Screening for Diabetes Mellitus after Pregnancy

Systematic Review for the Women's Preventive Services Initiative

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INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as glucose intolerance detected during pregnancy. GDM increases risk for maternal and fetal complications including preeclampsia,[1] fetal macrosomia causing shoulder dystocia and birth injury, and neonatal hypoglycemia.[2] Women diagnosed with GDM have increased risk for developing type 2 diabetes mellitus (DM) after pregnancy.[3] Follow-up screening of women with GDM provides early detection of women with continued glucose abnormalities, allowing for timely interventions to prevent progression and diabetes-related complications. Although screening for GDM is a long-established part of prenatal care that typically involves an oral glucose test administered after 24 weeks gestation,[4] screening for DM after GDM is not routinely performed.[5]

The prevalence of GDM in the United States was reported as 4.6% on birth certificates, 8.7% on the *Pregnancy Risk Assessment Monitoring System* (PRAMS) questionnaire, and 9.2% by either source.[6] Prevalence is higher among certain racial/ethnic groups including black, Asian, Hispanic, and Native American women compared with white women. Risk factors for GDM include older maternal age, history of GDM in a prior pregnancy, previous delivery of a large for gestational age infant, obesity, strong immediate family history of DM or GDM, and a history of unexplained fetal death.[7]

Approximately 15% to 60% of women with GDM develop DM within 5 to 15 years of delivery.[8] A meta-analysis of cohort studies of women with GDM estimated the risk of developing subsequent DM.[9] Results indicated a 7-fold increased risk in women with a history of GDM compared with those with a normoglycemic pregnancy (relative risk [RR] 7.43, 95% confidence interval [CI] 4.79 to 11.51).

Current Recommendations

Recommendations from the U.S. Preventive Services Task Force (USPSTF)[10] and Women's Prevention Services Initiative (WPSI)[11] address screening for GDM, but they do not provide recommendations for screening for DM after a pregnancy in which GDM was diagnosed.

Currently, standards and practices for screening for DM after GDM vary. Although follow-up testing is recommended beginning at the 6 week postpartum visit by the American Congress of Obstetricians and Gynecologists (ACOG),[12] the American Diabetes Association (ADA),[13] and other groups[14,15] (**Table 1**), only 33% to 58% of women with previous GDM are tested for DM during the postpartum period.[16]

Table 1. Postpartum Screening Recommendations of Professional Organizations

Organization	Recommendation
American Congress of Obstetricians and Gynecologists (ACOG)[12]	All women with GDM should be screened 6 to 12 weeks postpartum for DM, impaired fasting glucose, or impaired glucose tolerance. Women with positive screening results should be referred for preventive therapy, and women with negative screening results should receive follow-up testing every 3 years. A fasting plasma glucose test or a 75-g, 2-hour OGTT is appropriate for postpartum screening.
American Diabetes Association (ADA)[13]	A 75-g OGTT is recommended at the 6- to 12-week postpartum visit. Test women with GDM every 1-3 years if her 6- to 12-week OGTT is normal. The frequency of screening is based on the presence of risk factors: family history, pre-pregnancy BMI, or need for insulin or oral medications during pregnancy. Ongoing screening may be done with any glycemic test (HbA1c, fasting plasma glucose, OGTT) using nonpregnancy cut points.
Canadian Diabetes Association (CDA)[14]	Women who have had GDM should be screened for DM 6 weeks to 6 months postpartum with a 2 hour 75 g OGTT; before a future pregnancy; and every 3 years or more often, depending on the presence of other risk factors for DM.
Fifth International Workshop Conference on Gestational Diabetes[15]	Follow-up for women with GDM should be performed with a 75-g OGTT at 6-12 weeks postpartum.
British National Institute for Clinical Excellence (NICE)[17]	Women with GDM should be tested with a fasting plasma glucose test at 6-12 weeks postpartum, then with yearly fasting plasma glucose tests.

Abbreviations: BMI=body mass index; DM=type 2 diabetes mellitus; GDM=gestational diabetes mellitus; HbA1c=hemoglobin A1c test; OGTT=oral glucose tolerance test.

In a separate recommendation, the USPSTF recommends screening adults in the general population for DM who are 40 to 70 years old and obese.[18] The recommendation states that a history of GDM may increase risk for DM at a younger age or at a lower body mass index, and clinicians should consider screening women with these characteristics earlier than the general guidelines. The USPSTF report cites modeling studies to support screening every 3 years as a reasonable screening interval.

The American Diabetes Association (ADA)[19] recommends screening for DM in adults age 45 years and older and screening those with risk factors regardless of age. Most other groups, including the American Association of Clinical Endocrinologists,[20] the American Academy of Family Physicians,[21] and the Canadian Task Force on Preventive Health Care,[22] recommend screening adults with risk factors for DM.

