Can Breastfeeding Protect Babies From Asthma?
New results and current research from the CHILD Study

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Manitoba Breastfeeding Rounds – June 2017
“Human breastmilk is not only a perfectly adapted nutritional supply for the infant, but probably the most specific personalized medicine that he or she is likely to receive, given at a time when gene expression is being fine tuned for life.”

Victora et al. 
The Lancet Breastfeeding Series (2016)
Objectives

- Review previous research on the association of breastfeeding and asthma development

- Understand how breastfeeding mode, duration, and exclusivity modify the health effects of breastfeeding

- Identify bioactive components of human milk and describe their potential role in asthma development.

- Discuss opportunities for healthcare providers to support breastfeeding
Developmental Origins of...

**Allergies**
1 in 4 Canadians have seasonal allergies
1 in 13 have food allergies

Canadian Allergy, Asthma and Immunology Foundation & 2013 SCAAALAR survey

**Asthma**
1 in 6 Canadian children have asthma


**Obesity**
1 in 3 Canadian children are overweight

Overweight and obesity in children and adolescents. Results from the 2009 to 2011 Canadian Health Measures Survey
Canadian Asthma Primary Prevention Study (CAPPS)

- 545 high-risk infants born in 1995 (Manitoba & BC)
- Prenatal randomization to multifaceted intervention
- Clinical follow up: 1, 2, 7, 15 years (N=326)

Wheezing Risk Factors

- **More Wheeze:**
  - Boys
  - Winnipeg
  - Early atopy

- **Less Wheeze:**
  - Intervention Group
  - Exclusive breastfeeding >4m

... HOW?

(Azad et al. JAMA Pediatrics 2016)
The Canadian Healthy Infant Longitudinal Development (CHILD) Study

How do genes and the environment influence child health and development?

$30M Invested
500,000 Samples: Blood, Urine, Stool, Nasal Swabs, Dust, Breast Milk
200,000 Questionnaires
3600 Families
40+ Researchers
20+ Disciplines
5(+) Years Follow-Up
93% Retention

www.canadianchildstudy.ca

CHILD Study
HELP CHILDREN GROW UP HEALTHY
**Asthma**

Early infancy microbial and metabolic alterations affect risk of childhood asthma

Marie-Claire Arieta, {#2,5} Leah T. Siemsma, {#2,5} Pedro A. Dimitriu, {#3} Lisa Thorson, {#3} Shannon Russell, {#1,2} Sophie Yurist-Dutsch, {#1,2} Boris Kuzeljevic, {#3} Matthew J. Gold, {#1} Heidi M. Britton, {#1} Diana L. Lefebvre, {#1} Padmaa Subbarao, {#1} Piush Mandhane, {#1} Allan Becker, {#10} Kelly M. McGagny, {#10} Malcolm R. Sears, {#2} Tobias Kollmann, {#11} the CHILD Study Investigators, {#7} William W. Mohn, {#2,11} Stuart E. Turvey, {#1,11} B. Brett Finlay {#1,11}

![Graph showing microbial diversities](image)

“Infants at risk of asthma exhibited transient gut microbial dysbiosis during the first 100 days of life.”

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**Impact of maternal intrapartum antibiotics, method of birth and breastfeeding on gut microbiota during the first year of life: a prospective cohort study**

MB Azad, {#2,6} T Konya, {#6} BR Persaud, {#6} DS Guterman, {#6} RS Charl, {#1} C J Field, {#9} MR Sears, {#9} PJ Mandhane, {#9} SE Turvey, {#1} P Subbarao, {#1} AB Becker, {#1} JA Scott, {#1} AL Kuczyski, {#1} the CHILD Study Investigators

![Graph showing breastfeeding duration](image)

Breastfeeding favours: ↑ Bifidobacteria, ↓ Clostridium difficile, ↑↑ Diversity...
Research Questions

1) DOES breastfeeding protect against asthma?
   - Optimal dose, duration…?

2) HOW does breastfeeding protect against disease?

3) Why do effects VARY between mothers? studies?
   - Variation in milk? Feeding modes? Definitions? Analyses?

4) How can we SUPPORT mothers to achieve their breastfeeding goals?
Breastfeeding & Asthma

~30% reduced risk of “asthma” before 6 years
117 Studies

Limitations of previous studies:
- Defining breastfeeding
- Defining asthma
- High drop out rates
- Short follow-up
- Confounding factors

Limitations of previous studies:

Dogaru et al. AJE 2013
Breastfeeding in the CHILD Study

Breastfeeding in the CHILD Study

(Vehling, Azad et al. Unpublished)

(Vehling, Azad et al. Unpublished)
Breastfeeding in the CHILD Study

Lifetime Feeding?
Exclusive BF since birth according to maternal report
BUT
N=268 received formula in hospital

Mode of Feeding?
Direct breastfeeding?
Pumped breast milk?

