cow’s milk protein was first introduced into their diet and were also introduced to solids earlier than the control infants.

**REVIEWER COMMENTS.** The authors conclude that early introduction of solids was associated with the development of food allergy, which supports the current recommendations by the American Academy of Pediatrics to breastfeed exclusively and to delay introduction of solids until 4 to 6 months of age. Data are accumulating to suggest that breastfeeding seems protective against food allergies and that there is a critical window in which solid foods, including highly allergenic foods such as cow’s milk, eggs, and peanut, should be introduced in infancy. Breastfeeding should also continue concurrently for 2 to 3 months while cow’s milk and solids are introduced into the diet because it is thought to play a role in the development of oral tolerance.

**RESULTS.** Total IgE and atopic sensitization was significantly reduced in subjects who received probiotics. This reduction was more pronounced with longer follow-up for total IgE levels (correlation coefficient: −1.95 [95% confidence interval: −3.69 to −0.21]; P = .028). The effect on atopic sensitization was only significant when probiotics were administered both prenatally and postnatally (relative risk: 0.08 [95% confidence interval: 0.78 to 0.99]; P = .035) but not when only administered postnatally (P = .825). However, probiotics did not significantly reduce the prevalence of asthma or wheeze. *Lactobacillus* was found to be associated with increased atopic sensitization.

**CONCLUSIONS.** Early probiotic administration reduces the risk of atopic sensitization, but it does not reduce the risk of developing asthma. There was no significant association in subgroup analysis according to age group or treatment length.

**REVIEWER COMMENTS.** Results on atopy and asthma in association with probiotic administration have been conflicting. This study showed that probiotic administration was significant in reducing atopic sensitization but not disease. Similar to the hygiene hypothesis, in which a relative lack of microbial exposure during infancy and early childhood could result in an imbalance with a shift of Th1/Th2 cytokine balance toward a more allergic Th2 response, probiotics may promote a healthy gut microbiome, shifting this balance to a nonallergic Th1 response. Future trials are still needed to achieve more consistency among studies.

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**Probiotic Administration in Early Life, Atopy, and Asthma: A Meta-Analysis of Clinical Trials**


**PURPOSE OF THE STUDY.** Some studies suggest that early probiotic administration reduces the risk of allergies and asthma in childhood. This study evaluates the effects of probiotic supplementation on asthma and atopic sensitization.

**STUDY POPULATION.** The study included 4031 subjects in 20 cohorts primarily in Europe, Asia, and Australia. Probiotics were administered prenatally to pregnant mothers (2 studies), prenatally and postnatally (10 studies), or only postnatally directly to the child (9 studies).

**METHODS.** This meta-analysis included 25 double-blind, randomized, placebo-controlled trials published between 2001 and 2012. Meta-regression was performed to evaluate the effect of potential factors on probiotic efficacy. The pooled risk estimates were calculated by using random effect models. Atopic sensitization was measured by a positive skin prick test or elevated serum-specific IgE level to any food or inhalant allergen. Asthma was diagnosed directly by a physician or indirectly by parental report of a physician diagnosis.

**RESULTS.** Total IgE and atopic sensitization was significantly reduced in subjects who received probiotics. This reduction was more pronounced with longer follow-up for total IgE levels (correlation coefficient: −1.95 [95% confidence interval: −3.69 to −0.21]; P = .028). The effect on atopic sensitization was only significant when probiotics were administered both prenatally and postnatally (relative risk: 0.08 [95% confidence interval: 0.78 to 0.99]; P = .035) but not when only administered postnatally (P = .825). However, probiotics did not significantly reduce the prevalence of asthma or wheeze. *Lactobacillus* was found to be associated with increased atopic sensitization.

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**No Effect of Probiotics on Respiratory Allergies: A Seven-Year Follow-up of a Randomized Controlled Trial in Infancy**


**PURPOSE OF THE STUDY.** The goal of this study was to determine if supplementation with the probiotic *Lactobacillus reuteri* during the perinatal period and infancy, which had reduced the incidence of allergic sensitization and allergic eczema at age 2 years, reduces the incidence of asthma and allergic rhinoconjunctivitis in school-aged children.

**STUDY POPULATION.** The study population included 184 of 232 Swedish children who had participated in a double-blind, placebo-controlled, randomized controlled trial (RCT) of probiotic supplementation perinatally and during infancy. To be eligible for the RCT, children had to have a family history of allergic disease.

**METHODS.** Families were contacted when the children were 7 years old, and the follow-up visit included administration of questionnaires, physical examination, spirometry, measurement of fractional exhaled nitric oxide, and assessment of eczema. Skin prick testing and IgE testing were also performed by using a panel of common food and environmental allergens. The outcome of allergic disease was defined as symptomatic asthma, allergic rhinoconjunctivitis, and allergic rhinoconjunctivitis.
Supplementation With Probiotics in the First 6 Months of Life Did Not Protect Against Eczema and Allergy in At-Risk Asian Infants: A 5-Year Follow-up


PURPOSE OF THE STUDY. The authors had previously reported that supplementing infants at risk for allergic disease with probiotics did not prevent eczema or allergen sensitization in the first year of life. The present study evaluated the allergic outcomes of these same subjects at 5 years of age.

STUDY POPULATION. In this Singaporean study, qualifying term infants had a first-degree relative who not only had a diagnosis of asthma, allergic rhinitis, or eczema but also a positive result on skin prick testing to Dermatophagoidespteronyssinus and/or Blomia tropicalis. A total of 124 infants were given cow’s milk formula with probiotics and 121 infants were given cow’s milk formula without probiotics from the first day of life until 6 months of age. By 5 years, 87% had completed the study (112 who were on probiotics and 108 who did not receive probiotics).

METHODS. Subjects received at least 60 mL (9.26 g) per day of commercially available cow’s milk–based infant formula in this double-blind, placebo-controlled randomized study. Probiotic supplementation was with Bifidobacterium longum (BL999) and Lactobacillus rhamnosus (LPR). During regular follow-up visits over the next 5 years, children were assessed for asthma, allergic rhinitis, eczema, and food allergy.

RESULTS. At the age of 5 years, presence of eczema and eczema severity according to the SCORAD (Scoring Atopic Dermatitis) index were not significantly different between the probiotic group and the placebo group (16.9 vs 15.3; \(P = .295\)). There was also no significant difference between the 2 groups for asthma development, food allergy, and dust mite sensitization. Of note, those subjects who consumed probiotics on their own accord after the initial 6-month treatment period were statistically associated with a reduced incidence of asthma and allergic rhinitis at 5 years of age. There was no difference in growth rate (for height and weight) between the 2 study populations.

CONCLUSIONS. Early-life supplementation with probiotics did not change allergic outcomes at 5 years of age.

REVIEWER COMMENTS. Studies in Scandinavia, Australia, and Germany have had similar negative findings. Nevertheless, the authors noted that those infants who continued probiotic supplementation once a week from the age of 2 years for at least 1 year did have a reduced incidence of asthma and allergic rhinitis, no matter which study group they were part of. It seems we are not yet able to reach any final conclusions regarding probiotic supplementation and its influence on atopy.
No Effect of Probiotics on Respiratory Allergies: A Seven-Year Follow-up of a Randomized Controlled Trial in Infancy

Elizabeth Matsui

Pediatrics 2014;134;S141
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