Role of Early Life Environment in Shaping the Gut Microbiota

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HCEO Workshop: Microbiome & Health Disparities – November 2017
How the first nine months shape the rest of your life
The new science of fetal origins

The first 100 days
“Developmental Origins”

- **1990s: Fetal Origins of Adult Disease (FOAD)**
  Environmental exposures during **fetal life** influence adult health

- **2000s: Developmental Origins of Health and Disease (DOHaD)**
  Both the **prenatal and postnatal** environment shape developmental trajectories that influence health throughout the lifecourse
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
DOHaD: What are the important *early-life exposures*?
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
**Prenatal Exposures**

- Home Environment (Chemicals, Tobacco Smoke, Pets, etc.)
- Air Pollution (GIS Modelling)
- Maternal Nutrition
- Child Nutrition
- Breastfeeding
- Viral Infections
- Maternal Stress

**Postnatal Exposures**

- Birth
- 3 month
- 12 month
- 3 year
- 5 year

**Prevalent Period:** 2009-2012

- Clinic Visit
- Hospital Data
- Home Visit
- Clinic Visit
- Clinic Visit
- Clinic Visit
Perinatal Exposures

- **Cesarean Section** (WHO 2013)
  - Brazil 56%, USA 33%, Canada 27%, Sweden 17%

- **Intrapartum Antibiotics** (CDC)
  - 25% of US population (1 million women annually) exposed for GBS prophylaxis

- **Infant Feeding:** (CDC 2008)
  - WHO recommends: exclusive breastfeeding for 6 months, continued BF to 2 years+
  - Most US infants initiate breastfeeding, BUT
    - Within the first week, >50% are receiving formula
    - By 6 months, <50% are breastfed at all

Asthma?
Cesarean Section & Asthma

Meta-analysis of
23 studies:

20% increased risk
in children delivered by
Cesarean section.

(Thavagnanam et al. Clin Exp Allergy. 2008 38:4)
Antibiotics & Asthma

Meta-analysis of 20 studies:

50% increased risk following infant antibiotic* exposure

(Murk et al. 2011)

*Few studies on intrapartum antibiotics
Breastfeeding & Asthma

Meta-analysis of 117 Studies:

~30% reduced risk in breastfed infants

(Dogaru et al. AJE 2013)
Breast(milk)feeding & Asthma

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?
- Milk/skin microbiota?
- Physical lung exercise?
- Infant→Mother signalling?
- Toxins from bottles?

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

*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. J Pediatrics 2017)
Early Life Exposures

- **Pets** during infancy
  - 66% ↓ risk of asthma (age 12) (Hesselmar et al. Clin Exp Allergy 1999)

- **Tobacco smoke** exposure; prenatal and postnatal:
  - 22% ↑ risk of asthma (age 6+) (Silvestri et al. Pediatri Pulmonol 2015)

- **Maternal depression / anxiety:**
  - 25% ↑ risk of asthma (age 7) (Kozyrskyj et al. Am J Respir Crit Care Med. 2008 177:2)
DOHaD: Asthma, Allergies & Obesity

- Early **risk** factors:
  - Cesarean section
  - Antibiotics
  - Tobacco smoke
  - Maternal stress

- Early **protective** factors:
  - (Direct) Breastfeeding
  - Pets

**Biological Mechanisms?**
Gut Microbiota

- Complex “super organ” of ~100 trillion commensal microbes living in the gastrointestinal tract
- Prevent colonization by pathogens
- Educate the developing immune system
- Influence nervous system: ‘gut-brain-axis’
- Contribute to host metabolism
  - Digestion of complex carbohydrates
  - Vitamin production
  - Energy harvest
100 TRILLION
The human microbiome is made up of more than 100 trillion bacteria, fungi, protozoa, and viruses that live on and inside the body.

10X
We have 10 times more microbial cells in our body than human cells and the majority live in our guts—especially the large intestine, or colon.

The bacteria in our microbiomes are essential to human health and aid in biological processes such as:

- **E=mc²**
  - Extracting energy from food

- **FOLATE**
  - Producing essential vitamins

- **BIOFLAVONOID**
  - Regulating our immune system

- **NIACIN**
  - Regulating our glucose levels and metabolism

- **保护我们免受致病微生物的侵害**

**SYMBIOTIC**
The beneficial and symbiotic relationship between humans and our microbiomes has likely evolved and changed throughout human development.