Screening for DM in nonpregnant adults is performed in the United States by fasting plasma glucose (FPG), 2-hour plasma glucose following oral glucose tolerance test (OGTT), or hemoglobin A1c (HbA1c).[19] Diagnostic cut points described by the ADA are indicated below (**Table 2**).[19] All positive test results should be confirmed with repeated testing. Although the HbA1c test is considered a diagnostic test for DM by the ADA and the World Health Organization (WHO),[19,23] it may be less sensitive than FPG or OGTT when using the currently recommended diagnostic cut point of greater than or equal to 6.5%.[24-26] HbA1c reflects average glycemic levels over a 3- month period and tests obtained during early postpartum screening may not represent conditions following pregnancy. An advantage of HbA1c is that it does not require fasting prior to collection.

Table 2. Screening Tests and Diagnostic Cut points[19]

Screening Test	Normal	IFG or IGT	DM
2-hour OGTT			
mmol/l	7.8	7.8-11.0	≥11.1
mg/dl	<140	140-199	≥200
FPG			
mmol/l	<5.6	5.6-6.9	≥7.0
mg/dl	<100	100-125	≥126
HbA1c, %	<5.7	5.7-6.4	≥6.5

FPG = fasting plasma glucose; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; OCTT = oral glucose tolerance test.

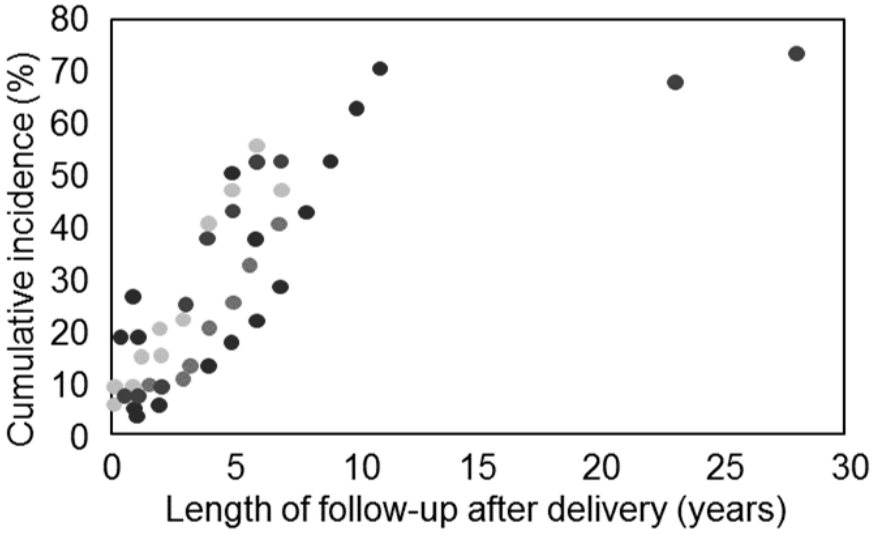
Risk Factors

Most practice guidelines advise using the presence of risk factors to determine the appropriateness of screening for DM. Traditional risk factors for DM in nonpregnant populations include obesity, physical inactivity, smoking, and older age.[27]

Among women with histories of GDM, additional risk factors are also relevant to screening. A systematic review of 28 studies examined the cumulative incidence of DM in women with GDM, and identified elevated fasting glucose during pregnancy as the most predictive risk factor.[8] Other risk factors including high BMI, older maternal age, previous history of GDM, family history of DM, and high parity, yielded mixed results with inconsistent or little predictive value.

In these studies, the cumulative incidence of DM increased markedly across studies during the first 5 years following GDM, while incidence at 10 years appeared to plateau (**Figure 1**). Differences in rates of progression from GDM to DM across ethnic groups were reduced after adjusting for various lengths of follow-up and testing rates in these studies.

Figure 1. Cumulative Incidence of DM following GDM (adapted from Kim, 2002)[8]

