# *Probiotics in Pregnancy*: Are Probiotics Preventative Against Infantile and Childhood Atopic Dermatitis?

Faculty of Health Sciences (HSS4303)
Presented by Miya Ismayilova, Muhammed Qureshi, Justin Lee, Jeffrey Lao
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## ABSTRACT

**Background:** Atopic dermatitis (AD), also known as atopic eczema, affects 3.5% of the global population[5]. Peak prevalence of AD occurs during infancy. No cure exists but certain preventative measures, such as probiotic use, have been proposed. Probiotic preventative treatments for AD most commonly involve Lactobacillus and Bifidobacterium strains. **Objective:** To comprehensively analyze the impact of prenatal and postnatal maternal probiotic supplements on the prevention of infantile and childhood atopic dermatitis. **Methods:** A structured literature review was conducted through the University of Ottawa Search+ database using the following keywords: probiotic, pregnancy, atopic dermatitis. Search+ was employed for its collection of databases available. Only peer-reviewed articles published from 2006 to 2016 were considered for the literature review. Results were filtered by terms in the inclusion and exclusion criteria. The search produced 82 publications from which 10 were eligible for the literature review. **Results:** Out of the 10 publications reviewed, 4 were RCTs and the remaining were systematic reviews and meta-analyses on mostly RCTs. 1 RCT did not discover a preventative effect from probiotic supplements in pregnancy on infantile and childhood atopic dermatitis. The remaining 9 publications provided evidence towards a statistically significant relationship between probiotics during pregnancy and a reduced risk of AD. **Conclusion:** Little heterogeneity exists in the findings; however, a consensus has not been reached. More research is needed to ascertain a clear relationship.

## BACKGROUND

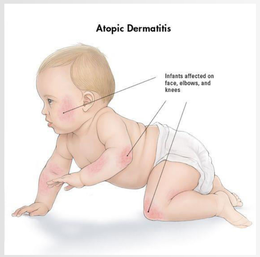



**Figure 1**: Atopic Dermatitis in Infant

Atopic dermatitis (AD) is a chronic , or chronically recurrent, inflammatory skin disease. Peak prevalence occurs during infancy - 20% of infants and young children have AD[4]. Globally, AD affects 3.5% of the population worldwide[5]. Although it is not known what causes AD, there is speculation that it is related to family history of the disease, maternal nutrition while she is carrying the child, and gut microbes that babies might lack during infanthood[5]. Since there is no known cure for the condition, the focus is on prevention. One of the most common prevention options is through the use or probiotics, specifically strains from the *Lactobacillus and Bifidobacterium* genera. The mechanism of action of probiotics is not known; however, the hygiene hypothesis suggests that children are more susceptible to allergic diseases because of a lack of exposure to microbes in early life[9].

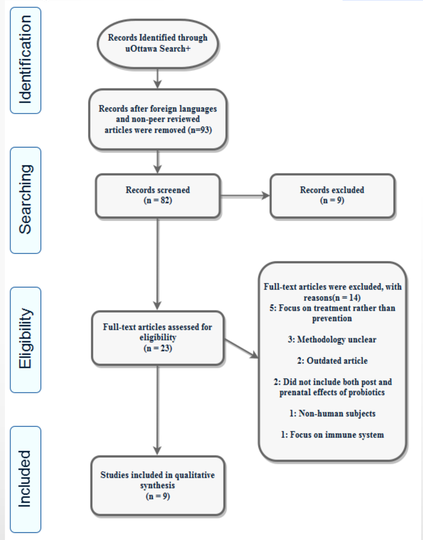
**Rationale**: Incidences of allergic diseases are rising across the world, and with no treatment available, research into prevention is key

**Research Question:** Do probiotic supplements in pregnancy and breastfeeding prevent the development of infantile and childhood atopic dermatitis?

