Glucose challenge test for detecting gestational diabetes mellitus: a systematic review
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CRD summary
The authors concluded that higher accuracy measures were needed for the 50g glucose challenge test to be used as a definite diagnostic test in place of the oral glucose tolerance test. This was a well-conducted review but limitations in the evidence available and potential for missing unpublished studies make the reliability and generalisability of the pooled results uncertain.

Authors' objectives
To determine the diagnostic accuracy of the 50g glucose challenge test for gestational diabetes mellitus.

Searching
MEDLINE and EMBASE were searched without methodological filter or other restrictions up to October 2010. Search terms were reported. A cited reference search was performed in Web of Science. Reference lists were searched and authors of primary studies contacted for further published articles. Abstracts were not included.

Study selection
Eligible studies compared the 50g glucose test (index test) with either the 75g or 100g oral glucose tolerance test (reference standard) in pregnant women (before 32 weeks gestation) at any level of risk for gestational diabetes mellitus. Studies had to report sufficient data to construct a 2x2 contingency table. Studies in which the oral glucose tolerance test was performed only in screen-positive women and case-controlled studies that compared women with and without gestational diabetes mellitus were excluded.

The most common reference test used was the 100g oral glucose tolerance test; some studies used the 75g oral glucose tolerance test. Gestational age ranged from seven to 40 weeks; testing was performed between 24 and 28 weeks in most studies. There was variation in threshold values of the index test used to define test positivity (range 4.0mmol/L to 16.0mmol/L). Some studies used a low threshold for the oral glucose tolerance test to define gestational diabetes mellitus and others used a high threshold. Few studies reported exclusion criteria: preterm birth, foetal death, medication, preeclampsia, preterm premature rupture of membranes (PPROM), delivery elsewhere or chronic disease. Incidence of gestational diabetes mellitus ranged from 3% to 33% in unselected populations and 11% to 17% in high risk populations.

Two reviewers independently selected studies for inclusion in the review. Any disagreements were resolved through discussion with a third reviewer.

Assessment of study quality
Methodological quality was assessed using a modified version of the QUADAS tool. Partial verification criteria were split to assess complete verification for women with a positive and negative index test separately and correction for verification bias replaced the differential verification criterion.

Two reviewers assessed study quality. Disagreements were resolved through discussion or arbitration with a third reviewer.

Data extraction
Data to populate a 2x2 contingency tables were extracted and used to calculate sensitivity and specificity. Where data were missing on test accuracy or other relevant characteristics the author of the primary study was contacted.

Two reviewers extracted data. Disagreements were resolved through discussion or arbitration with a third reviewer.

Methods of synthesis
Pooled estimates of sensitivity and specificity and their 95% confidence intervals (CI) were calculated using a random-effects bivariate regression model; positive and negative likelihood ratios (LR+/-) were derived from these estimates.
Summary estimates were calculated using studies that reported on a threshold of 7.8mmol/L on the index test. Summary estimates were reported for two additional thresholds (7.5mmol/L and 8.0mmol/L).

Covariates examined for their effect on test accuracy were reference test (75g versus 100g oral glucose tolerance test), risk level of women in the study (consecutive inclusion versus inclusion of women with risk factors) and high versus low oral glucose tolerance test threshold values. Accuracy as a function of the index test threshold values was calculated by including this as a continuous covariate in the model.

Results of the review

Twenty-six studies based on 25 articles (13,564 women, range 42 to 3,836; included 1,027 with gestational diabetes mellitus) were included in the review. There was one randomised controlled trial, one cross-sectional study and 24 cohort studies. The reference test was performed independently and consistently in all studies. Most studies did not blind interpreters of the oral glucose tolerance test from the results of the glucose challenge test. Most studies did not perform correction for verification. Twenty studies had consecutive (unselected) recruitment and four recruited a high risk population. Four studies reported inclusion based on the presence of risk factors; one study did not report methods used. Withdrawals were explained in approximately 70% of the included studies.

Low threshold oral glucose tolerance test: Based on a threshold value of 7.8mmol/L and low threshold oral glucose tolerance test, the 50g glucose challenge test had a pooled sensitivity of 74% (95% CI 62 to 87), specificity of 85% (95% CI 80 to 90), positive likelihood ratio of 4.9 (95% CI 3.5 to 7.0) and negative likelihood ratio of 0.31 (95% CI 0.20 to 0.47) for studies with an unselected population. For studies with a high risk population sensitivity was 74% (95% CI 62 to 87), specificity was 77% (95% CI 66 to 89), positive likelihood ratio was 3.2 (95% CI 2.0 to 5.2) and negative likelihood ratio was 0.34 (95% CI 0.22 to 0.53).

High threshold oral glucose tolerance test: Based on a threshold value of 7.8mmol/L and high threshold oral glucose tolerance test, the 50g glucose challenge test had a pooled sensitivity of 83% (95% CI 75 to 91), specificity of 81% (95% CI 75 to 87), positive likelihood ratio of 4.4 (95% CI 3.2 to 6.0) and negative likelihood ratio of 0.21 (95% CI 0.14 to 0.32) for studies with an unselected population. For studies with a high risk population sensitivity was 83% (95% CI 75 to 91), specificity was 72% (95% CI 60 to 84), positive likelihood ratio was 3.0 (95% CI 2.0 to 4.5) and negative likelihood ratio was 0.24 (95% CI 0.15 to 0.37).

The only covariate to impact on results was threshold of the 50g glucose test which was statistically significant for both sensitivity and specificity. Results for 7.5 and 8.0 thresholds and summary ROC curves were reported.

Authors’ conclusions

The 50g glucose challenge test was acceptable to screen for gestational diabetes mellitus but higher accuracy measures were needed for it to be used as a definite diagnostic test to replace the oral glucose tolerance test.

CRD commentary

The review question was clear. Well-defined inclusion and exclusion criteria were presented. Several sources were searched without limitations but the authors did not appear to seek unpublished data and abstracts were not included. Procedures for study selection, data extraction and study quality assessment minimised risks of error and bias. Relevant criteria were used to evaluate methodological quality; results were reported in an online supplement. Considerable uncertainty surrounding blinding of interpreters of the reference standard may have overestimated accuracy. Some uncertainty regarding use of uninterpretable results and reporting of withdrawals may have affected the reliability of the results of the primary studies.

The authors acknowledged potential limitations due to incomplete reporting of study and sample characteristics of the primary studies. There was heterogeneity across the included studies in terms of patient population, thresholds used and samples on which the test was conducted. Overall the synthesis appeared appropriate. A robust SROC model maintained the within-study relationship between sensitivity and specificity when deriving the pooled estimates. Results were not reported consistently (text and tables reported different estimates) and it appeared that two specificities were given for one patient population.

Overall this was a well-conducted review. Methodological limitations in the included studies may impact on the reported estimates of accuracy. Substantial clinical heterogeneity and potential for missing unpublished studies make...
reliability and generalisability of the pooled results unclear.

**Implications of the review for practice and research**

**Practice**: The authors suggested that a one step-method (such as using the oral glucose tolerance test for screening in a selected population) might be less of a burden for women and potentially more cost-effective than a two-step method in which a glucose loading test might be performed more than once.

**Research**: The authors stated that individual patient data meta-analyses would be required to evaluate the true effect of clinical variables and different threshold values and suggested that combining the 50g glucose challenge test with other screening strategies should be explored. They also suggested comparing the cost effectiveness of a strategy involving selection based on various risk factors followed by screening with a 50g glucose test (and an oral glucose tolerance test in the case of an abnormal result) with other screening strategies in an RCT.

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