubinemia (0.51 [CI, 0.29 to 0.91]) were also lower with more frequent dosing.

Diagnosis and Treatment before 24 Weeks’ Gestation: Early versus Late Screening

We identified no randomized, controlled trials of screening and treatment before 24 weeks’ gestation in high-risk women. However, in a fair-quality prospective cohort study (23), women with early-onset gestational diabetes were more likely to have hypertension (18.5% vs. 5.9%; P = 0.006), mostly because of a higher rate of preexisting chronic hypertension (10.8% vs. 2.4%; P = 0.010); were more likely to have preeclampsia (6.2% vs. 0.6%; P = 0.020); and had higher mean fasting, 2-hour postprandial, and predinner glucose levels. In addition, 33.9% of women with an early diagnosis of gestational diabetes required insulin, compared with 7.1% of those given a late diagnosis (P < 0.001). The neonates of women with an early diagnosis were more likely to have perinatal death (6% vs. 0%; P = 0.020) and hypoglycemia (8% vs. 0%; P = 0.005) but not respiratory distress (5-minute Apgar score <7) or admission to an intensive care unit.

Key Question 4

What are the adverse effects associated with screening for gestational diabetes?

Three fair-quality studies (2 prospective cohort and 1 cross-sectional) addressed the psychological effect and burden of screening, which we considered to be the primary harms associated with screening (24–26).

The first cohort study assessed 209 Australian women by using the Spielberger State-Trait Anxiety Inventory, the Edinburgh Postnatal Depression Scale, and the Short-Form 36 (SF-36) before gestational diabetes screening at 24 to 28 weeks and again at about 36 weeks (24). The investigators found no statistically significant associations of anxiety, depression, or concern for the baby’s health with glucose challenge test results. Of note, women in the late third trimester who had negative results reported less vitality and greater social functioning than those who had positive results, but the researchers found no differences in any other SF-36 domain. Women with negative glucose challenge results were more likely than those with positive results to rate their screening experience as positive (77% vs. 57%; P < 0.010), but they did not differ in likelihood of requesting screening during subsequent pregnancies.

The other cohort study involved 50 women with gestational diabetes and 50 with normal glucose tolerance. The gestational diabetes group had higher mean scores on the Mental Health Inventory 5 (13.9 [SD, 4.8] vs. 11.4 [SD, 3.8]; P = 0.004) and higher mean anxiety scores on the Spielberger State-Trait Anxiety Inventory (40.6 [SD, 13.3] vs. 34.2 [SD, 9.9]; P = 0.007) than women with normal glucose tolerance at 30 weeks’ gestation (26). There were no statistically significant differences, however, at 36 weeks’ gestation or 6 weeks’ postpartum. The gestational diabetes and control groups also did not differ in attitudes about gestational diabetes testing during any assessment period.

The cross-sectional study assessed psychological status around 35 weeks’ gestation in 68 women with gestational diabetes and 50 nondiabetic pregnant controls (25). The
researchers found no differences between groups in mood according to the Profile of Mood States Bipolar Form.

**Key Question 5**

*What are the adverse effects associated with treatment of gestational diabetes?*

Potential adverse effects of gestational diabetes treatment included physical (maternal hypoglycemia, maternal side effects of oral hypoglycemic agents or insulin, teratogenicity in the neonate) and psychological effects. Two good-quality (16, 19) and 5 fair-quality (15, 17, 18, 21, 27) studies addressed this question.

**Treatment versus No Treatment of Gestational Diabetes**

An analysis of ACHOIS compared measures of quality of life, depression, and anxiety between subsets of 332 (of 490) treated and 350 (of 510) untreated women (16). Six weeks after diagnosis, the treated and untreated groups differed significantly on 6 quality-of-life components on the SF-36, with all differences favoring treatment (32, 33). At 3 months’ postpartum, 3 SF-36 components (physical functioning, general health, and overall physical component) were better with treatment. Five of the 6-week differences, however, were no longer statistically significant (16). The relative risk for postpartum depression was 0.46 (CI, 0.29 to 0.73) with gestational diabetes treatment compared with no treatment. Scores on the Spielberger State-Trait Anxiety Inventory did not differ between treated and untreated women 6 weeks after diagnosis or 3 months’ postpartum. These analyses did not report hypoglycemia rates.

**Studies Comparing Gestational Diabetes Treatments**

A good-quality randomized, controlled trial evaluated potential harms of glyburide versus insulin (19). Only 4 women in the glyburide group, compared with 41 in the insulin group, experienced hypoglycemia (glucose level <2.2 mmol/L [<40 mg/dL]; P = 0.030), and none of the women reported severe hypoglycemia.

