Impact of maternal supplementation with probiotics during pregnancy on atopic eczema in childhood – a meta-analysis

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CRD summary
The authors concluded that probiotics, particularly *Lactobacillus*, taken during pregnancy, reduced the risk of children developing atopic eczema. The reliability of the authors’ conclusions is unclear, due to limitations in the review methods and reporting, relatively small trial samples, and a small effect size.

Authors' objectives
To assess the impact of taking probiotics during pregnancy, on the development of atopic eczema, in children.

Searching
PubMed, EMBASE, and EBM Reviews were searched for relevant publications, from database inception to June 2009. Limited search terms were reported. Reference lists of relevant articles were screened for additional publications.

Study selection
Eligible for inclusion were double-blind, placebo randomised controlled trials (RCTs) assessing the effects of women’s probiotic intake, during pregnancy, on the development of atopic eczema, in their children, during their first years of life. Only RCTs with ethics approval were eligible for inclusion.

The primary objective, of each included trial, was not always specifically the assessment of atopic eczema. The probiotics were *Lactobacillus rhamnosus* GG, *Bifidobacterium breve*, or a mixture of bacteria, including *Propionibacterium freudenreichii shermanii*, *Bifidobacterium animalis lactis*, and *Lactobacillus reuteri*. Probiotic or placebo intake started between the first trimester of pregnancy and two to four weeks before birth. Intake (via lactation) continued up to between three months and two years after birth. Approximately half the children were male.

Two reviewers independently screened articles for inclusion.

Assessment of study quality
Two reviewers independently assessed trial quality according to guidance published by the Centre for Reviews and Dissemination. There were nine criteria, covering randomisation, blinding, inclusion and exclusion criteria reported, similarity between treatment groups and treatment appearance, and reporting of drop-out rates.

Data extraction
The incidence of atopic eczema, in the intervention and placebo groups, was extracted to calculate risk ratios and their 95% confidence intervals.

Two reviewers independently extracted the data. Discrepancies were resolved by referral to a third reviewer.

Methods of synthesis
A random-effects model was used to combine the risk ratios and 95% confidence intervals, weighted by sample size. Separate meta-analyses were performed for trials using *Lactobacillus* and trials using mixed probiotics. Statistical heterogeneity was assessed using *I²*.

Results of the review
Seven RCTs, with 2,843 children (range 94 to 925), were included in the review. Four trials did not describe their randomisation methods in detail; four did not specify whether outcome assessment was blinded; and two trials did not describe their drop-out rates. One trial did not specify whether the appearance of the probiotics and the placebo were similar. The other quality criteria were met by each trial. In one trial follow-up was reported at two, four, and seven years.
Mothers taking *Lactobacillus* during pregnancy showed a statistically significant reduction in the risk of developing atopic eczema, compared to mothers taking placebo (RR 0.82, 95% CI 0.71 to 0.95; four RCTs). There was no evidence of statistical heterogeneity ($I^2=0$).

There were no statistically significant differences between mothers taking mixed bacteria, and those taking placebo, during pregnancy, and the risk of their child developing atopic eczema (three RCTs; $I^2=0$).

**Authors' conclusions**

Probiotics, particularly *Lactobacillus*, taken during pregnancy, reduced the risk of children developing atopic eczema.

**CRD commentary**

The review question and supporting inclusion criteria were broadly defined. Three databases were searched for relevant articles, but the full search details were not given, and there did not appear to be a specific search for unpublished trials. Trial quality was assessed using appropriate criteria. With the exception of one trial, they appeared to meet most criteria. The actual drop-out rates were not reported. Each stage of the review process was performed by two people, minimising the potential for reviewer error and bias.

Few participant details were provided, so it was unclear whether there were significant differences in the maternal characteristics, and whether other interventions were given. Only two trials showed statistically significant findings, and these were only just significant. Appropriate methods were used to assess statistical heterogeneity and the results showed no evidence of variation. One trial reported long-term results; the follow-up times for the other trials were not reported. Trial samples were generally small.

The reliability of the authors' conclusions is unclear, due to limitations in the review methods and reporting, relatively small samples, and a small effect size.

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

**Practice:** The authors stated that *Lactobacillus* probiotics could be recommended during pregnancy and lactation, but probiotics consisting of various bacterial strains could not be recommended.

**Research:** The authors stated that further longitudinal trials were needed to assess the effects, the best time to start taking probiotics, and any differing effects for each bacterial strain.

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