## METHODS

- Via UOttawa's "Search+", a structured literature review was conducted by first using the following keywords: probiotics, and pregnancy, and atopic dermatitis (see Figure 2).
- A date range of 2006 to 2016 was imposed. Non peer-reviewed articles were omitted. Foreign language results were omitted.
- The inclusion criteria terms were: pregnant women, pregnancy, prevention, probiotics, dietary supplements, atopic dermatitis, and dermatitis atopic.
- The exclusion criteria terms were: prebiotics, food hypersensitivity, asthma, and food microbiology.
- Following this procedure yielded 82 publications - the abstracts were used to determine which full-text articles would be assessed for eligibility. This yielded 23 full-text articles, which were judged based upon their relevance to the research question and their quality (see Figure 3 and 4).
- 10 articles were deemed relevant these articles were randomized control trials, systematic reviews, and meta-analyses. The 10 publication were agreed upon through multiple raters – the overall agreement within the group was 0.74

**Figure 2**: PRISMA flowchart




## RESULTS

**Figure 5**: Summary table of results

| Authors (year) | Type of study | No. of participants or publications | Study population or Databases utilized | Treatment or Measurements of risk | Results |
|---|---|---|---|---|---|
| **R.J. Boyle et al (2011)** | RCT | 250 women-infant pairs | Pregnant women and their infants | LGG daily from 36 weeks gestation until delivery | Prenatal treatment with *Lactobacillus rhamnosus GG* was not sufficient for preventing eczema (RR 0.39) |
| **C.K. Dotterud et al (2010)** | RCT | 415 women-infant pairs | Pregnant and lactating women and their infants | Probiotic milk containing LGG and Bb-12 daily from 36 weeks of gestation to 3 months postnatal | Odds ratio for the cumulative incidence of AD was 0:51 in the probiotic group and the placebo group, respectively. Probiotics given to mothers reduced the cumulative incidence of AD. |
| **A. Huurre (2009)** | RCT | 171 women-infant pairs | Pregnant and lactating women with no past or current chronic or metabolic disease and their infants | LGG and Bb12 strains supplemented from first trimester until the end of exclusive breastfeeding | Atopic eczema was diagnosed at the age of 12 months in 9.7% of the infants in the probiotic group and in 17.6% of the infants in the placebo group (OR 0.3) |
| **S. Rautava et al (2012)** | RCT | 205 woman-infant pairs | Pregnant and lactating women with atopic sensitization and a history of or active allergic disease, and their infants | Dietary supplement with minerals, vitamins, and probiotic mix of LPR and BL999 or ST11 and BL999. Treated from 2 months before delivery until child was 2 months. | LPR + BL999 (OR 0.17) or ST11 + BL999 (OR 0.16) were both associated with a statistically significant reduction in the risk of developing eczema and chronically persistent eczema during the first 24 months of life compared with infants whose mothers received placebo |
| **K. Doege et al (2012)** | Systematic review and meta-analysis | 7 RCTs | PubMed and Ovid | Relative risk of 0.92 | Significant risk reduction by the administration of *Lactobacillus* in children age 2-7 but not for a mix of probiotics |
| **N. Foolad et al (2013)** | Systematic review | 20 RCTs and 1 follow up study | Medline, Cochrane Central Register of Controlled Trials and LILACS | N/A | *Lactobacillus rhamnosus GG* was the most effective in low risk atopic dermatitis whereas *L. rhamnosus* H019 was most effective in high risk of atopic dermatitis |
| **J.A. Mansfield et al (2014)** | Systematic review and meta- analysis | 27 total publications, 6 RCTs | EMBASE, PubMed, Medline, and Central | Relative risk of 0.74 (for the RCTs) | Use of probiotics supplementation beginning in gestation through the first 6 months of life has been shown to decrease incidence of atopic dermatitis to 26% |
| **C.A. Naaktgeboren (2010)** | Systematic review and meta-analysis | 39 total publications, 25 RCTs | PubMed and Cochrane | Odds ratio of 0.88 | Probiotic consumption during pregnancy is associated with a reduced risk of AD in infants |
| **M. Panduru et al. (2015)** | Systematic review and meta-analysis | 16 RCTs | PubMed, Scopus, Web of knowledge, EBSCO, ARTO, Google Scholar and ClinicalTrails.gov | Odds ratio of 0.70 | Probiotic administration has protective role in atopic dermatitis prevention especially when administered in the last weeks of pregnancy followed by the supplementation of infants during the first months of life. |
| **C. Pelucchi et al (2012)** | Systematic review and meta-analysis | 18 RCTs | Medline, EMBASE, and Cochrane Library | Relative risk of 0.80 | A moderate 20% decrease in atopic dermatitis due to probiotics is seen |