A fair-quality randomized, controlled trial of primarily Latina women randomly assigned to neutral protamine Hagedorn insulin (NPH) plus insulin lispro (an insulin analogue) versus NPH plus regular insulin assessed the safety of lispro (18). Maternal hypoglycemia (glucose level <3.1 mmol/L [<55 mg/dL]) was rare in both groups before all meals. However, the only statistically significant difference in number of hypoglycemic episodes was for fasting prebreakfast measurements (a mean of 0.93% [SD, 1.04%] of measures in the regular insulin group were in the hypoglycemic range vs. 0.65% [SD, 0.13%] of those in the lispro group; P = 0.025).

Of the remaining fair-quality studies, only 1 reported on maternal hypoglycemia (21). Of 274 Israeli women with gestational diabetes who were randomly assigned to insulin treatment 4 times daily (compared with 2 times daily), excellent glycemic control further improved with 4-times-daily insulin (mean hemoglobin A1c value, 5.5% vs. 5.8%; mean difference, −0.3% [CI, −0.4% to −0.2%]) but did not increase hypoglycemic episodes necessitating help from another person (21). Another trial comparing preprandial versus postprandial glucose monitoring to guide insulin treatment in gestational diabetes did not report specific rates of maternal hypoglycemia (17). However, there were no significant differences between the treatment groups in hospitalization to optimize glycemic control during pregnancy (relative risk, 0.7 [CI, 0.2 to 3.1] for preprandial vs. postprandial monitoring) (17). One fair-quality prospective cohort study used the Profile of Mood States Bipolar Form to evaluate emotional adjustment to diagnosis and treatment of gestational diabetes in 206 women with newly diagnosed gestational diabetes who required diet or insulin therapy and 95 pregnant controls (27). The overall mean values on each of the 6 mood scales did not statistically significantly differ between the diet- or insulin-treated groups. In analyses that stratified good versus poor glycemic control, women with better control had significantly better mood scores.

**DISCUSSION**

We identified no randomized, controlled trials of gestational diabetes screening at 24 weeks’ gestation or later. We believe it is unlikely that such a study will ever be conducted in the United States given the relatively common clinical practice of gestational diabetes screening and institutionalized ethical constraints for research in human subjects. We also found no high-quality evidence on sensitivity or specificity of gestational diabetes screening for primary neonatal outcomes (stillbirth; neonatal death; brachial plexus injury; clavicular fracture; and neonatal intensive care for hypoglycemia, hyperbilirubinemia, or the respiratory distress syndrome) or for primary maternal outcomes (death and preeclampsia or pregnancy-induced hypertension). However, we did find new good-quality evidence that treatment of a screening-detected population with mild gestational diabetes reduced serious neonatal (as a composite outcome) and maternal (preeclampsia or gestational hypertension) outcomes in a population similar to the United States in ethnicity and obesity (16). This new evidence adds to evidence from a 1966 study that found a reduction in macrosomia with gestational diabetes treatment compared with no treatment (22). Several of the trials comparing gestational diabetes treatments also suggest that improved glycemic control with intensified management (whether preprandial monitoring or insulin given 4 times daily) reduces perinatal complications.

Regarding potential harms associated with gestational diabetes screening at 24 weeks’ gestation or later and treatment, evidence suggests that during the first few weeks after screening, women with positive results on screening for gestational diabetes may report higher anxiety, more psychological distress, and poorer perceptions of their gen-
eral health than women with negative results. However, these differences do not persist into the late third trimester or postpartum period. There also appears to be no long-term differences between women with positive and those with negative screening results in the experience of screening or likelihood of requesting screening for gestational diabetes during future pregnancies. Limited evidence suggests that quality of life is not worse in women receiving gestational diabetes treatment than in women not receiving treatment.

Our review found limited evidence on screening and treating gestational diabetes diagnosed before 24 weeks’ gestation. One fair-quality prospective cohort study suggests that an early diagnosis of gestational diabetes may represent pregestational diabetes, because women given an early diagnosis were more likely to require insulin and had a higher proportion of perinatal deaths and neonatal hypoglycemia than those with a late diagnosis. The number of U.S. women who are obese and thus are at risk for both type 2 diabetes and gestational diabetes is increasing; thus, data on the risks and benefits of early gestational diabetes screening would be useful.

