CRD summary
The review concluded that all current tocolytic agents were superior to no treatment at delaying delivery of newborns for both 48 hours and seven days. In light of the limited assessment of study quality, questionable statistical techniques used and an absence of any statistical investigation into variation between studies, the authors’ conclusions are not likely to be reliable.

Authors’ objectives
To determine the optimal first-line tocolytic agent for treatment of premature labour.

Searching
MEDLINE, EMBASE, CINAHL and Cochrane Database of Clinical Trials were searched (without language restrictions) for full published papers with dates that ranged from 1950 to January 2008; search terms were reported. Cochrane reviews were checked.

Study selection
Randomised controlled trials (RCTs) that compared different tocolytic drugs (or compared with placebo or usual care) in women with a mean gestational age of between 28 and 33 weeks were eligible for inclusion. Studies where assigned treatments were not adequately concealed were excluded.

Interventions included different types of betamimetics, calcium-channel blockers, magnesium sulphate, nitrates, oxytocin receptor antagonists and prostaglandin inhibitors. Control treatments included placebo, usual care, bed rest and intravenous fluids. Outcomes of interest were rates of delayed delivery (at various time points), drug-related adverse events, neonatal survival and neonatal respiratory distress syndrome.

It was unclear how many reviewers were involved in selecting relevant abstracts, but two reviewers selected full articles for inclusion. Disagreements were resolved by consensus.

Assessment of study quality
Allocation concealment (using the Cochrane Collaboration A, B, C criteria) and blinding were assessed by two reviewers independently.

Data extraction
Means and standard errors were extracted and grouped by drug category. If gestational ages were significantly different between treatment groups, neonatal outcome data were not extracted. Authors were contacted where necessary to clarify use of antenatal corticosteroids (neonatal outcomes were not extracted if clarification was not provided).

Two reviewers independently extracted data. Disagreements were resolved by consensus.

Methods of synthesis
Meta-analyses with a random-effects model were used to calculate pooled percentage rates and 95% confidence intervals (by individual treatment category only). Studies were weighted by sample size. A decision analysis was conducted to produce treatment rankings.

Results of the review
Fifty-eight RCTs (n=7,176) were included in the review. It appeared that around two-thirds of the trials had adequate allocation concealment.

All tocolytic agents were better than placebo or control treatments at delaying delivery for at least 48 hours and also for
at least seven days, but none were significantly better for delaying delivery to 37 weeks of gestation. Rates of both neonatal death and neonatal respiratory distress syndrome did not differ significantly between groups. Women who took betamimetics had significantly higher rates of treatment-related adverse events (leading to treatment discontinuation) compared with other treatment groups. Results of the decision analysis indicated that prostaglandin inhibitors provided superior results for all outcomes except delayed delivery until 37 weeks.

Authors’ conclusions
Although all current tocolytic agents were superior to no treatment at delaying delivery for both 48 hours and seven days, prostaglandin inhibitors were superior to the other agents and may be considered the optimal first-line agent before 32 weeks of gestation to delay delivery.

CRD commentary
The review addressed a clear question supported by appropriate inclusion criteria. Several databases were searched for relevant studies without language restrictions. Excluding studies published only as abstracts may have introduced publication bias. Suitable methods (such as independent duplicate data extraction) were used throughout the review to minimise risks of reviewer error and bias. Study quality assessment was limited to examination of allocation concealment and blinding, so it was unclear whether studies used appropriate randomisation procedures. The authors excluded studies where assigned treatments were not adequately concealed, but few details of the quality assessment results were provided and so it was difficult to assess the strength of the evidence. Very few details were provided about individual studies. Aggregated characteristics omitted reporting drug dose details. The synthesis involved pooling treatment data separately from comparator data within a given trial instead of using both groups to derive an effect size. Statistical heterogeneity was not assessed. By doing this the analyses did not utilise the benefits of randomisation, so the results should be interpreted with much caution. In light of the limited quality assessment, the questionable synthesis and an absence of any assessment of statistical heterogeneity, the authors' conclusions are not likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that prostaglandin inhibitors and calcium channel blockers had the best combination of tolerability and efficacy and should be considered the best choices for first-line tocolysis, taking into account maternal and foetal factors that might influence the choice of tocolytic agent.

The authors did not state any implications for research.

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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.