(Vehling, Azad et al. Unpublished)
Breastfeeding in the CHILD Study

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Partial</th>
<th>Exclusive</th>
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<tr>
<td>In Hospital</td>
<td>3.4</td>
<td>24.7</td>
<td>71.9</td>
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<td>3 months</td>
<td>14.3</td>
<td>59.6</td>
<td>26.0</td>
</tr>
<tr>
<td>6 months</td>
<td>23.9</td>
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<td>12 months</td>
<td>54.0</td>
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</tr>
<tr>
<td>24 months</td>
<td>91.1</td>
<td></td>
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</tbody>
</table>

Formula vs. Food
Partial = Breast Milk + Solids (32%)
Formula (6%)
Solids + Formula (21%)

N=2773 Canadian infants from the CHILD Study
- 21% of mothers had asthma
- 46% breastfed >12 months
- 21% of infants wheezed in 1st year

Less Breastfeeding & More Infant Wheezing:
- Smokers (mother or others in household)
- Lower maternal education
- Young mothers (<25 years)
- Lower gestational age (<37 weeks)

Analysis controlled for these confounders
Among infants born to mothers with asthma, breastfeeding associated with significantly reduced risk of infant wheezing, after controlling for maternal smoking, education, age, etc.

**DOSE EFFECTS:** stronger association with longer / more exclusive breastfeeding:
- 62% reduced risk with 6 months exclusive BF
- 37% with partial BF (without formula)

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**“We are facing an Armageddon of COPD death...”**

“The public health implications are stark.

The extent of use of formula feeds described in this study is nothing short of a disgrace.

Although it is clear that there are some women who cannot breast feed for the best of medical reasons... there is no reason at all why more than half these mothers did not breast feed for more than a year.

Women with asthma need to understand the benefits to their child of avoiding formula.

Would it be too radical to suggest formula milk should be made prescription only for children of asthmatic mothers? Perhaps, but something needs to be done; and that effectively and soon.”
Research Questions

1) DOES breastfeeding protect against asthma?
   - Optimal dose, duration...?

2) HOW does breastfeeding protect against disease?

3) Why do effects VARY between mothers? studies?
   - Variation in milk? Feeding modes? Definitions? Analyses?

4) How can we SUPPORT mothers to achieve their breastfeeding goals?

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Physical Exercise: Breast vs. Bottle

- ↓ Rate of swallowing, interruption of breathing
- ↑ Negative pressure (98 mmHg; 3x higher)
- ↑ Sucking exercise (8 min; 2x longer)
- ↑ Ventilator efforts
- ↑ Lung capacity

Ogbuanu et al. Paediatrics 2009
"Milk is really a genius fluid that was outrageously understudied. If we can identify components of human breast milk that are important, then we can understand the wisdom of milk—and take advantage of them."

David Mills, UC Davis

Nature's first functional food
Breast milk feeds helpful microbes, fights harmful ones, provides immunity, and jump-starts a newborn's life.
**Milk Bioactives**

**CHILD Breast Milk (N~2800):**
- 1 sample per mother
- Mix of fore + hind milk, multiple feeds
- Median lactation = 16 weeks (IQR 14-19)

**Representative Subset (N=430):**
- Fatty Acids (C. Field, U. Alberta)
- Endocrine Hormones (C. Field, U. Alberta)
- Microbiota (E. Khafipour, U. Manitoba)
- Oligosaccharides (L. Bode, UC San Diego)
- Wish list: Toxins/Chemicals, Food antigens, Artificial Sweeteners, Cytokines...

**Human Milk Oligosaccharides (HMOs):**
- Non-digestible carbohydrates
- Structurally diverse
  - Cows: ~40 vs. Humans: >100
- Highly variable between mothers
- Small studies (N<50):
  - Possible associations with HIV transmission, allergy, infant adiposity
  - Maternal determinants (besides genetics) unknown

(Bode Glycobiology 2012 –“Every baby needs a sugar mama”)
HMOs in the CHILD Cohort

(Azad, Bode, Robertson, et al. Unpublished)
HMOs & Allergy?

N=430 dyads; 19 HMOs
Partial Least Squares Discriminant Analysis (PLS-DA) P<0.001 (robust to leave-one-out cross validation)

While no single HMO predicts food sensitization, the overall HMO profile is significantly associated with food sensitization.

(Azad, Sharma, Bode et al. Unpublished)

Milk Microbiota

- Human milk is not sterile!
  - Breastfed infants consume $10^5$–$10^7$ bacteria daily.