This review had several limitations. First, there is no consistent standard for gestational diabetes screening or diagnosis. The USPSTF limited this review to current national and international standard criteria for gestational diabetes diagnosis to maintain consistency in interpreting potential benefits and harms. This consistent definition resulted in eliminating some studies considered in other reviews. Second, we only assessed potential benefits of gestational diabetes screening during the perinatal and immediate postpartum period. It is well recognized that women who develop gestational diabetes during pregnancy have an increased risk for future type 2 diabetes after pregnancy (34), and long-term benefits to a mother or her future child might arise from gestational diabetes screening during pregnancy. Third, we reviewed a select group of outcomes. We did not systematically review intermediate outcomes (such as macrosomia, cesarean section/operative delivery, induction of labor, perineal lacerations, shoulder dystocia), but we did abstract and describe these outcomes when they were reported in the studies that addressed our primary outcomes (available in the full review at www.ahrq.gov/clinic/uspsfix.htm). Of note, ACHOIS found that, in women receiving gestational diabetes treatment, there was improvement in a composite outcome that included intermediate outcomes plus the primary outcomes that were the focus of this review. Fourth, the USPSTF also explicitly excluded antepartum surveillance (for example, ultrasound and non–stress test evaluations of the pregnancy to determine whether delivery should be induced) from the scope of this review. Finally, the economics of gestational diabetes screening was beyond the scope of this update.

Ongoing studies will address important gaps in the literature. The Hyperglycemia and Adverse Pregnancy Outcome study, a prospective cohort study of 25 000 pregnant women screened at 24 to 32 weeks’ gestation in 10 countries, is nearing completion. This study will provide information on how glycemic level may relate to outcomes (cesarean section rates, fetal size, neonatal hypoglycemia, and fetal hyperinsulinemia) and will help to identify an ideal diagnostic threshold (35). A multicenter randomized, controlled trial in the Maternal-Fetal Medicine Units Network is studying outcomes with treatment versus no treatment of mild gestational diabetes detected by a 2-step approach. For the 1-hour 50-g glucose challenge test, values were 7.5 mmol/L (135 mg/dL) to 11.1 mmol/L (200 mg/dL); for the 3-hour 100-g oral glucose challenge test, a normal fasting level was less than 5.3 mmol/L (<95 mg/dL), and 2 of the 3 remaining postchallenge measurements were abnormal (36–38). Other trials are evaluating the efficacy and safety of metformin in pregnancy (39, 40).

Unfortunately, no high-quality evidence is available on screening and treatment of gestational diabetes among high-risk women in the first trimester. Screening can identify previously unrecognized type 2 diabetes and the transient abnormality of glucose tolerance during pregnancy—both currently defined as gestational diabetes. It is important to evaluate the effect of these gestational diabetes conditions on maternal and fetal outcomes separately in future studies.

From Kaiser Permanente Northwest, Portland, Oregon, and Sansum Diabetes Research Institute, Santa Barbara, California.

Acknowledgment: The authors thank their expert reviewers for feedback and guidance, in particular Marie-Aline Charles, MD; David Hadden, MD; Boyd Metzger, MD; and Catherine Spong, MD. They also thank Martie Succe and Kevin Lutz, MFA, for their editorial assistance; Taryn Cardenas for her technical assistance; and Paula Smith for her overall help with managing the project.

Grant Support: This study was conducted by the Oregon Evidence-based Practice Center under contract to the Agency for Healthcare Research and Quality (contract 290-02-0024, task order 2).

Potential Financial Conflicts of Interest: None disclosed.


Current author addresses are available at www.annals.org.

References
Screening for Gestational Diabetes Mellitus

CLINICAL GUIDELINES

www.annals.org

20 May 2008 | Annals of Internal Medicine | Volume 148 • Number 10 | 775

9704245


Current Author Addresses: Drs. Hillier, Vesco, and Whitlock; Ms. Pedula; and Ms. Beil: The Center for Health Research, Kaiser Permanente Northwest, 3800 North Interstate Avenue, Portland, OR 97227. Dr. Pettitt: Sansum Diabetes Research Institute, 2219 Bath Street, Santa Barbara, CA 93105.
### Appendix Table 1. Search Strategies

**Systematic review**

**Databases:** MEDLINE, Database of Abstracts of Reviews of Effects, Health Technology Assessment Database, Cochrane Database of Systematic Reviews

2000–15 November 2007

1. “Diabetes, Gestational”[MeSH:NoExp]
2. “Fetal Macrosomia”[MeSH]
3. “gestational diabetes”[ti]
4. gdm[ti]
5. macrosomia[ti]
6. antepartum[tiab] AND surveillance[tiab]
7. OR 2 OR 3 OR 4 OR 5 OR 6
8. “gestational diabetes”[tiab]
9. “gestational diabetic*”[tiab]
10. gdm[tiab]
11. macrosomia[tiab]
12. 8 OR 9 OR 10 OR 11
13. 12 AND (in process[sb] OR publisher[sb])
14. 7 OR 13
15. 14 AND systematic[sb]