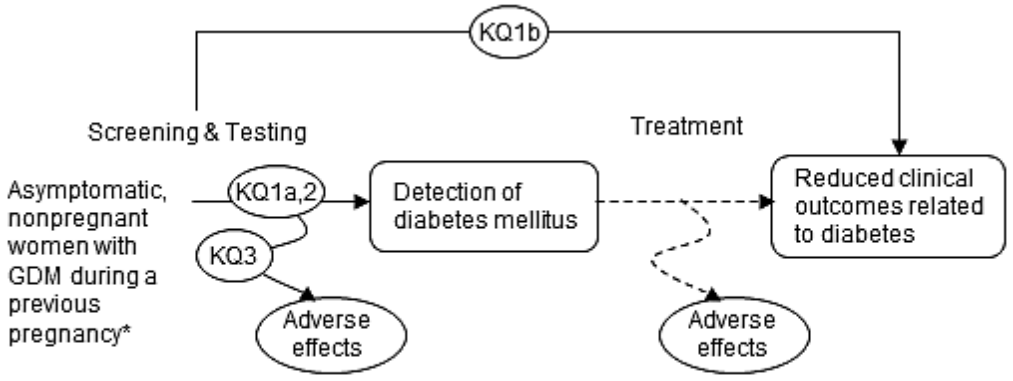


A subsequent systematic review of 14 studies, all based on convenience sampling, identified risk factors associated with the development of DM in women with GDM.[28] These included anthropometric measures of obesity, early gestational age at the time of diagnosis of GDM, and the method of glucose control. Results of these analyses were limited by differences in how risk factors were defined in the studies.

METHODS

The WPSI Advisory Group determined the scope and key questions for this review. Investigators created an analytic framework outlining the key questions and patient populations, interventions, and outcomes (**Figure 2**). The target population includes nonpregnant women with previously diagnosed GDM who have no symptoms of DM and who have not been previously diagnosed with DM when not pregnant.

Figure 2. Analytic Framework



*Women have not been previously diagnosed with diabetes when not pregnant.

Key Questions

For asymptomatic, nonpregnant women with GDM during a previous pregnancy who have not been previously diagnosed with DM when not pregnant:

1. What is the effectiveness of screening for DM in
   a) Identifying women with diabetes?
   b) Reducing clinical outcomes related to diabetes?
2. What screening methods and approaches are most effective (tests, timing after pregnancy, intervals)?
3. What are the harms of screening for DM?

Literature Searches

A research librarian conducted electronic database searches in Ovid MEDLINE, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews from 1946 to October 13, 2017. Search strategies are provided in **Appendix 1**. Investigators also manually reviewed reference lists of relevant systematic reviews and articles.

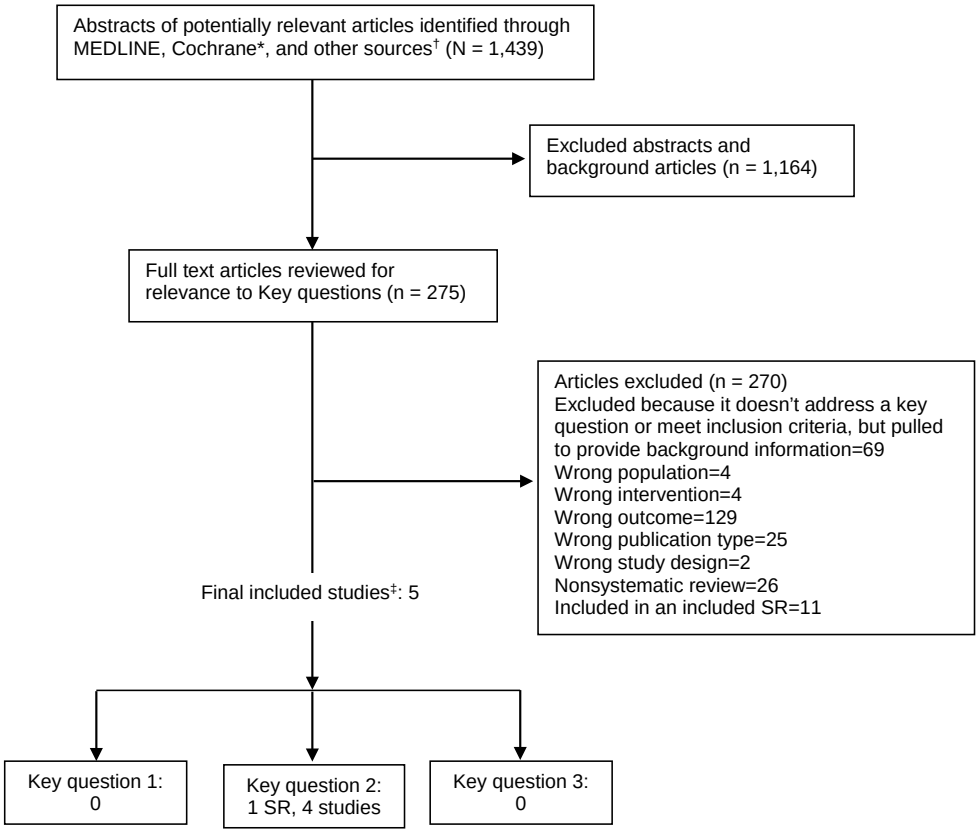
Study Selection

All titles and abstracts identified through searches were independently reviewed for eligibility against pre-specified inclusion/exclusion criteria organized by PICOTS (population, intervention,

comparator, outcome, timing, study design) by a trained member of the research team (**Appendix 2**). Studies marked for possible inclusion by a reviewer underwent a full-text review. All results were tracked in an EndNote® database (Thomson Reuters, New York, NY).

