AllerGen

Allergy, Genes and Environment Network

Le réseau des allergies, des gènes et de l'environnement

CHILD: The Canadian Healthy Infant Longitudinal Development study:

NFASt Workshop June 23 2015

Canada

The origins of the CHILD study: converging research questions

Allergy Genes & Environment Network (AllerGen) of Centres of Excellence:

What are the underlying causes of the epidemic of allergic diseases, including asthma?

Health Canada / CIHR:

What impact does the built environment have on the health of the growing child, especially allergies and asthma?

The DOHaD Hypothesis

Environmental influences during pre- and post-natal life induce changes leading to disease susceptibility (possibly through epigenetic mechanisms)

Factors Critical to the Development of Allergy & Asthma

- Genetics
- Environmental

gene X environment

X time

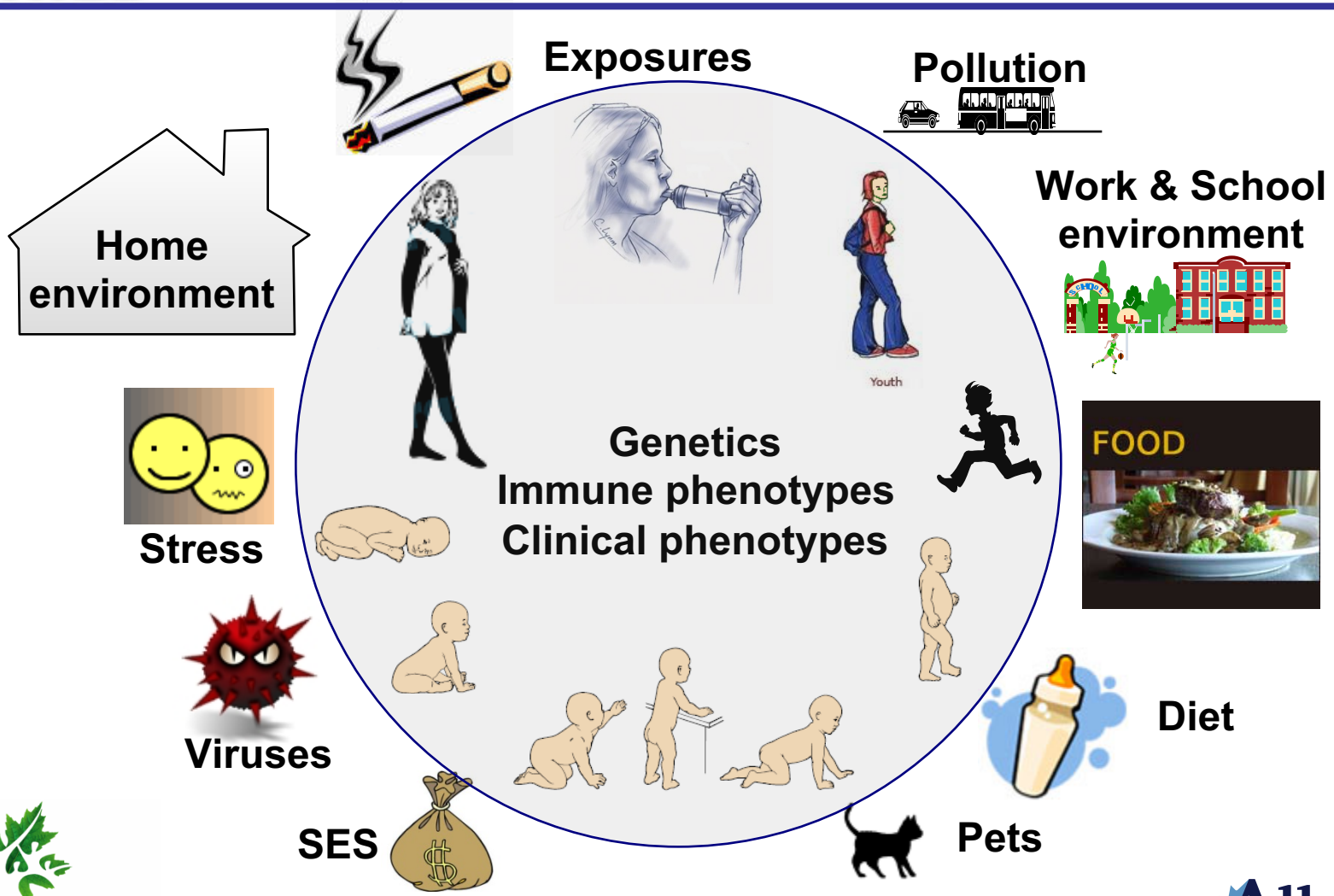
Development of Allergy

- Is there a "Window of Opportunity" during pregnancy and in early life that defines the likelihood of developing allergy?

Development of Allergy

- What are the critical early life events that influence development of allergic diseases?

CHILD Study www.canadianchildstudy.ca



Canadian Healthy Infant Longitudinal Development

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

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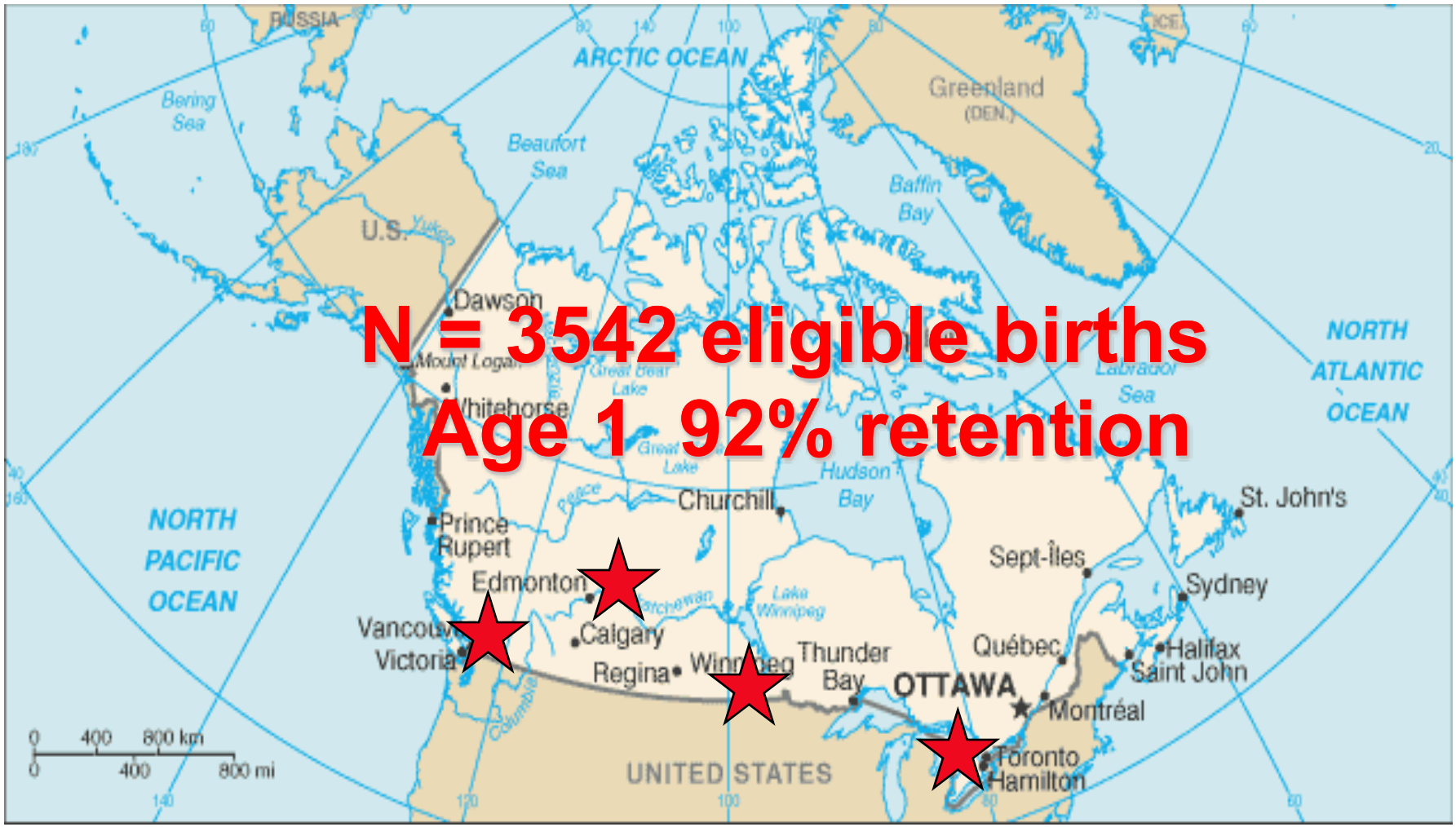
CHILD Outcomes