**Screening**

**Database:** MEDLINE

2000–15 November 2007

1. Diabetes, Gestational/
2. gestational diabetic$[ti,ab].
3. 1 or 2
4. Mass Screening/
5. screen$[ti,ab].
6. 4 or 6
7. 3 and 6
8. Diabetes, Gestational/di [Diagnosis]
9. 7 or 8
10. limit 9 to english language
11. limit 10 to humans
12. limit 10 to animals
13. 12 not 11
14. 10 not 13
15. limit 14 to yr = “2000 - 2006”

**Early screening**

**Database:** MEDLINE

1966–1999

1. Diabetes, Gestational/
2. gestational diabetic$[ti,ab].
3. Pregnancy in Diabetics/
4. 1 or 2 or 3
5. Mass Screening/
6. screen$[ti,ab].
7. 5 or 6
8. 4 and 7
9. Diabetes, Gestational/di [Diagnosis]
10. Pregnancy in Diabetics/di [Diagnosis]
11. 8 or 9 or 10
12. Pregnancy Trimester, First/
13. first trimester.ti,ab.
14. first pregnancy trimester.ti,ab.
15. Pregnancy Trimester, Second/
16. second trimester.ti,ab.
17. second pregnancy trimester.ti,ab.
18. early.ti,ab.
19. earlier.ti,ab.
20. 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21. 11 and 20
22. limit 21 to english language
23. limit 22 to humans
24. limit 22 to animals
25. 24 not 23
26. 22 not 25
27. limit 26 to yr = “1966 - 1999”

Continued on following page
### Screening tests

**Database:** MEDLINE  
2000–15 November 2007

1. Glucose Tolerance Test/
2. oral glucose tolerance.ti,ab.
3. ogtt.ti,ab.
4. glucose challenge test$.ti,ab.
5. Glucose Intolerance/
6. Blood Glucose/
7. Diabetes, Gestational/
8. gestational diabetes.ti,ab.
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. Pregnancy/
11. pregnancy.ti,ab,hw.
12. 10 or 11
13. 9 and 12
14. “Sensitivity and Specificity”/
15. “Predictive Value of Tests”/
16. ROC Curve/
17. specificity.ti,ab.
18. sensitivity.ti,ab.
19. predictive value.ti,ab.
20. accuracy.ti,ab.
21. False Negative Reactions/
22. False Positive Reactions/
23. Diagnostic Errors/
24. exp “Reproducibility of Results”/
25. Reference Values/
26. Reference Standards/
27. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
28. 13 and 27
29. 1 or 2 or 3 or 4
30. 12 and 29
31. limit 30 to (clinical trial or controlled clinical trial or randomized controlled trial)
32. clinical trials/ or controlled clinical trials/ or randomized controlled trials/
33. double-blind method/ or random allocation/ or single-blind method/
34. random$.ti,ab.
35. 32 or 33 or 34
36. 30 and 35
37. Glucose Tolerance Test/st [Standards]
38. 28 or 31 or 36 or 37
39. limit 38 to english language
40. limit 39 to humans
41. limit 39 to animals
42. 41 not 40
43. 39 not 42
44. limit 43 to yr=“2000 - 2006”

### Clinical trials

**Databases:** MEDLINE, Cochrane Central Registry of Controlled Trials  
2000–15 November 2007

1. Diabetes, Gestational/
2. gestational diabetes.ti,ab.
3. 1 or 2
4. limit 3 to (clinical trial or controlled clinical trial or randomized controlled trial)
5. clinical trials/ or controlled clinical trials/ or randomized controlled trials/
6. double-blind method/ or random allocation/ or single-blind method/
7. random$.ti,ab.
8. 5 or 6 or 7
9. 3 and 8
10. 4 or 9
11. limit 10 to english language
12. limit 11 to humans
13. limit 11 to animals
14. 13 not 12
15. 11 not 14
16. limit 15 to yr=“2000 - 2006”

### Treatment harms

**Database:** MEDLINE

---

Downloaded From: http://annals.org/pdfaccess.ashx?url=/data/journals/aim/20160/ on 05/31/2017
**Appendix Table 1—Continued**