**Figure 3**: Quality Assessment of Reviews

| Study | K. Doege et al (2012) | N. Foolad et al (2013) | J.A. Mansfield et al (2014) | C. Naaktgeboren (2010) | M. Panduru et al (2015) | C. Pelucchi et al (2012) |
|---|---|---|---|---|---|---|
| Methodology described in detail | Yes | Yes | Yes | Yes | Yes | Yes |
| Mata-analysis | Yes | No | Yes | Yes | Yes | Yes |
| Majority RCTs | Yes | Yes | Yes | Yes | Yes | Yes |

**Figure 4**: Quality Assessment of Experiments

| Experiment | R.J. Boyle et al (2010) | C.K. Dotterud et al (2010) | S. Rautava et al (2012) | S.E. Scranton et al (2008) |
|---|---|---|---|---|
| Randomized | Yes | Yes | Yes | Yes |
| Randomization described | Yes | Yes | Yes | Yes |
| Double-blinded | Yes | Yes | Yes | Yes |
| Placebo-controlled | Yes | Yes | Yes | Yes |
| Dropouts described | Yes | Yes | Yes | Yes |

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## DISCUSSION

**Key findings:**
- Out of the 10 publications reviewed only 1 did not find a preventative association between probiotic use in pregnancy and infantile atopic dermatitis.
- 7 publications analyzed probiotic mixes while 3 researched individual strains and found *Lactobacillus* strains to be more effective than probiotic mixes.
- 7 publications analyzed probiotic mixes of *Lactobacillus* and *Bifidobacterium* strains and found the mixes beneficial.
- Prenatal and postnatal probiotic supplementation impacts infantile AD more than childhood AD.
- The majority of publications included postnatal supplementation of probiotics and some suggested that the postnatal supplementation during breastfeeding might have a larger impact than prenatal probiotic supplementation.
- The majority of our findings emphasized a need for more research on probiotics and atopic dermatitis

**Limitations of study:**
- The study populations in the RCTs were varied which can lead to differing results
- The treatments in the RCTs were varied which can lead to differing results
- Relatively few RCTs in the literature leading to
- Foreign language bias in our searches

**Strengths:**
- Only placebo-controlled, double-blinded, and randomized experiments were included into the structured literature review
- Only literature reviews on majorly RCTs were included into the structured literature review
- For one exception, all literature reviews were accompanied by meta-analyses

**Our Results Contextualized:**
- This structured literature review reflects the findings of other systematic reviews. Heterogeneity exists in the literature however, the majority of findings are reporting a positive association between probiotics and decreased incidences of atopic dermatitis.

**Future Implications:**
- As previously mentioned, incidences of allergic diseases are rising worldwide. Some risk factors are known; however, no cure has yet been discovered. In place of treatment, preventative measures have been proposed and are currently being researched.
- With more RCTs conducted, a clear relationship can be found. Probiotic supplements can become an affordable preventative treatment if they are proven to prevent the development of infantile and childhood atopic dermatitis.

## CONCLUSION

The majority of findings in the literature indicate that prenatal and postnatal probiotic supplements in pregnancy and breastfeeding have a preventative and protective effect on infantile and childhood atopic dermatitis. More research is necessary as heterogeneity can still be found in the results. More research on the differing effects of probiotic strains has also been proposed.

## ACKNOWLEDGEMENT

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