Each full-text article was independently reviewed by two trained members of the research team for inclusion or exclusion based on pre-specified eligibility criteria. A best evidence approach was applied when reviewing abstracts and selecting studies to include for this review that involves using the most relevant studies with the strongest methodologies.[29-31] Disagreements were resolved by discussion and consensus. Results of the full text review were tracked in the EndNote® database, including the reason for exclusion. Results of searches and study selection are described in **Figure 3**.

Figure 3. Literature Flow Diagram



*Cochrane databases include the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews.
†Identified from reference lists, hand searching, etc.
‡Studies that provided data and contributed to the body of evidence were considered 'included'.

Studies were included that enrolled nonpregnant women with a history of GDM during a previous pregnancy who have not been previously diagnosed with DM when not pregnant. Studies of screening tests for DM used methods currently in practice settings in the United States. Comparisons included screening methods, approaches, and specific tests to diagnose DM

after pregnancy compared with usual care; or one method compared with another method. Outcomes of studies included clinical outcomes related to screening and subsequent treatment (KQ 1); measures of test performance in detecting DM (sensitivity, specificity; likelihood ratios; c-stats) (KQ 2); and false positive/negative results, anxiety, distress, and other adverse events impacting quality of life (KQ 3). Studies reporting the diagnosis of "pre-diabetes," impaired fasting glucose, impaired glucose tolerance, or other intermediate measure related to testing were not included. Studies of the efficacy and harms of diabetes treatment were outside the scope of this review. Studies conducted in settings applicable to the United States were particularly relevant. Findings related to population subgroups were specifically included when available.

Randomized controlled trials, large (>100) prospective cohort studies, diagnostic accuracy studies, and systematic reviews were included if they met inclusion criteria. Other study designs, such as case-control and modeling studies, were included when evidence from other study designs was lacking.

Data Management and Analysis

For studies meeting inclusion criteria, data were abstracted into tables to summarize relevant information including characteristics of study populations, interventions, comparators, outcomes, study designs, settings, and methods. All data abstractions were reviewed for completeness and accuracy by another member of the team.

Predefined criteria were used to assess the quality of individual controlled trials, systematic reviews, and observational studies,[32] rating them as "good," "fair," or "poor," depending on their methodological limitations.[32] Each study was independently rated for quality by two team members and disagreements were resolved by consensus.

No statistical meta-analyses were conducted because studies were lacking to provide estimates. Studies were qualitatively synthesized according to interventions, populations, and outcomes measured. Studies and their findings are described in a narrative, descriptive format to provide an overview of relevant evidence for each key question.

Assessing Applicability

Applicability is defined as the extent to which the effects observed in published studies are likely to reflect the expected results when a specific intervention is applied to the population of interest under "real-world" conditions.[31] It is an indicator of the extent to which research included in a review might be useful for informing clinical decisions. Factors important for understanding the applicability of studies were considered including differences in the interventions, comparators, populations, and settings.

Establishing the Strength of Recommendations

Investigators created evidence maps to provide a descriptive summary of supporting evidence for each key question. Results of systematic reviews and research studies, epidemiologic data,

USPSTF recommendations, clinical best practices, and other relevant sources were included in the evidence maps.

RESULTS

Key Question 1. Effectiveness of Screening Following Pregnancy

No studies were identified that evaluate the effectiveness of screening for DM among women with previous GDM during the postpartum period, the year following pregnancy, or later in reducing clinical outcomes related to DM.

In a systematic review of screening for DM in nonpregnant adults for the USPSTF,[33] two European trials of adults in their 50s (36% to 54% women) found no benefit of screening in reducing risks for all-cause mortality, cardiovascular mortality (hazard ratio [HR] 1.02, 95% CI 0.75 to 1.38), cancer-related mortality (HR 1.08, 95% CI 0.90 to 1.30), or diabetes-related mortality (HR 1.26, 95% CI 0.75 to 2.10).[34,35] However, the applicability of these studies to clinical practice in the United States is limited by differences in health care systems, racial distributions of populations, and screening approaches in the trials.