- The study is powered on the primary outcome of diagnosed asthma at 5 years
  - Intermediate outcomes of food allergy, allergic eczema, atopy and recurrent wheeze will be assessed throughout

CHILD study sites: 3629 families



CHILD outcomes: Age 1

Age 1 assessments completed

Fall 2013 (age 3, fall 2015):

Skin test positive to:

Foods	11.5%
Inhalants	5.1%

CHILD outcomes Age 1

Skin test positives to food - Most Common

1. Milk
2. Egg
3. Peanut
4. Soy
5. Wheat

5%

CHILD Study

www.canadianchildstudy.ca

Exposures

Pollution

Home environment

Work & School environment

Stress

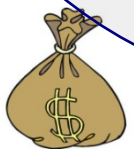
Genetics
Immune phenotypes
Clinical phenotypes

Microbes

Viruses

Diet

SES



Pets

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Canadian Healthy Infant Longitudinal Development

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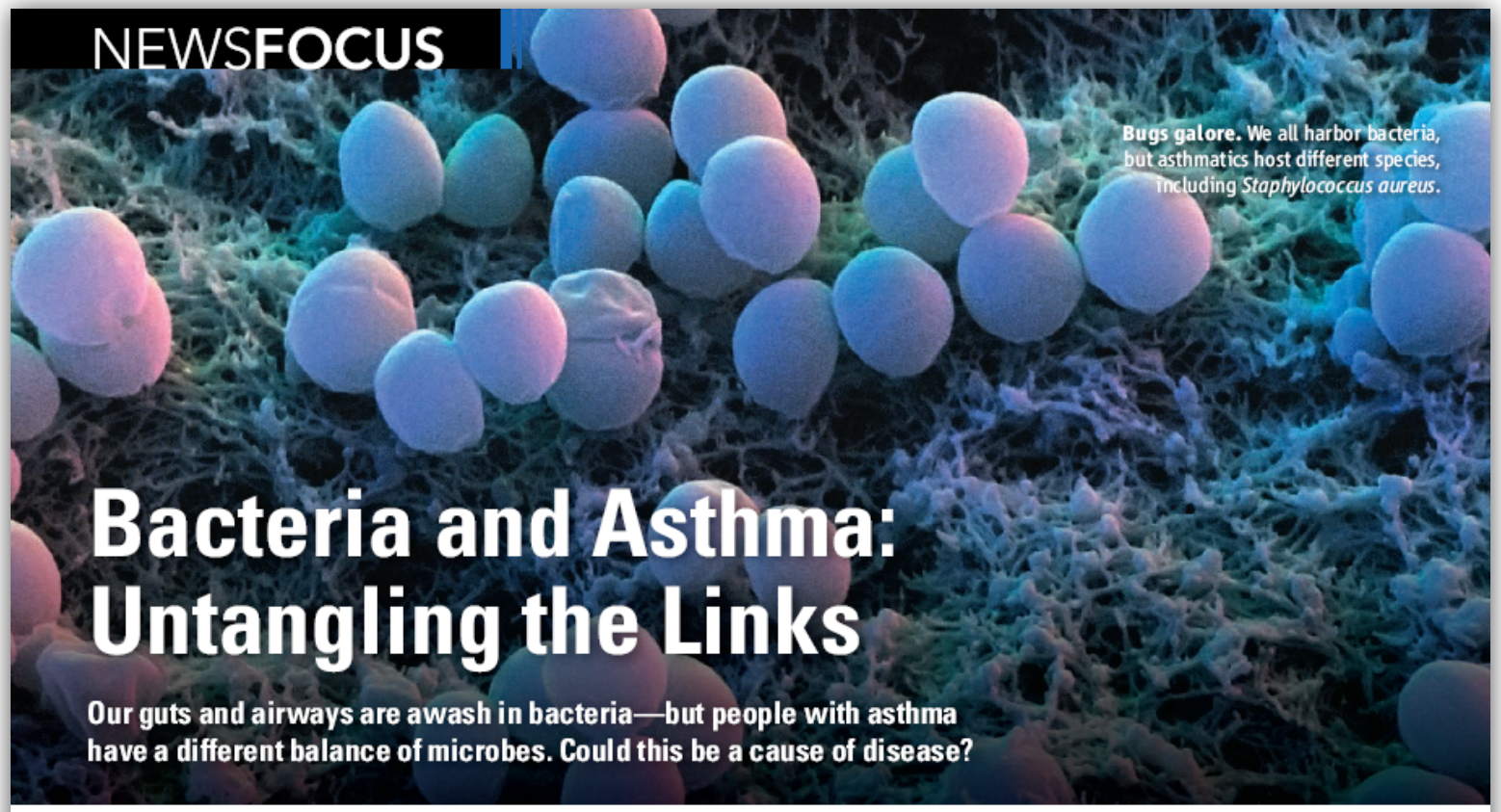
Discoveries from Dirty Diapers: Environmental Exposures and the Infant Gut Microbiome