- Source of gut microbiota
  - Many health effects…

- A few small studies (N < 30):
  - Variation by birth mode, obesity, time postpartum, gestational age, genetics, country… ???
  - None examined infant health

(Hunt et al. PLOS One 2011)
Milk Microbiota Clusters?

Research Questions

1) **DOES** breastfeeding protect against allergy, asthma, obesity...?
   - Optimal dose, duration...?

2) **HOW** does breastfeeding protect against disease?
   - Milk bioactives? Epigenetics? Self regulation? Psychosocial effects?

3) **Why do effects VARY** between mothers? studies?
   - Variation in Milk Composition? Feeding Modes? Definitions? Analyses?

4) How can we **SUPPORT** mothers to achieve their breastfeeding goals?
Variation in “Breastfeeding” Definitions

*Adjusted for maternal age, ethnicity, asthma, smoking during pregnancy, postsecondary education, and gestational age.


Variation in Mode of Breastmilk Feeding

DBM = Direct Breast Milk
IBM = Indirect (pumped) Breast Milk

Compared to direct breastfeeding, any other mode of infant feeding was associated with an increased risk of possible or probable asthma by 3 years of age.

- Bioactivity of milk?
- Physical lung exercise?
- Skin-to-skin contact?
- Infant→Mother signalling?
- Toxins from plastic bottles?

*Adjusted for infant sex, maternal diagnosis of asthma, ethnicity, method of birth, daycare attendance, gestational age and solid food introduction; with multiple imputation of missing data.

(Klopp et al. submitted)
Variation in Milk Oligosaccharides, Fatty Acids...

**Research Questions**

1) **DOES** breastfeeding protect against asthma...?
   - Optimal dose, duration...?

2) **HOW** does breastfeeding protect against disease?

3) Why do effects **VARY** between mothers? studies?
   - Variation in Milk Composition? Feeding Modes? Definitions? Analyses?

4) How can we **SUPPORT** mothers to achieve their breastfeeding goals?
Supporting Breastfeeding

Compared to newborns who received formula supplementation, those who were exclusively breastfed in hospital had a 21% reduced risk of breastfeeding cessation over time. (HR 0.79; 95%CI: 0.72-0.88)

Newborn Feeding & Breastfeeding (in)Equity

(Vehling, Azad et al. Submitted)
Newborn Feeding & Breastfeeding (in)Equity

(Vehling, Azad et al. Submitted)

Inequity in breastfeeding duration reduced by 55% with exclusive breastfeeding in hospital.

Prenatal Care & Newborn Feeding

Chart review:
N=147 mother-infant dyads at HSC Winnipeg

Lower breastfeeding rates among women attending <5 prenatal care visits

(Coneys, Azad et al. Unpublished)
Breastfeeding

Mechanisms
• Gut Microbiota
• Epigenetics
• Metabolism
• Lung Function
• Immunity

Milk Composition
• Microbiota
• Oligosaccharides
• Immune Factors
• Nutrients
• Hormones
• Toxins

Maternal Factors
Modifiable: Obesity, Nutrition, Self-Efficacy, Smoking, Birth Mode, Pro/Antibiotics… Fixed: Age, Ethnicity, Genetics, Parity, Asthma…

Objectives

- Review previous research on the association of breastfeeding and asthma development
  - Protective. Limitations addressed by CHILD study.

- Understand how breastfeeding mode, duration, and exclusivity modify the health effects of breastfeeding
  - Dose effects. Mode matters. Formula (not food) diminishes benefits.

- Identify bioactive components of human milk and describe their potential role in asthma development.
  - Nutrients, microbiota, oligosaccharides… Highly variable. Fixed & modifiable factors.

- Discuss opportunities for healthcare providers to support breastfeeding
  - Prenatal (community) and early postpartum (hospital)
New Project!

“Breastfeeding is the responsibility of a society, not an individual woman.”
– Cesar Victora, Gairdner Laureate


Breastfeeding Education in Manitoba Schools

A Breastfeeding Information and Activity Kit for Secondary School Teachers

OPHA Breastfeeding Promotion Taskgroup

Ideas?
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Acknowledgements

Azad Lab
Faisal Atakora, Jana Slaught, Lorena Vehling, Michelle La, Kozeta Miliku, Deborah Chan, Hasantha Sinnock, Annika Klopp, Olivia Coneys

CHILD Study
Manitoba: Allan Becker, Rishma Chooniedass & Team
National: Malcolm Sears, Diana Lefebvre (McMaster) & Team

Collaborators
Atul Sharma, George & Fay Yee Centre for Healthcare Innovation
Ehsan Khafipour, Shirin Moosavi (U. Manitoba)
Catherine Field, Sue Goruck (U. Alberta)
Lars Bode, Bianca Robertson (U. California San Diego)
Nathan Nickel (Manitoba Centre for Health Policy / U. Manitoba)

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Questions?