Key Question 2. Effective Screening Methods and Approaches

Studies of Tests Used to Screen for DM after GDM

Fasting blood glucose. A systematic review included 11 studies reporting the sensitivity and specificity of postpartum screening tests for DM in women with prior GDM.[36] Studies compared fasting blood glucose (FBG) with the 2 hour 75-g OGTT using different diagnostic thresholds and criteria (WHO 1985 or WHO 1999 criteria). All were cross-sectional studies published between 1999 and 2008, and most used convenience samples from clinical populations. Although race and ethnicity varied across studies, results were not determined for specific population sub-groups. Eight studies screened for DM within 1 year following pregnancy, two studies had wide testing periods (1 to 86 months), and 1 study screened 4 to 8 years after pregnancy.

The most currently relevant studies in this review compared a single FBG test to a 2 hour 75-g OGTT test using the WHO 1999 criteria (FBG ≥7.0 mmol/l; 2-hour OGTT ≥11.1 mmole/l).[37-41] With specificity fixed at 100%, sensitivity in the five studies ranged from 16% to 89%. The wide range of sensitivity likely reflected the heterogeneity of participants in the studies. The study with the highest sensitivity screened women 4 to 8 years after pregnancy, had low loss to follow-up (26%), and included mostly nonwhite participants.[37]

Two studies published since the systematic review also determined the sensitivity and specificity of FBG compared with 2 hour 75-g OGTT using the WHO 1999 criteria (**Table 3**).[42,43] Both studies included clinical populations in the United Kingdom and met criteria for fair-quality. In a study of 470 women with FBG and OGTT obtained during the year following GDM, FBG of 7.1 mmol/l or greater had sensitivity of 89.5% and specificity of 91.7% compared with OGTT.[42] In a second study that screened 876 women with GDM at 6 weeks postpartum, FBG of 7.0 mmol/l or

greater had sensitivity of 77.1% and specificity of 100% compared with OGTT.[43] Women in this study were predominantly nonwhite (70% South Asian, 26% white European, 4% other).

Hemoglobin A1c. Two fair-quality studies evaluated the sensitivity and specificity of HbA1c compared with OGTT using the WHO 1999 criteria (2-hr OGTT ≥11.1 mmole/l). [44,45] In a study of 203 women in the United Kingdom with GDM who were screened at 6-week postpartum visits, HbA1c values of 6.5% or greater had diagnostic sensitivity of 100% and specificity of 92.3% compared to OGTT.[45] In a study of 354 women with GDM in Spain who returned within the first year postpartum, HbA1c values of 6.5% or greater had diagnostic sensitivity of 16.7% and specificity of 100% compared to OGTT.[44]

Timing after Pregnancy and Screening Intervals

No studies addressed when or how frequently to screen for DM after pregnancy.

Key Question 3. Harms of Screening

No studies were identified that address the harms of screening for DM after pregnancy in women with previous GDM.

In a systematic review of screening for DM in nonpregnant adults for the USPSTF,[33] a fair-quality study of 116 adults invited for screening in a European trial found that a new diagnosis of diabetes was associated with increased short-term anxiety 6 weeks after screening compared with no new diagnosis, based on short-form Spielberger State-Trait Anxiety Inventory scores (46.7 vs. 37.0; $P = 0.031$).[46] No other studies addressed harms of screening or estimated the rate of false-positive results, psychological effects, or other harms associated with a diagnosis of DM, including studies of impaired fasting glucose or impaired glucose tolerance.[33]

Table 3. Recent Studies of Diagnostic Accuracy of Screening Tests for DM after GDM

Author, Yr, Quality	Setting; Sample Size; Population	Screening Test	Reference standard	Definition of DM	Outcomes Measured	Accuracy for Diagnosis of DM (sensitivity; specificity)
Kakad, 2010[42] Fair	UK; 470 women with GDM followed with postpartum OGTT	FPG	OGTT	FPG ≥7.1 mmol/l; 2-hour glucose >11.0 mmol/l	Detection of DM	**Cutoff ≥7.1 mmol/l** 89.5%; 91.7%
McClean, 2010[43] Fair	UK; 876 women with GDM tested at 6 weeks postpartum; 70% South Asian, 26% white, 4% other	FPG	OGTT	FPG ≥7.0 mmol/l; 2-hour glucose ≥11.1 mmol/l	Detection of DM	**Cutoff ≥7.0 mmol/l** 77.1% (95% CI 68.0% to 84.6%); 100% (95% CI 99.6% to 100.0%)*
Katreddy, 2013[45] Fair	UK; 203 women with GDM tested at 6 weeks postpartum	HbA1c	OGTT	FPG ≥7.0 mmol/l; 2-hour glucose ≥11.1 mmol/l	Detection of DM	**Cutoff ≥6.5%** 100%; 92.3%
Megia, 2012[44] Fair	Spain; 364 women with GDM who returned within the first year postpartum	HbA1c	OGTT or FPG	FPG 7.0 mmol/l; 2-hour glucose ≥11.1 mmol/l	Detection of DM	**Cutoff ≥6.5%** OGTT: 16.7%; 100% FPG: 28.6%; 100%

Abbreviations: CI=confidence interval; DM=diabetes mellitus; FPG=fasting plasma glucose; GDM=gestational diabetes mellitus; HbA1c=hemoglobin A1c; g=grams; l=liters; mol=moles; mmol=millimoles; N=sample size; OGTT=oral glucose tolerance test.
*Calculated.