2000–15 November 2007

| 1. Diabetes, Gestational/dh, dt, pc, th [Diet Therapy, Drug Therapy, Prevention & Control, Therapy] |
| 2. Insulin/ |
| 3. Glyburide/ |
| 4. Metformin/ |
| 5. Sulfonlurea Compounds/ |
| 6. Hypoglycemic Agents/ |
| 7. (administration dosage or “therapeutic use”).fs. |
| 8. treat$.ti,ab,hw. |
| 9. therapy.ti,ab,hw. |
| 10. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 |
| 11. Diabetes, Gestational/ |
| 12. gestational diabet$.ti,ab. |
| 13. 11 or 12 |
| 14. 10 and 13 |
| 15. 1 or 14 |
| 16. (adverse effects or mortality or poisoning or toxicity).fs. |
| 17. adverse effect$.ti,ab. |
| 18. harm$.ti,ab. |
| 19. Prenatal Exposure Delayed Effects/ |
| 20. Abnormalities, Drug-Induced/ |
| 21. anxiety.ti,ab,hw. |
| 22. depression.ti,ab,hw. |
| 23. Depressive Disorder/ |
| 24. labeling.ti,ab. |
| 25. labelling.ti,ab. |
| 26. labeled.ti,ab. |
| 27. labelled.ti,ab. |
| 28. Hypoglycemia/ |
| 29. Hypoglycemia$.ti,ab. |
| 30. Hypoglycaemia$.ti,ab. |
| 31. Acidosis/ |
| 32. Acidosis, Lactic/ |
| 33. acidosis.ti,ab. |
| 34. Teratogens/ |
| 35. teratogen$.ti,ab. |
| 36. pain.ti,ab,hw. |
| 37. unnecessary.ti,ab,hw. |
| 38. Pre-Eclampsia/ |
| 39. Pre-Eclamps$.ti,ab. |
| 40. preeclamp$.ti,ab. |
| 41. Hypertension, Pregnancy-Induced/ |
| 42. pregnancy induced hypertension.ti,ab. |
| 43. gestational hypertension.ti,ab. |
| 44. Hypertension/ and Pregnancy Complications, Cardiovascular/ |
| 45. Infant Mortality/ |
| 46. infant mortality.ti,ab. |
| 47. neonatal mortality.ti,ab. |
| 48. perinatal mortality.ti,ab. |
| 49. hyperbilirubinemia, neonatal/ or jaundice, neonatal/ |
| 50. hyperbilirubin$.ti,ab. |
| 51. Phototherapy/ |
| 52. phototherapy.ti,ab. |
| 53. Polycythemia/ |
| 54. Polycythem$.ti,ab. |
| 55. Polycythaemia$.ti,ab. |
| 56. Respiratory Distress Syndrome, Newborn/ |
| 57. Respiratory Distress.ti,ab. |
| 58. Intensive Care, Neonatal/ |
| 59. neonatal intensive care.ti,ab. |
| 60. nicu.ti,ab. |
| 61. Infant, Small for Gestational Age/ |
| 62. Small for Gestational Age.ti,ab. |
| 63. Fetal Growth Retardation/ |
| 64. Intrauterine Growth Retardation.ti,ab. |
| 65. Intrauterine Growth Restriction.ti,ab. |
| 66. IUGR.ti,ab. |
| 67. Fetal Growth Retardation.ti,ab. |
| 68. Fetal Growth Restriction.ti,ab. |
Appendix Table 1—Continued

69. 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68
70. 15 and 69
71. limit 70 to English language
72. limit 71 to humans
73. limit 71 to animals
74. 73 not 72
75. 71 not 74
76. limit 75 to yr = "2000–2006"
Appendix Table 2. Inclusion Criteria*

Key Question 1
1. Study evaluates screening for gestational diabetes <24 wk or ≥24 wk in a population relevant to primary care
2. Acceptable screening methods: 1-step (75 g or 100 g); 2-step (50 g/100 g; 50 g/75 g); fasting glucose for <24 wk
3. Positive result on screening includes
   a. 50 g: glucose value ≥130 mg/dL or ≥140 mg/dL
   b. 75 g: Carpenter and Coustan, ADA, or WHO criteria
   c. 100 g: Carpenter and Coustan or NDDG criteria
4. Primary outcomes systematically identified
   a. Maternal: mortality; preeclampsia/pregnancy-induced hypertension
   b. Perinatal outcomes: mortality; brachial plexus injury; fractured clavicle; admission to NICU for treatment of hypoglycemia, hyperbilirubinemia, or the respiratory distress syndrome
   c. Secondary or intermediate outcomes (not systematically included): macrosomia; cesarean section; induction of labor; preterm birth; maternal third- or fourth-degree perineal lacerations
5. Study design: RCT, CCT, or prospective cohort if no RCT available