**Personal microbial communities shift throughout a person’s life and are influenced by diet, exercise, medications such as antibiotics, pathogens, and other environmental factors.**

Early infancy microbial and metabolic alterations affect risk of childhood asthma

Marie-Claire Arrieta,1,2,* Leah T. Stiensma,2,3* Pedro A. Dimitriu,2 Lisa Thorson,1 Shannon Russell,1,2 Sophie Yurist-Doutch,1,2 Boris Kuzeljevic,3 Matthew J. Gold,4 Heidi M. Britton,1 Diana L. Lefebvre,5 Padmaja Subbarao,6,7 Piush Mandhane,8,9 Allan Becker,10 Kelly M. McNagny,4 Malcolm R. Sears,5 Tobias Kollmann,3,11 the CHILD Study Investigators,† William W. Mohn,2 Stuart E. Turvey,3,11§ B. Brett Finlay1,2,12‡
“Infants at risk of asthma exhibited transient gut microbial dysbiosis during the first 100 days of life.”
Human microbiota: onset and shaping through life stages and perturbations.
(Ottman et al. Front Cell Infect Microbiol 2012)
What early life exposures shape the gut microbiome?
What early life exposures shape the gut microbiome?

- **Birth**
  - Vaginal delivery
  - Cesarean delivery

- **Infant (<1 year)**
  - Milk consumption
  - Solid food introduction

- **Toddler (1–3 years)**
  - Full adult diet

**Maternal factors**
- Gut microbiota
- Vaginal infection
- Periodontitis

**Postnatal factors**
- Antibiotics
- Breast-feeding
- Host genetics
- Environment

(Tamburini et al. 2017 Nat Med Rev)
Gut Microbiota: Development & Health

Increased risk of disease

Factors influencing mother gut microbiota
- Pregnant weight gain
- Antibiotic exposure
- Hygiene and social condition
- Bacteria in amniotic fluid
- Smoking in pregnancy
- Gestational metabolic abnormalities

Accumulation enhances the development of dysbiotic microbiota

Dysbiotic microbiota of the mother
- Antibiotics
- Urban environment / overly hygienic lifestyle

Genetic predisposition
- Small family size / no pets
- Non-optimal nutrition / processed foods
- Pre-term birth
- Caesarian delivery
- Formula feeding

Optimal nutrition of the mother
- Optimal nutrition / fresh foods
- Vaginal delivery
- Term birth
- Large family size / pets

Normal microbiota of the healthy mother
- Rural environment / contact with environmental microbes

Factors influencing child gut microbiota
- High-fat mother’s milk
- Intensive care at birth
- Delivery and feeding modality
- Weight at birth
- Gestational age

Health

(Putignani et al. Pediatric Research 2014 76:1)

(Nylund et al. Proc Nut Soc 2014)
**MICROBIOTA PROFILE**

**RISK FACTORS:**
- Birth Mode
- Infant Diet
- Antibiotic Use
- Environment

**HEALTH OUTCOMES**
- Allergic Disease
- Immune Function
- Obesity...

**Fecal Sample** → Gut Microbes → Microbial Genomes

**DNA sequence alignment**

**MiSeq**

**16S rRNA**

**Phylogenetic Analysis**

**PIs**
- James Scott (Toronto)
- Anita Kozyrskyj (Alberta)
Vaginally-delivered infants acquire gut microbiota from birth canal, C-section infants acquire microbiota from skin

(Dominguez-Bello et al. PNAS 2010 107:26) (Madan et al. JAMA Pediatrics 2016)
Perinatal Exposures & Gut Microbiota

Gut microbiota of healthy Canadian infants: profiles by mode of delivery and infant diet at 4 months

Meghan B. Azad PhD, Theodore Konya MPH, Heather Maughan PhD, David S. Guttman PhD, Catherine J. Field PhD, Radha S. Charl MD, Malcolm R. Sears MB, Allan B. Becker MD, James A. Scott PhD, Anita L. Kozynskij PhD, on behalf of the CHILD Study Investigators

Background: The gut microbiota is essential to human health throughout life, yet the acquisition and development of this microbial community during infancy remains poorly understood. Meanwhile, there is increasing concern over many rates of cesarean delivery and insufficient exclusive breastfeeding of infants in developed countries. In this article, we characterize the gut microbiota of healthy Canadian infants and describe the influence of cesarean delivery and formula feeding.

Methods: We included a subset of 24 term infants from the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort. Mode of delivery was obtained from medical records, and mothers were asked to report on infant diet and medication use. Fecal samples were collected at 4 months of age, and we characterized the microbiota composition using high-throughput DNA sequencing.