CONCLUSIONS

Few studies have addressed screening for DM after GDM, and none provide evidence of benefits and harms of screening. Several studies evaluate the discriminatory accuracy of screening tests in women with previous GDM by comparing the performance of FBG (7 studies) and HbA1c (2 studies) against OGTT, the reference standard. While some studies indicate high sensitivity and specificity, others report lower values. This discrepancy largely reflects the heterogeneity of studies that vary by study populations and methods. Studies generally enrolled small convenience samples of patients and only two studies were conducted in the United States.

FUTURE RESEARCH NEEDS

Studies of screening in women with previous GDM for DM after pregnancy are lacking. Future research that evaluates benefits and harms of screening with long term clinical outcomes and compares the effectiveness of different screening intervals and strategies would provide direct supporting evidence for clinical recommendations. Research is needed to determine the optimal timing of testing after pregnancy, methods for improving compliance with postpartum testing for both patients and providers, and the value of patient counseling and continued screening for women with initial negative screening results. Research to improve testing procedures should focus on establishing when HbA1c becomes a more reliable screening test after pregnancy; the impact of weight changes, anemia correction, and lactation on screening test results; and identifying tests or protocols that improve accuracy for detecting DM in the immediate postpartum period. Additional studies to determine predictors that lead to the development of DM in women after pregnancy and in subsequent pregnancies, particularly for those with initial negative or borderline screening test results, could lead to the development of effective prevention strategies and programs.

CONCLUSIONS

Women diagnosed with GDM have an increased risk for developing DM in the years after pregnancy. Current clinical guidelines recommend screening women with GDM after pregnancy, however, many women are not screened in practice. Clinical procedures, including the OGTT, FBG, and HbA1c, demonstrate adequate sensitivity and specificity for screening, and are currently available to test eligible women during their routine health care. Screening for DM after pregnancy provides an opportunity for early detection and intervention to prevent progression of DM and diabetes-related complications, and may ultimately reduce the burden of DM among women.

EVIDENCE MAP

KQ 1: Effectiveness of screening for DM after GDM in reducing clinical outcomes related to diabetes.		
Systematic Reviews	**Additional Studies**	**Recommendations**
Systematic review for the USPSTF[33] on screening for abnormal blood glucose and DM in nonpregnant adults (2015): Two trials of non-pregnant adults in their 50s (36% to 54% women) found no benefit of screening in reducing risk for all-cause mortality, cardiovascular mortality (HR 1.02, 95% CI 0.75 to 1.38), cancer-related mortality (HR 1.08, 95% CI 0.90 to 1.30), or diabetes-related mortality (HR 1.26, 95% CI 0.75 to 2.10).[34,35]	No studies in women with a history of GDM address effectiveness of screening after pregnancy in reducing clinical outcomes related to diabetes.	• USPSTF recommendation[18,47] for screening for abnormal blood glucose and DM in nonpregnant adults (2015): Screen asymptomatic adults age 40 to 70 years who are overweight or obese for DM. Individuals with risk factors* may be at increased risk for diabetes at a younger age or lower BMI. Clinicians should consider screening earlier in those with one or more of these characteristics. • ACOG:[12] All women with GDM should be screened postpartum for DM.

KQ 2: Screening methods and approaches.		
Systematic Reviews	**Additional Studies**	**Recommendations**
A systematic review of five studies comparing a single FBG ≥7.0 mmol/l to a 2 hour 75-g OGTT (≥11.1 mmol/l) indicated sensitivity of 16% to 89%. (specificity 100%).[36]	• Two recent studies of FBG compared with OGTT indicated sensitivity 89.5%, specificity 91.7% for FBG ≥7.1 mmol/l;[42] and sensitivity 77.1% and specificity 100% for FBG ≥7.0 mmol/l.[43] • Two recent studies of HbA1c (≥6.5%) compared with OGTT indicated sensitivity 100%, specificity 92.3%;[45] and sensitivity 16.7%, specificity 100%.[44] • No studies address when or how frequently to screen for DM after pregnancy.	• ACOG:[12] All women with GDM should be screened 6 to 12 weeks postpartum for DM, impaired fasting glucose, or impaired glucose tolerance. Women with positive screening results should be referred for preventive therapy, and women with negative screening results should receive follow-up testing every 3 years. A fasting plasma glucose test or a 75-g, 2-hour OGTT is appropriate for postpartum screening. • ADA:[13] A 75-g OGTT is recommended at the 6- to 12-week postpartum visit. Test women with GDM every 1-3 years if her 6- to 12-week OGTT is normal. The frequency of screening is based on the presence of risk factors.** Ongoing screening may be done with any glycemic test (HbA1c, fasting plasma glucose, OGTT) using nonpregnancy cut points.