Key Question 2
1. Study evaluates screening test sensitivity, specificity, reliability, and yield
2. Acceptable screening methods: 1-step (75 g or 100 g); 2-step (50 g/100 g; 50 g/75 g); fasting glucose for <24 wk
3. Positive result on screening includes
   a. 50 g: glucose value ≥130 mg/dL or ≥140 mg/dL
   b. 75 g: Carpenter and Coustan, ADA, or WHO criteria
   c. 100 g: Carpenter and Coustan or NDDG criteria
4. Primary outcomes systematically identified
   a. Maternal: mortality; preeclampsia/pregnancy-induced hypertension
   b. Perinatal outcomes: mortality; brachial plexus injury; fractured clavicle; admission to NICU for treatment of hypoglycemia, hyperbilirubinemia, or the respiratory distress syndrome
   c. Secondary or intermediate outcomes (not systematically identified): macrosomia; cesarean section; preterm birth; maternal third- or fourth-degree perineal lacerations
5. Study design: RCT, CCT, observational
6. Uses sensitivity and specificity criteria to assess primary health outcomes specified in the analytic framework

Key Question 3
1. Study evaluates treatment of gestational diabetes, including glyburide, any sulfonylurea, metformin, insulin, diet, and/or exercise therapy
2. Acceptable screening methods: 1-step (75 g or 100 g); 2-step (50 g/100 g; 50 g/75 g); fasting glucose for <24 wk
3. Positive result on screening includes
   a. 50 g: glucose value ≥130 mg/dL or ≥140 mg/dL
   b. 75 g: Carpenter and Coustan, ADA, or WHO criteria
   c. 100 g: Carpenter and Coustan or NDDG criteria
4. Primary outcomes systematically identified
   a. Maternal: mortality; preeclampsia/pregnancy-induced hypertension
   b. Perinatal outcomes: mortality; brachial plexus injury; fractured clavicle; admission to NICU for treatment of hypoglycemia, hyperbilirubinemia, or the respiratory distress syndrome
   c. Secondary or intermediate outcomes (not systematically identified): macrosomia; cesarean section; preterm birth; maternal third- or fourth-degree perineal lacerations
5. Study design: RCT, CCT, or prospective cohort if no RCT available

Key Question 4
1. Study presents harms of screening tests accepted in key questions 1 or 3
2. Acceptable screening methods: 1-step (75 g or 100 g); 2-step (50 g/100 g; 50 g/75 g); fasting glucose for <24 wk
3. Positive result on screening includes
   a. 50 g: glucose value ≥130 mg/dL or ≥140 mg/dL
   b. 75 g: Carpenter and Coustan, ADA, or WHO criteria
   c. 100 g: Carpenter and Coustan or NDDG criteria
   d. Exception allowed if used an accepted screening method and nonstandard cutoff criteria
4. Study design: all considered

Key Question 5
1. Study presents harms of treatment accepted in key question 3
2. Acceptable screening methods: 1-step (75 g or 100 g); 2-step (50 g/100 g; 50 g/75 g); fasting glucose for <24 wk
3. Positive result on screening includes
   a. 50 g: glucose value ≥130 mg/dL or ≥140 mg/dL
   b. 75 g: Carpenter and Coustan, ADA, or WHO criteria
   c. 100 g: Carpenter and Coustan or NDDG criteria
   d. Exception allowed if used an accepted screening method and nonstandard cutoff criteria
4. Study design: all considered

Exclusion Criteria
1. Not an acceptable study design, including method of accepted study types or mixing gestational diabetes/impaired glucose tolerance/normal groups
2. Not generalizable to U.S. population
3. Did not address specified conditions and/or mortality
4. Not 1 of established screening criteria used (hemoglobin A1c), or 50-g OGTT used as a diagnostic test (nonstandard) or 75-/100-g or 100-g OGTT diagnostic tests using different diagnostic criteria than the current standards as outlined in our workplan (e.g., cutoffs plus SD to a different population mean)
5. No information on yield (prevalence), sensitivity, specificity, or reliability
6. Not 1 of established screening criteria used (e.g., hemoglobin A1c)
### Appendix Table 2—Continued