Results: We observed high variability in the profiles of fecal microbiota among the infants. The profiles were generally dominated by Actinobacteria (mainly the genus Bifidobacterium) and Firmicutes (with diverse representation from numerous genera). Compared with breastfed infants, formula-fed infants had increased richness of species, with overrepresentation of Clostridium difficile. Escherichia-Shigella and Bacteroides species were underrepresented in infants born by cesarean delivery. Infants born by elective cesarean delivery had particularly low bacterial richness and diversity.

Interpretation: Those findings advance our understanding of the gut microbiota in healthy infants. They also provide new evidence for the effects of delivery mode and infant diet as determinants of this essential microbial community in early life.

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, a T Konya, a RR Persaud, a DS Guttman, a RS Charl, a CJ Field, a MR Sears, b PJ Mandhane, a SE Turvey, a P Subbarao, a AB Becker, b JA Scott, b AL Kozynskij, a the CHILD Study Investigators

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Correspondence: AL Kozynskij, PhD, Department of Pediatrics, University of Alberta, 3-527 Edmonton Clinic Health Academy, 11405 – 87th Avenue, Edmonton, AB, Canada T6G 1C9. Email: kozynskij@ualberta.ca

Acepted 17 Jun 2013. Published Online 28 September 2015.
Intrapartum Antibiotic Prophylaxis (IAP) administered for:
- ALL Cesarean (CS) deliveries
- 27% of Vaginal deliveries:
  - GBS (76%)
  - PROM (24%)

(Azad et al. BJOG 2015)
C-Section, Antibiotics, Breastfeeding & Microbiota

Microbiota dysbiosis after CS, regardless of feeding

(Azad et al. BJOG 2015)
C-Section, Antibiotics, Breastfeeding & Microbiota

Microbiota “recovery” in breastfed infants

(Azad et al. BJOG 2015)
Increased weight gain by C-section: Functional significance of the primordial microbiome

Keith A. Martinez II,1,2a Joseph C. Devlin,1,2a Corey R. Lacher,1 Yue Yin,1 Yi Cai,1 Jincheng Wang,1 Maria G. Domínguez-Bello1,2b

Epidemiological evidence supports a direct association between early microbiota impact—including C-section—and obesity. We performed antibiotic-free, fostered C-sections and determined the impact on the early microbiota and body weight during development. Mice in the C-section group gained more body mass after weaning, with a stronger phenotype in females. C-section-born mice lacked the dynamic developmental gut microbiota changes observed in control mice. The results demonstrate a causal relationship between C-section and increased body weight, supporting the involvement of maternal vaginal bacteria in normal metabolic development.
Intestinal microbiome is related to lifetime antibiotic use in Finnish pre-school children

Katri Korpela¹, Anne Salonen¹, Lauri J. Virta², Riina A. Kekkonen³, Kristoffer Forslund⁴, Peer Bork⁴ & Willem M. de Vos¹,⁵,⁶

Macrolide (M) Antibiotics:
- ↓ Actinobacteria (Bifidobacteria)
- ↑ Proteobacteria, Bacteroidetes
- Recovery by 12 months
(No phylum-level effect from Penicillins (P))

Figure 1 | Microbiota composition in 257 fecal samples as arranged per group. C denotes control group, no antibiotics for the past 2 years and in total <1 course per year of life on average. E denotes early-life exposure group, no antibiotics for the past 2 years and >1 course per year of life on average. M6 denotes macrolide course within 6 months; M12 denotes macrolide course within 6–12 months; M24 denotes macrolide course within 12–24 months. P6, P12 and P24 denote penicillin courses within 6, 6–12 and 12–24 months, respectively. (a) Phyla composition. (b) Genus-level microbiota composition according to PCoA analysis. The background colour indicates interpolated time since the last macrolide course.

N=142 children (Finland)
Microbiota “recovery”?  

- Antibiotics used to disrupt microbiota in newborn mice
- Microbiota **recovered** after antibiotic exposure, but immune function and adiposity were **permanently** altered
Antibiotics, birth mode, and diet shape microbiome maturation during early life

Nicholas A. Bokulich, Jennifer Chung, Thomas Battaglia, Nora Henderson, Melanie Jay, Huilin Li, Amon D. Lieber, Fen Wu, Guillermo I. Perez-Perez, Yu Chen, William Schweizer, Xuhui Zheng, Monica Contreras, Maria Gloria Dominguez-Bello, Martin J. Blaser

N=43 infants (USA)

Normal development of gut microbiota, birth – 23 months

Fig. 1. Microbial and dietary succession viewed over the first 2 years of life. Mean relative abundance (RA) of fecal bacteria at the genus level at each month of life, for taxa with >1% mean RA across all samples. (A) All 43 infant subjects during the first 2 years of life. (B to E) The first 6 months of life for the...
Antibiotics, birth mode, and diet shape microbiome maturation during early life