KQ 3: Harms of screening		
Systematic Reviews	**Additional Studies**	**Recommendations**
USPSTF systematic review on screening for abnormal blood glucose and DM in nonpregnant[33] adults[18,47] (2015): One study indicated that a new diagnosis of DM was associated with increased short-term anxiety 6 weeks after screening compared with no new diagnosis; no other studies addressed harms of screening.	No studies in women with a history of GDM address harms of screening after pregnancy.	USPSTF recommendation for screening for abnormal blood glucose and DM in nonpregnant adults[18,47] (2015): The USPSTF considered the potential harms of measuring blood glucose and initiating lifestyle modifications to be small to none.

Abbreviations: ADA=American Diabetes Association; ACOG=American College of Obstetricians and Gynecologists; BMI=body mass index; CI=confidence interval; DM=diabetes mellitus; FBG=fasting blood glucose; GDM=gestational diabetes mellitus; HbA1c=hemoglobin A1c; HR=hazard ratio; OGTT=oral glucose tolerance test; USPSTF=U.S. Preventive Services Task Force.
*Risk factors include a family history of DM, history of GDM or polycystic ovarian syndrome, or relationship to certain racial/ethnic groups with high prevalence of DM (African Americans, American Indians or Alaskan Natives, Asian Americans, Hispanics or Latinos, or Native Hawaiians or Pacific Islanders).
**Family history of DM, pre-pregnancy BMI, or need for insulin or oral medications during pregnancy.

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APPENDIX 1

Searches

Database: Ovid MEDLINE(R)
Search Strategy:
---
1 exp Diabetes, Gestational/ (9250)
2 exp Pregnancy in Diabetics/ (11966)
3 (gdm or gestational diabet*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (9252)
4 2 and 3 (1943)
5 1 or 4 (10102)
6 Diabetes Mellitus/di, ep, eh, et, pc [Diagnosis, Epidemiology, Ethnology, Etiology, Prevention & Control] (30974)
7 5 and 6 (306)
8 exp Diabetes Mellitus, Type 2/di, ep, eh, et, pc [Diagnosis, Epidemiology, Ethnology, Etiology, Prevention & Control] (29322)
9 5 and 8 (759)
10 exp Prediabetic State/di, ep, eh, et, pc [Diagnosis, Epidemiology, Ethnology, Etiology, Prevention & Control] (2138)
11 5 and 10 (69)
12 7 or 9 or 11 (1045)
13 exp Risk/ (985946)
14 exp Prognosis/ (1318869)
15 exp biomarkers/ (770112)
16 exp disease susceptibility/ (135509)
17 ep.fs. (1387044)
18 et.fs. (2262485)
19 exp epidemiologic studies/ (1983814)
20 exp epidemiologic factors/ (1312468)
21 exp 'specificity/ and sensitivity'/ (0)
22 exp mass screening/ (111306)
23 exp comparative study/ (1764732)
24 exp postpartum period/ (55752)
25 exp time/ (1234735)
26 13 or 14 or 15 or 16 or 17 or 18 or 19 or 21 or 23 or 24 or 25 (7981436)
27 12 and 26 (919)
28 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 ((follow* or postnatal* or post-natal* or postpartum* or post-partum or subseq* or futur* or after* or earlier or preced* or past or previous* or prior) adj5 (pregnan* or (gestat* adj3 diabet*) or gdm))).mp. (229)

29 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 ((follow* or subseq* or postnatal* or post-natal* or postpartum* or post-partum or after* or preced* or prior or previous*) adj5 ((gestat* adj3 diabet*) or gdm))).mp. (172)
30 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 ((follow* or subsequen* or later or after*) adj5 pregnan*)).mp. (56)
31 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 (postnatal* or post-natal* or postpartum* or post-partum*)).mp. (87)
32 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 ((follow* or subsequen* or later or after* or giv* or gave) adj5 birth*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (27)
33 28 or 29 or 30 or 31 or 32 (318)
34 27 or 33 (1151)
35 limit 34 to (english language and humans) (1032)