<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Not 1 of the included treatments for gestational diabetes (e.g., thiazolidinediones)</td>
</tr>
<tr>
<td>8</td>
<td>Editorials, comments, and letters</td>
</tr>
<tr>
<td>9</td>
<td>Nonsystematic reviews</td>
</tr>
<tr>
<td>10</td>
<td>Did not address 1 of the key questions</td>
</tr>
<tr>
<td>11</td>
<td>Systematic review, but search strategy too old to be relevant for our interval update of the USPSTF 2003 gestational diabetes review</td>
</tr>
<tr>
<td>12</td>
<td>SER used as source document</td>
</tr>
<tr>
<td>13</td>
<td>Prevalence outside United States</td>
</tr>
<tr>
<td>14</td>
<td>Prevalence-only articles</td>
</tr>
<tr>
<td>15</td>
<td>Natural history-only articles</td>
</tr>
<tr>
<td>16</td>
<td>Did not report sensitivity and specificity criteria to assess specified health outcomes in the analytic framework</td>
</tr>
<tr>
<td>17</td>
<td>Poor quality</td>
</tr>
</tbody>
</table>

*To convert glucose values in mg/dL to mmol/L, multiply by 0.05551. ADA = American Diabetes Association; CCT = clinical controlled trial; NDDG = National Diabetes Data Group; NICU = neonatal intensive care unit; OGTT = oral glucose tolerance test; RCT = randomized, controlled trial; SER = systematic evidence review; USPSTF = U.S. Preventive Services Task Force; WHO = World Health Organization.*
# Appendix Table 4. Summary Characteristics of Treatment Trials after 24 Weeks’ Gestation (Key Question 3)*

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Patients, n</th>
<th>Treatment</th>
<th>Setting</th>
<th>Population, %</th>
<th>BMI, kg/m²</th>
<th>Gestational Age at Screening, wk</th>
<th>Screening Test Used</th>
<th>Quality Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment vs. untreated</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crowther et al., 2005 (16)</td>
<td>1000</td>
<td>Treatment of mild gestational diabetes vs. no treatment</td>
<td>Australia, United Kingdom</td>
<td>White: 75 Asian: 16 Other: 8</td>
<td>Intervention group: 26.8 (23.3–31.2) Control group: 26.0 (22.0–30.9)</td>
<td>29.1 (28.2–30.0)</td>
<td>Step 1: Risk factors or 50-g GCT (&lt;7.8 mmol/L); 1-h cutoff (95% were positive in 50-g test) Step 2: 75-g OGTT: 1) fasting glucose value &gt;7.8 mmol/L and 2) 2-h glucose value, 7.8–11.0 mmol/L</td>
<td>Good</td>
</tr>
<tr>
<td>O’Sullivan et al., 1966 (22)</td>
<td>943</td>
<td>Treatment of screening-positive patients vs. no treatment of screening-positive patients vs. no treatment of screening-negative patients</td>
<td>Boston</td>
<td>NR</td>
<td>n &lt;20% over ideal body weight Intervention group: 37.7 Control group: 39.5</td>
<td>NR</td>
<td>Step 1: 90-g GCT, whole-blood glucose value &gt;130 mg/dL Step 2: 100-g OGTT with ≥2 abnormal glucose values</td>
<td>Fair</td>
</tr>
</tbody>
</table>