Differences in microbiome development by birth mode and diet

Fig. 1. Microbial and dietary succession viewed over the first 2 years of life. Mean relative abundance (RA) of fecal bacteria at the genus level at each month of life, for taxa with >1% mean RA across all samples. (A) All 43 infant subjects during the first 2 years of life. (B to E) The first 6 months of life for the.
Pets & Microbiota

Infants living with pets have: (Azad et al AACI 2013)

- ↑ gut microbiota diversity
- Different gut microbiota composition

↑ Peptostreptococcaceae (including C. difficile)
↑ Clostridiaceae
↑ Veillonaceae (D)
↑ Coprococcus
↓ Bifidobacteriaceae (C)
↓ Eggerthella (D)

“Say Hello to the 100 Trillion Bacteria That Make Up Your Microbiome”
May 15, 2013 ~ NYTimes Magazine
MICHAEL POLLAN
Smoking & Microbiota?

- Second-hand smoke induced significant changes in gut microbiota in mice
  (Wang et al. World J Gastroenterol 2012)

- Maternal smoking during pregnancy associated with altered human infant gut microbiota profiles at birth.
  (Gosalbes et al. Clin Exp Allergy 2012)
Stress & Microbiota

- No (?) human evidence yet, but...


Breastfeeding favours:
↑ Bifidobacteria, ↓ Clostridium difficile, ↓↑ Diversity…

(Azad et al. CMAJ 2013, and BJOG 2015)
DOHaD: Asthma, Allergies & Obesity

- Early risk factors:
  - Cesarean section
  - Antibiotics
  - Tobacco smoke
  - Maternal stress

- Early protective factors:
  - (Direct) Breastfeeding
  - Pets
“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
DID YOU EVER WONDER WHAT’S IN... ?

**Breastmilk**

**PLUS:**

- Probiotic Bacteria
- Prebiotic Oligosaccharides
Probiotics:
Live beneficial bacteria

Prebiotics:
Non-digestible carbohydrates that select for beneficial bacteria
WHAT'S IN HUMAN MILK

Human milk oligosaccharides (HMOs) are food for friendly bacteria like *Bifidobacterium infantis*. Shorter chain HMOs in particular are almost entirely consumed by this microbe.

(Petherick *Nature* 2010)
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”)
(Bode Glycobiology 2012 –“Every baby needs a sugar mama”)
Human Milk Oligosaccharides (HMOs)

N=410 mothers (9 countries)

(McGuire et al. AJCN 2017)
HMOs in the CHILD Cohort

**Absolute HMO Concentration (nmol/mL)**

**Relative HMO Composition (%)**

- **HMOs:**
  - 2,3-FL
  - 3FL
  - LNT
  - 3,6-GL
  - DFLac
  - 6,8-SIL
  - LNT
  - LNFP_I
  - LNFP_II
  - LNFP_III
  - LSTb
  - LSTc
  - DFLNT
  - LNH
  - GSLNT
  - FLN
  - DFLNH
  - FDSL
  - DGLNH

(Lars Bode, Bianca Robertson, Azad et al. Unpublished)
Milk Microbiota

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

- Source of gut microbiota

- 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 in the CHILD Cohort

(Shirin Moossavi, Ehsan Khafipour, Azad et al. Unpublished)
Association Between Breast Milk Bacterial Communities and Establishment and Development of the Infant Gut Microbiome

N=107 mother-infant pairs (USA)
What early life factors contribute to health disparities?
Suboptimal breastfeeding & child mortality

All causes attributable to Suboptimal breastfeeding
Both sexes, Under 5 years, 2013, Percent of total deaths

http://vizhub.healthdata.org/gbd-compare
Breastfeeding Inequities

Less Breastfeeding:
- Lower education
- Maternal obesity
- Maternal smoking
- First Nations Ethnicity
- Younger maternal age