Meghan Azad, PhD
Postdoctoral Fellow
University of Alberta



Bugs galore. We all harbor bacteria, but asthmatics host different species, including *Staphylococcus aureus*.

Bacteria and Asthma: Untangling the Links

Our guts and airways are awash in bacteria—but people with asthma have a different balance of microbes. Could this be a cause of disease?

SIX YEARS AGO, GARY HUFFNAGLE, AN immunologist at the University of Michigan, Ann Arbor, conducted an experiment that reflects what happens to many of us early in life. He exposed mice to a triple whammy: yeast in their intestines, mold spores up their noses that migrated down the airways, and an antibiotic drug. The animals began showing signs of asthma; blood tests revealed disruption of their immune systems.

"They developed some fairly wicked

ean section, who experience a more sterile entry into the world than those born vaginally, are more likely to get asthma. So are young children treated with many courses of antibiotics. Along with animal studies, these observations suggest that the balance of bacteria and other microbes help guide immune development—and that when the balance is disrupted, disease may follow.

The picture can be dishearteningly complicated. Thousands of species of bacte-

who stay healthy. "It's really coming down to the bacterial community structure, who's there, and in what numbers, and where," Huffnagle says. Cataloging these inhabitants is a new frontier.

Lungs and guts

For many years Hans Bisgaard, a pediatrician at the University of Copenhagen, was puzzled by a classic feature of asthma: Very young children with the disease have abun-

CMAJ RESEARCH

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. Chari MD, Malcolm R. Sears MB, Allan B. Becker MD, James A. Scott PhD, Anita L. Kozyrskyj PhD, on behalf of the CHILD Study Investigators

See related commentary by Song and colleagues on page 373 and at www.cmaj.ca/lookup/doi/10.1503/cmaj.130147

Abstract

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 rising 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: These 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.

Competing interests: Allan Becker is an advisory board member for Merck, Novartis and AstraZeneca; his institution has received research grants from Merck and AstraZeneca. No competing interests were declared by the other authors.

This article has been peer reviewed.

Additional CHILD Study Investigators are listed at the end of the article.