## Treatment comparisons

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Patients, n</th>
<th>Treatment</th>
<th>Setting</th>
<th>Population, %</th>
<th>BMI, kg/m²</th>
<th>Gestational Age at Screening, wk</th>
<th>Screening Test Used</th>
<th>Quality Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Langen et al., 2005, 2005 (19, 20)</td>
<td>404</td>
<td>Glyburide vs. insulin treatment</td>
<td>San Antonio, Texas</td>
<td>Hispanic: 83 White: 12 Black: 5</td>
<td>Intervention group: 27.3 (SD, 3.1) Control group: 26.7 (SD, 3.2)</td>
<td>27.3 before intervention</td>
<td>Step 1: 100-g OGTT with ≥2 abnormal glucose values by Carpenter and Coustan criteria</td>
<td>Good</td>
</tr>
<tr>
<td>Bancroft et al., 2000 (15)</td>
<td>68</td>
<td>Diet plus intensive glucose monitoring vs. diet plus standard clinic glucose monitoring</td>
<td>United Kingdom</td>
<td>Asian: 31 White: 69</td>
<td>Mean: Diet plus intensive monitoring group: 32.2 (SD, 6.7) Diet plus standard monitoring group: 27.0 (SD, 6.1)</td>
<td>27.3 before intervention</td>
<td>75-g OGTT with fasting glucose value &gt;7.0 mmol/L and 2-h glucose value of 7.8–11.0 mmol/L GGT done at the discretion of individual clinicians</td>
<td>Fair</td>
</tr>
<tr>
<td>Jovanovic et al., 1999 (18)</td>
<td>42</td>
<td>NPH plus bipro insulin vs. NPH plus regular insulin</td>
<td>California</td>
<td>Hispanic: 39 Regular Insulin group: 100</td>
<td>Mean (1-SE): Regular insulin group: 31.5 ± 1.1</td>
<td>27.3 before intervention</td>
<td>NDDG criteria (2-step 50-g GCT, then 100-g OGTT)</td>
<td>Fair</td>
</tr>
<tr>
<td>Nachshen et al., 1999 (21)</td>
<td>274</td>
<td>4-times-daily insulin vs. 2-times-daily insulin</td>
<td>Israel</td>
<td>Jewish: 4-times-daily group: 57 2-times-daily group: 55</td>
<td>4-times-daily group: 27.9 (SD, 2.6) 2-times-daily group: 27.8 (SD, 2.7)</td>
<td>At diagnosis: 4-times-daily group: 25.9 (SD, 2.6) 2-times-daily group: 26.3 (SD, 2.7)</td>
<td>100-g OGTT with ≥2 abnormal glucose values &gt;5.5, 10.6, 9.2, 8.1 mmol/L, at 0, 1, 2, and 3 h, respectively</td>
<td>Fair</td>
</tr>
<tr>
<td>de Veciana et al., 1995 (17)</td>
<td>66</td>
<td>Preprandial vs. postprandial monitoring of glucose to inform treatment decisions</td>
<td>California</td>
<td>Hispanic: 85 White: 11 Black/Asian: 5</td>
<td>Preprandial group: 28.9 (SD, 3.2) Postprandial group: 28.4 (SD, 3.3)</td>
<td>27.3 before initiation of treatment</td>
<td>1-hour 50-g GCT value &gt;140 mg/dL but &lt;190 mg/dL; patients with glucose value &gt;190 mg/dL started insulin immediately Step 2: 3-h 100-g OGTT with ≥2 abnormal glucose values (fasting &gt;105 mg/dL, 1-h &gt;190 mg/dL, 2-h &gt;145 mg/dL, 3-h &gt;145 mg/dL)</td>
<td>Fair</td>
</tr>
</tbody>
</table>

* To convert glucose values in mg/dL to mmol/L, multiply by 0.05551; to convert glucose values in mmol/L to mg/dL, divide by 0.05551. BMI = body mass index; GCT = glucose challenge test; NDDG = National Diabetes Data Group; NPH = neutral protamine Hagedorn; NR = not reported; NS = not significant; OGTT = oral glucose tolerance test; P=Mediant (metachromatic range).
Appendix Table 5. Health Outcomes of Treatment Trials after 24 Weeks’ Gestation (Key Question 3)*

<table>
<thead>
<tr>
<th>Study; Year (Reference)</th>
<th>Multiple outcomes (Reference)</th>
<th>Mortality; n (%)*</th>
<th>Fracture; n (%)*</th>
<th>Brachial Plexus Injury; n (%)*</th>
<th>NICU Admissions; n (%)*</th>
<th>Hypoglycemia; n (%)*</th>
<th>Hypertension; n (%)*</th>
<th>Respiratory Distress; n (%)*</th>
<th>Death; n (%)*</th>
<th>Pregnancy-Induced Hypertension; n (%)*</th>
<th>NICU: NR</th>
<th>Neonatal Nurtury: Intervention group 357 (51) Control group: 321 (41) Adjusted RR: 1.42 (CI, 0.87–2.32)</th>
<th>NICU: NR</th>
<th>Neonatal Nurtury: Control group: 19 (6) Adjusted RR: 1.52 (CI, 0.86–2.71)</th>
<th>NICU: NR</th>
<th>Neonatal Nurtury: Intervention group: 58 (12) Control group: 91 (18) Adjusted RR: 0.51 (CI, 0.31–0.85)</th>
</tr>
</thead>
<tbody>
<tr>
<td>O’Sullivan et al., 1995 (16)</td>
<td>5 (0.7)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Bancroft et al., 2001 (17)</td>
<td>Preprandial glucose monitoring group: 8 (19) Insulin 4-times-daily group: 12 (16) RR: 1.7 (CI, 0.11–2.71)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nachum et al., 2000 (18)</td>
<td>Intensive care unit</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Devane et al., 1999 (17)</td>
<td>Preprandial glucose monitoring group: 7 (21) Postprandial glucose monitoring group: 0 (P = NS)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* NICU = neonatal intensive care unit; NR = not reported; NS = not significant; RR = relative risk.
† RR not calculated as zero in intervention group. A composite outcome (stillbirth, neonatal death, shoulder dystocia, bone fracture, and nerve palsy) was reported with an adjusted RR of 0.55 (CI, 0.14–0.75) with intervention group compared with control group. Seven shoulder dystocia events occurred in the intervention group and 16 in the control group.
‡ Original report was unclear on units for CI.