Benefits and harms of treating gestational diabetes mellitus: a systematic review and meta-analysis for the US Preventive Services Task Force and National Institutes of Health Office of Medical Applications of Research

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CRD summary
This well-conducted review concluded that treating gestational diabetes mellitus resulted in less pre-eclampsia, shoulder dystocia and macrosomia compared with no treatment. The evidence did not show an effect on neonatal hypoglycaemia or future poor metabolic outcomes. There was little evidence of short-term harm of treating gestational diabetes mellitus. These conclusions are likely to be reliable.

Authors' objectives
To assess the maternal and neonatal benefits and harms of treating gestational diabetes mellitus.

Searching
Fifteen databases (including MEDLINE, EMBASE and The Cochrane Library) were searched from 1995 to May 2012 for studies in English. Search terms were reported. Trial registries, conference abstracts and proceedings and websites of relevant organisations were searched from 2010 to 2012. Reference lists of relevant reviews and included studies were screened.

Study selection
Randomised controlled trials (RCTs), non-RCTs and cohort studies that compared any treatment of gestational diabetes mellitus with no treatment in pregnant women with no known pre-existing diabetes were eligible for inclusion. Eligible studies had to report important short-term and long-term maternal, foetal, neonatal and child outcomes.

All the included studies compared diet modification, glucose monitoring and insulin as required versus standard care. Where reported, diagnostic testing for gestational diabetes mellitus occurred at least of 24 weeks gestation. Glucose inclusion criteria for patients varied across studies and ranged from a positive screening on the 50 gram glucose challenge with non-diagnostic oral glucose tolerance tests to meeting the recognised criteria (such as National Diabetes Data Group criteria). Most studies were conducted in North America and Australia.

Two reviewers independently assessed studies for inclusion. Any disagreements were resolved by discussion.

Assessment of study quality
The quality of RCTs was assessed using the Cochrane risk of bias tool and the quality of cohort studies was assessed using the nine-point Newcastle-Ottawa Scale. The strength of evidence for primary outcomes was evaluated by using a Grading of Recommendations Assessment, Development and Evaluation approach.

Two reviewers independently performed quality assessment, with any disagreements resolved by discussion.

Data extraction
For dichotomous outcomes, data were extracted on event rates to enable the calculation of relative risks (RR) with 95% confidence intervals (CI). For continuous outcomes, data were extracted on mean and standard deviations to enable the calculation of mean differences with 95% CI.

One reviewer performed data extraction. A second reviewer checked for accuracy and consistency.

Methods of synthesis
Studies were combined in a meta-analysis when they were sufficiently similar in terms of statistical heterogeneity ($I^2 \leq 75\%$). Statistical heterogeneity was assessed using the $X^2$ and $I^2$ statistics. The random-effects Mantel–Haenszel model was used to calculate the pooled relative risks with 95% CI. The random-effects inverse variance method was used to calculate the weighted mean differences with 95% CI. Separate analyses were conducted by different types of study.
Results of the review
Five RCTs (2,643 patients) and six retrospective cohort studies (3,110 patients) were included in the review. Risk of bias was high for one RCT, low for one RCT and unclear for three RCTs. All cohort studies were judged as high quality (quality scores ranged from 7 to 9).

Compared with no treatment, treatment was significantly associated with fewer cases of pre-eclampsia (RR 0.62, 95% CI 0.43 to 0.89; three RCTs), shoulder dystocia (RR 0.42, 95% CI 0.23 to 0.77; three RCTs), and macrosomia (birthweight above 4,000g) (RR 0.50, 95% CI 0.35 to 0.71; five RCTs). Significant heterogeneity was observed only for the outcome of macrosomia ($I^2=50\%$) and not for the other two outcomes.

Two RCTs reported that treatment was significantly associated with less weight gain compared with no treatment; there was no difference for this outcome between the two groups in other two RCTs.

Two RCTs showed no difference in birth injury between the treatment and no treatment groups but one cohort study showed fewer cases with treatment than no treatment.

No difference between the treatment and no treatment groups was found for neonatal hypoglycaemia, cesarean delivery and admission to a neonatal intensive care unit and small-for-gestational-age neonates. There was insufficient evidence on long-term metabolic outcomes among infants.

There was no evidence from included studies for long-term maternal outcomes including type 2 diabetes mellitus, obesity and hypertension.

Authors' conclusions
Treating gestational diabetes mellitus resulted in less pre-eclampsia, shoulder dystocia, and macrosomia compared with no treatment. However, the current evidence did not show an effect on neonatal hypoglycaemia or future poor metabolic outcomes. There was little evidence of short-term harm of treating gestational diabetes mellitus other than an increased demand for services.

CRD commentary
The review question was clear and supported by appropriate inclusion criteria. Various relevant databases were searched. Efforts were made to find both published and unpublished studies and this minimised potential for publication bias. The search was limited studies in English so some relevant studies may have been missed. Sufficient attempts were made to minimise errors and biases during the review process. The quality of included studies was assessed using the appropriate criteria.

Interpretation of results took into account the strength of evidence for primary outcomes. The authors judged the overall strength of evidence to be moderate at best and insufficient for several outcomes. Statistical heterogeneity was assessed and appropriate methods were used to pool the results.

This was a well-conducted review and despite the moderate quality of the evidence the authors' conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that the evidence from this review supported the benefits of treating mild gestational diabetes mellitus.

Research: The authors stated a need for further studies to investigate the long-term metabolic effect on offspring whose mothers were treated for gestational diabetes mellitus. Well-conducted prospective cohort studies were required to evaluate the real-world effect of the treatment of gestational diabetes mellitus on health care utilisation. Future research was needed to determine glucose thresholds and treatment targets where benefits of treating gestational diabetes mellitus outweigh the risks of no treatment. Randomised controlled trials to evaluate the care of women diagnosed with gestational diabetes mellitus (including foetal surveillance protocols) were required in order to guide obstetric investigations and management of gestational diabetes mellitus.
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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.