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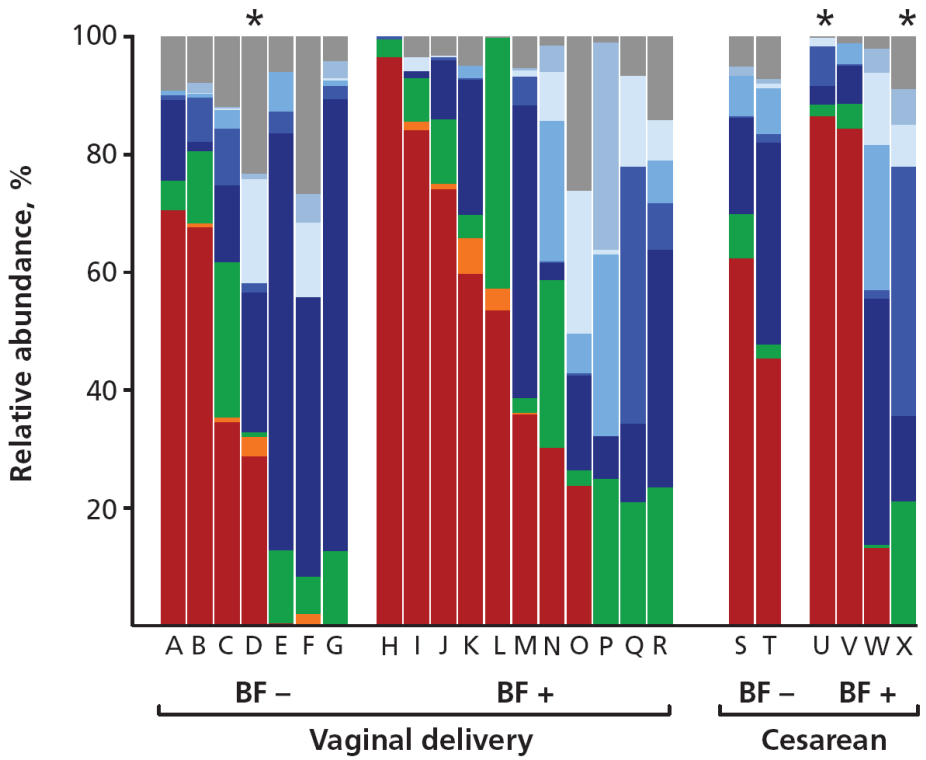


Each column = 1 infant
BF = breastfeeding

(Azad et al. *CMAJ* 2013)