Database: EBM Reviews - Cochrane Database of Systematic Reviews
Search Strategy:
---
1 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 ((follow* or postnatal* or post-natal* or postpartum* or post-partum or subseq* or futur* or after* or earlier or preced* or past or previous* or prior or histor*) adj5 (pregnan* or (gestat* adj3 diabet*) or gdm))).mp. (16)
2 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 ((follow* or subseq* or postnatal* or post-natal* or postpartum* or post-partum or after* or preced* or prior or previous* or histor*) adj5 ((gestat* adj3 diabet*) or gdm))).mp. (14)
3 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 ((follow* or subsequen* or later or after*) adj5 pregnan*)).mp. (7)
4 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 (postnatal* or post-natal* or postpartum* or post-partum*)).mp. (8)

5 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 ((follow* or subsequen* or later or after* or giv* or gave) adj5 birth*)).mp. [mp=title, abstract, full text, keywords, caption text] (1)
6 1 or 2 or 3 or 4 or 5 (18)

Database: EBM Reviews - Cochrane Central Register of Controlled Trials <January 2017>
Search Strategy:
---
1 (gdm or gestational diabet*).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword] (867)
2 exp Risk/ (31262)
3 exp Prognosis/ (121459)
4 exp biomarkers/ (6838)
5 exp disease susceptibility/ (1190)
6 ep.fs. (32659)
7 et.fs. (57717)
8 exp epidemiologic studies/ (131260)
9 exp epidemiologic factors/ (37863)
10 exp 'specificity/ and sensitivity'/ (0)
11 exp mass screening/ (3191)
12 exp comparative study/ (7)
13 exp postpartum period/ (1200)
14 exp time/ (59890)
15 2 or 3 or 4 or 5 or 6 or 7 or 8 or 10 or 12 or 13 or 14 (278747)
16 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 ((follow* or postnatal* or post-natal* or postpartum* or post-partum or subseq* or futur* or after* or earlier or preced* or past or previous* or prior or histor*) adj5 (pregnan* or (gestat* adj3 diabet*) or gdm))).mp. (51)
17 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 ((follow* or subseq* or postnatal* or post-natal* or postpartum* or post-partum or after* or preced* or prior or previous* or histor*) adj5 ((gestat* adj3 diabet*) or gdm))).mp. (31)
18 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 ((follow* or subsequen* or later or after*) adj5 pregnan*)).mp. (12)
19 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 (postnatal* or post-natal* or postpartum* or post-partum*)).mp. (9)

20 ((screen* or predispos* or suscept* or epidemiol* or etiol* or cause* or causal* or causat* or link* or predict* or risk* or chance* or percent* or probab* or develop* or diagnos* or exhibit* or symptom*) adj5 (diabetes mellitus or dm or niddm) adj7 ((follow* or subsequen* or later or after* or giv* or gave) adj5 birth*)).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword] (1)
21 16 or 17 or 18 or 19 or 20 (53)
22 1 and 15 (309)
23 21 or 22 (341)

APPENDIX 2

Inclusion/Exclusion Criteria

Category	Inclusion	Exclusion
Populations	Asymptomatic, nonpregnant women with a history of GDM during a previous pregnancy who have not been previously diagnosed with DM when not pregnant.	Pregnant women; women previously diagnosed with DM when not pregnant; women with overt symptoms of DM.
Interventions	KQ 1-3: Screening for DM using methods currently in U.S. practice.	Screening using laboratory tests or other methods not relevant to U.S. practice; other interventions. Studies of treatment or risk reduction.
Comparisons	KQ 2: Screening methods, approaches, and specific tests to diagnose DM after pregnancy compared with usual care; one method compared with another method.	Other comparisons.
Outcomes	KQ 1: Clinical outcomes related to screening and subsequent treatment. KQ 2: Measures of test performance to diagnose DM (sensitivity, specificity; likelihood ratios; c-stats). KQ 3: False positive/negative results; anxiety, distress; other adverse events impacting quality of life.	KQ 1: Intermediate, not clinical, health measures. KQ 2: Diagnosis of glucose intolerance, "pre-diabetes," or other intermediate measure related to testing. KQ3: Other outcomes not listed.
Setting	Primary care and maternity care clinical settings comparable to U.S. practice.	Practice settings dissimilar than those in the U.S.
Study Design	KQ 1, 3: RCTs, observational studies with or without comparison groups. KQ 2: Discriminatory accuracy studies.	Other study designs.
Study Quality	Good- and fair-quality studies for meta-analyses.	Studies rated poor-quality.

Abbreviations: DM=diabetes mellitus; GDM=gestational diabetes mellitus; KQ=key question; RCT=randomized controlled trial