More Breastfeeding:
- Vancouver

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<thead>
<tr>
<th>Site</th>
<th>N</th>
<th>Exclusive BF at 6 months %</th>
<th>p</th>
<th>Any BF at 12 months %</th>
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<tr>
<td>Edmonton</td>
<td>781</td>
<td>15.2 **</td>
<td>***</td>
<td>35.9 ***</td>
<td>***</td>
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<td>Toronto</td>
<td>777</td>
<td>16.6</td>
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<td>37.4</td>
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<td>Vancouver</td>
<td>740</td>
<td>25.3</td>
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<td>60.9</td>
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<td>Winnipeg</td>
<td>998</td>
<td>16.3</td>
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<th>Maternal age (years)</th>
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<th>Exclusive BF at 6 months %</th>
<th>p</th>
<th>Any BF at 12 months %</th>
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<tr>
<td>&lt;30</td>
<td>991</td>
<td>12.8 ***</td>
<td>***</td>
<td>32.6 ***</td>
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<td>30 to 35</td>
<td>1372</td>
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<td>35+</td>
<td>910</td>
<td>23.6</td>
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<td>49.8</td>
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<th>Pre-pregnancy BMI (kg/m²)</th>
<th>N</th>
<th>Exclusive BF at 6 months %</th>
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<td>Normal: &lt;25</td>
<td>1863</td>
<td>19.6 **</td>
<td>**</td>
<td>49.8 ***</td>
<td>***</td>
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<td>Overweight: ≥25 - 30</td>
<td>633</td>
<td>18.9</td>
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<td>43.9</td>
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<td>Obese: ≥30</td>
<td>440</td>
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<td>27.0</td>
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<th>Ethnicity</th>
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<th>Any BF at 12 months %</th>
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<td>Asian</td>
<td>508</td>
<td>19.5</td>
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<td>49.0 *</td>
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<td>Caucasian</td>
<td>2359</td>
<td>18.7</td>
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<td>42.8</td>
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<td>First Nations</td>
<td>143</td>
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<td>Other</td>
<td>225</td>
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<td>39.6</td>
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<th>Education</th>
<th>N</th>
<th>Exclusive BF at 6 months %</th>
<th>p</th>
<th>Any BF at 12 months %</th>
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<tr>
<td>≤ High school</td>
<td>280</td>
<td>8.7 ***</td>
<td>***</td>
<td>24.5 ***</td>
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<td>Some post-secondary</td>
<td>466</td>
<td>15.1</td>
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<td>Post-graduate</td>
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<td>23.6</td>
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<td>55.8</td>
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Compared to newborns who received formula supplementation, those who were exclusively breastfed in hospital breastfed 4 months longer and had a 21% reduced risk of breastfeeding cessation over time. (HR 0.79; 95%CI: 0.72-0.88)
Newborn Feeding & Breastfeeding (in)Equity

Newborn Feeding in Hospital:

- Breastfeeding + Formula

**Median Breastfeeding Duration (months):**

- Overweight Low Education: N=244
- Normal Weight Low Education: N=246
- Overweight High Education: N=586
- Normal Weight High Education: N=1046

Equity Gap with Formula Supplementation = 6.7 months

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

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

(Vehling, Azad et al. Submitted)
Early risk factors:
- Cesarean section
- Antibiotics
- Tobacco smoke
- Maternal stress

Early protective factors:
- (Direct) Breastfeeding
- Pets
Unanswered Questions…

- What is a ‘healthy microbiome’?

- What are the long-term health effects of microbiota “dysbiosis” resulting from early life exposures?

- **HOW** do microbiota influence disease risk?

- How can we **prevent** gut microbiota dysbiosis?
  - Vaginal delivery, **breastfeed**, avoid unnecessary antibiotics…

- How can we **repair** gut microbiota dysbiosis?
  - “Vaginal Seeding” after CS? **Breastfeed**? Pre/probiotics? Fecal Transplants?

- How can we target gut microbiota (in early life) to **reduce health disparities**?
Breastfeeding

Milk Composition

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

Interventions

Maternal Factors

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

Allergies, Asthma, Obesity, Diabetes, Cognitive Development…

Developmental Origins of CHILD HEALTH & Disease
Meghan Azad, PhD

Milk Composition
- Microbiota
- Oligosaccharides
- Immune Factors
- Fatty Acids
- Hormones
- Vitamins

Breastfeeding

Milk Composition

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

Interventions

Maternal Factors

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

Developmental Origins of CHILD HEALTH & Disease
Meghan Azad, PhD
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National: Malcolm Sears (McMaster) & Team
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(U. Toronto) & Team

Collaborators
Ehsan Khafipour, Shirin Moosavi (U. Manitoba)
Lars Bode (U. California San Diego)
“If breastfeeding did not already exist, someone who invented it today would deserve a dual Nobel Prize in medicine and economics.

Breastfeeding is a child’s first inoculation against death, disease, and poverty, but also their most enduring investment in physical, cognitive, and social capacity.”

Keith Hudson
VP Human Development
World Bank Group
Breastfeeding in the CHILD Study

N=3139 (Formula), 3159 (Any BF), 3057 (Exclusive BF)

(Vehling, Azad et al. Unpublished)