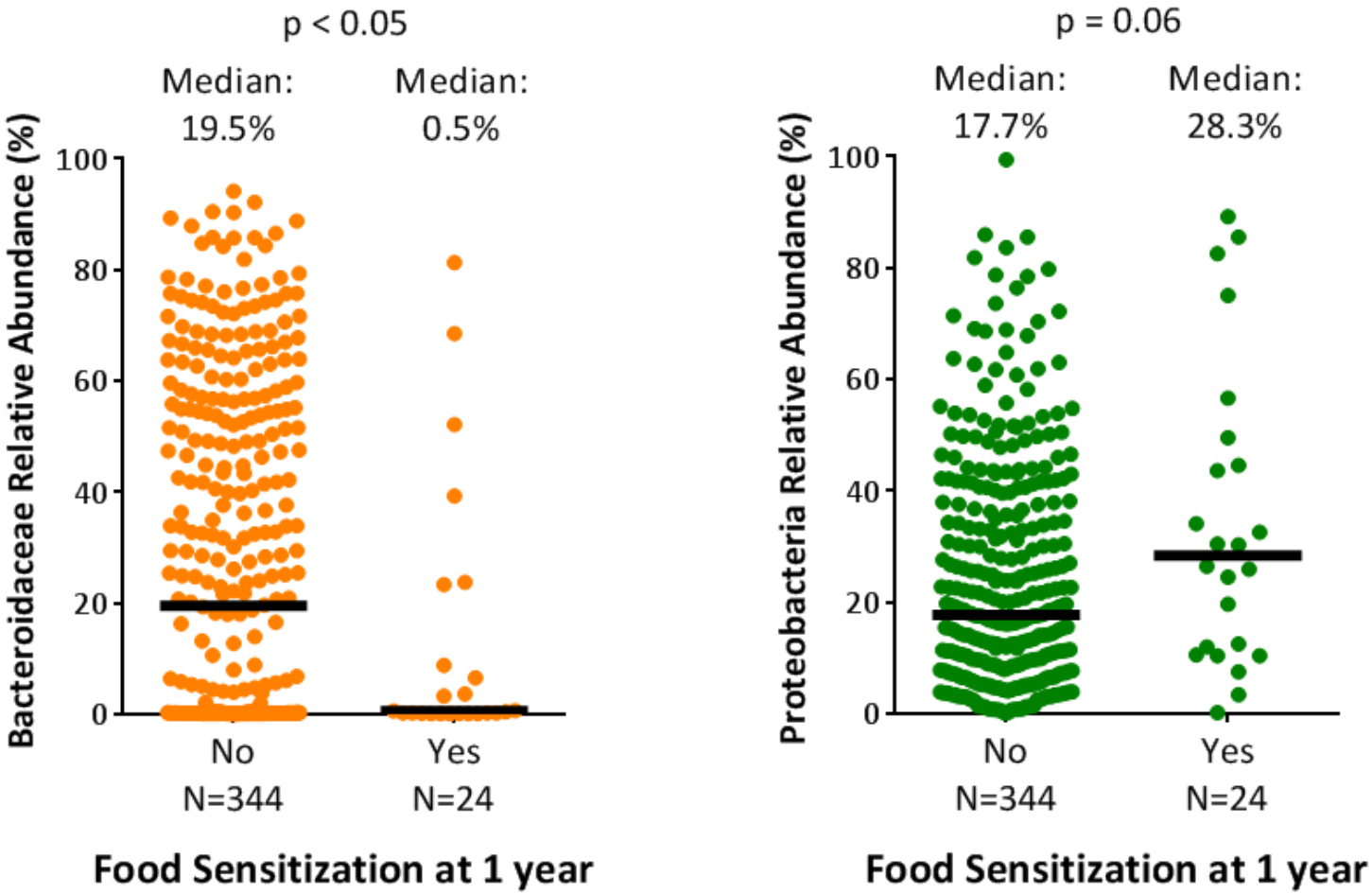
Major Findings:

- **Cesarean section:**
  ↓ Bacteroidetes
- **Breastfeeding:**
  ↓ Richness

Exposure	No. of infants	Richness score,* mean ± SD
Diet at 4 mo		
Exclusively breastfed	10	9.0 ± 4.1
Partially breastfed	5	12.6 ± 5.3
Not breastfed	9	15.0 ± 4.0

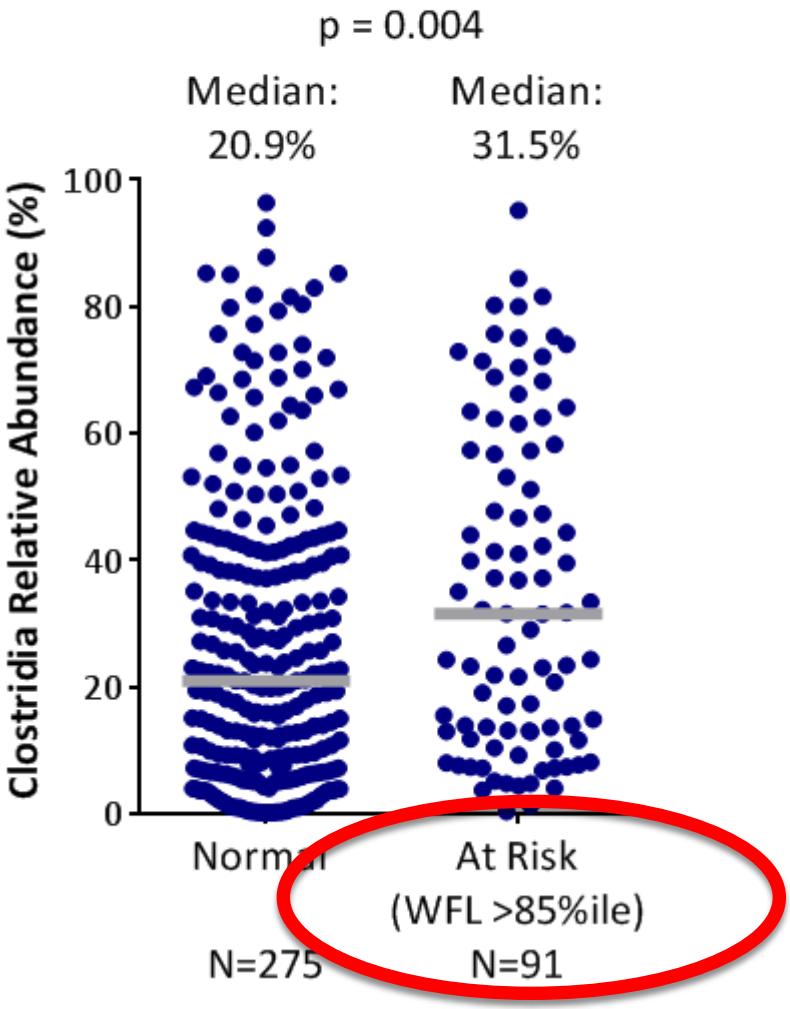
New data on Food Sensitization at age 1:

Bacteroidaceae Proteobacteria

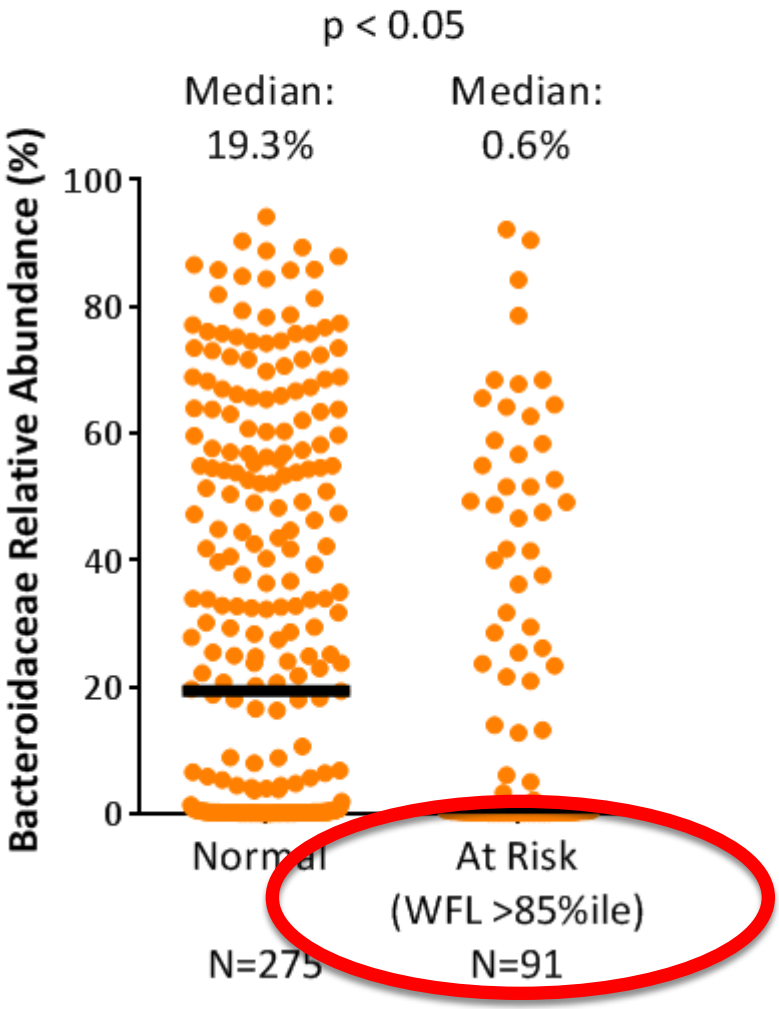


Overweight at 3 months :

Clostridia



Bacteroidaceae



CHILD Study LEGACY

Asthma, food and other allergy

- New knowledge – development of disease, gene-environment interactions, epigenetics – psycho-social effects, built environments
- Enhance understanding of personalized medicine
- Provide a basis for personalized health management based on genetics and potential where "environmental" modification is possible