Vaginal Seeding and Placentophagy

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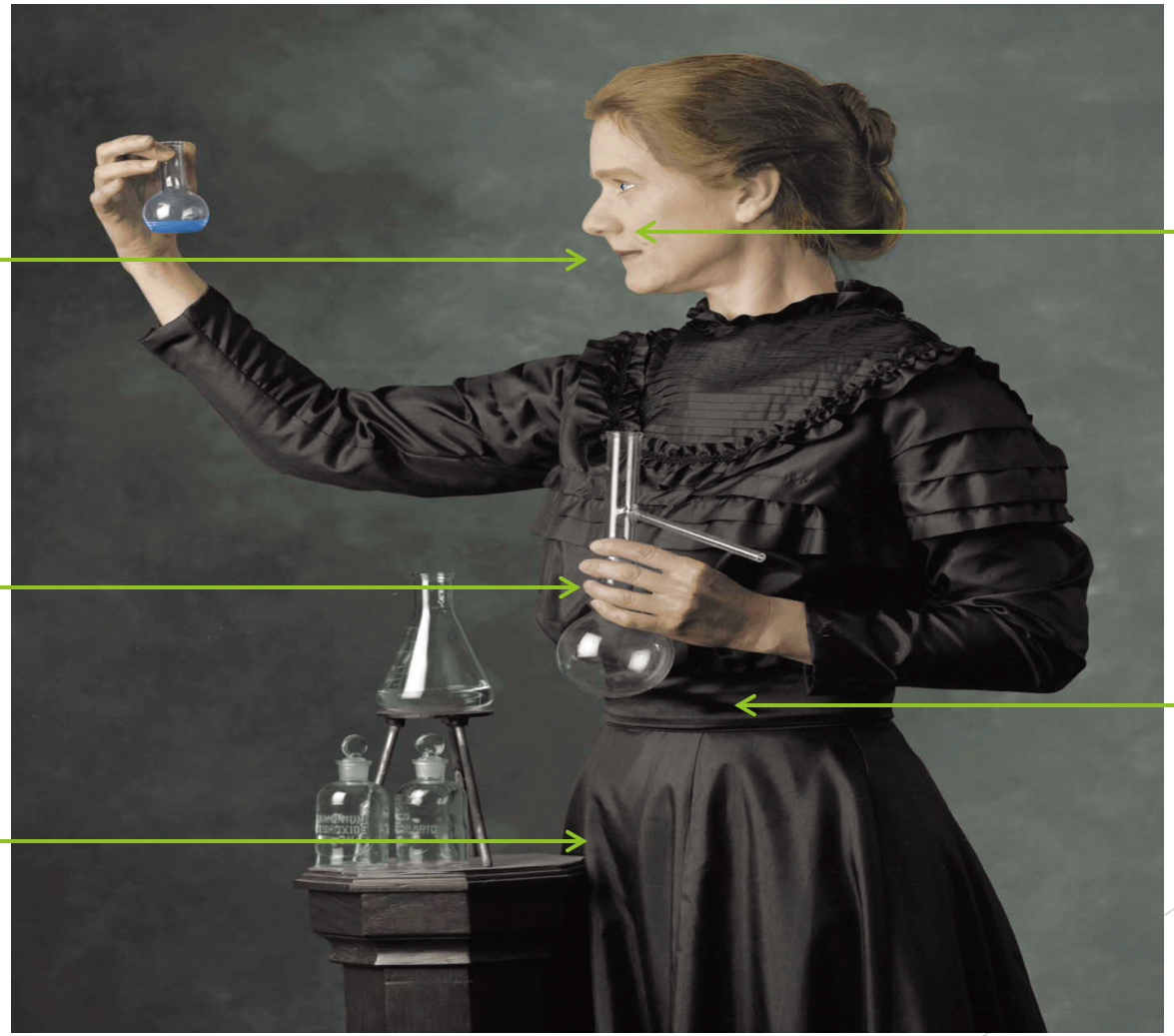
WOMEN'S HEALTH RESEARCH INSTITUTE AT BC WOMEN'S

Disclosures

- None

The Allen-Carey Award of Excellence
in Women's Health

The Microbiome



Culture Independent Investigations

- Large scale 16SrRNA-based studies in healthy, asymptomatic women (*Zhou 2007, Zhou 2009, Ravel 2011, Gajer 2012, Drell 2013*)
- Clusters of 4-7 defined as community state types (CST) distinguished by dominant bacterial taxa
- Most prevalent and dominant- *Lactobacillus* (*L*) *iners*, followed by *L crispatus*, *L gasseri*, *L jensenii*
- Suggestion that non-lactobacillus dominant communities may be “healthy” in some women

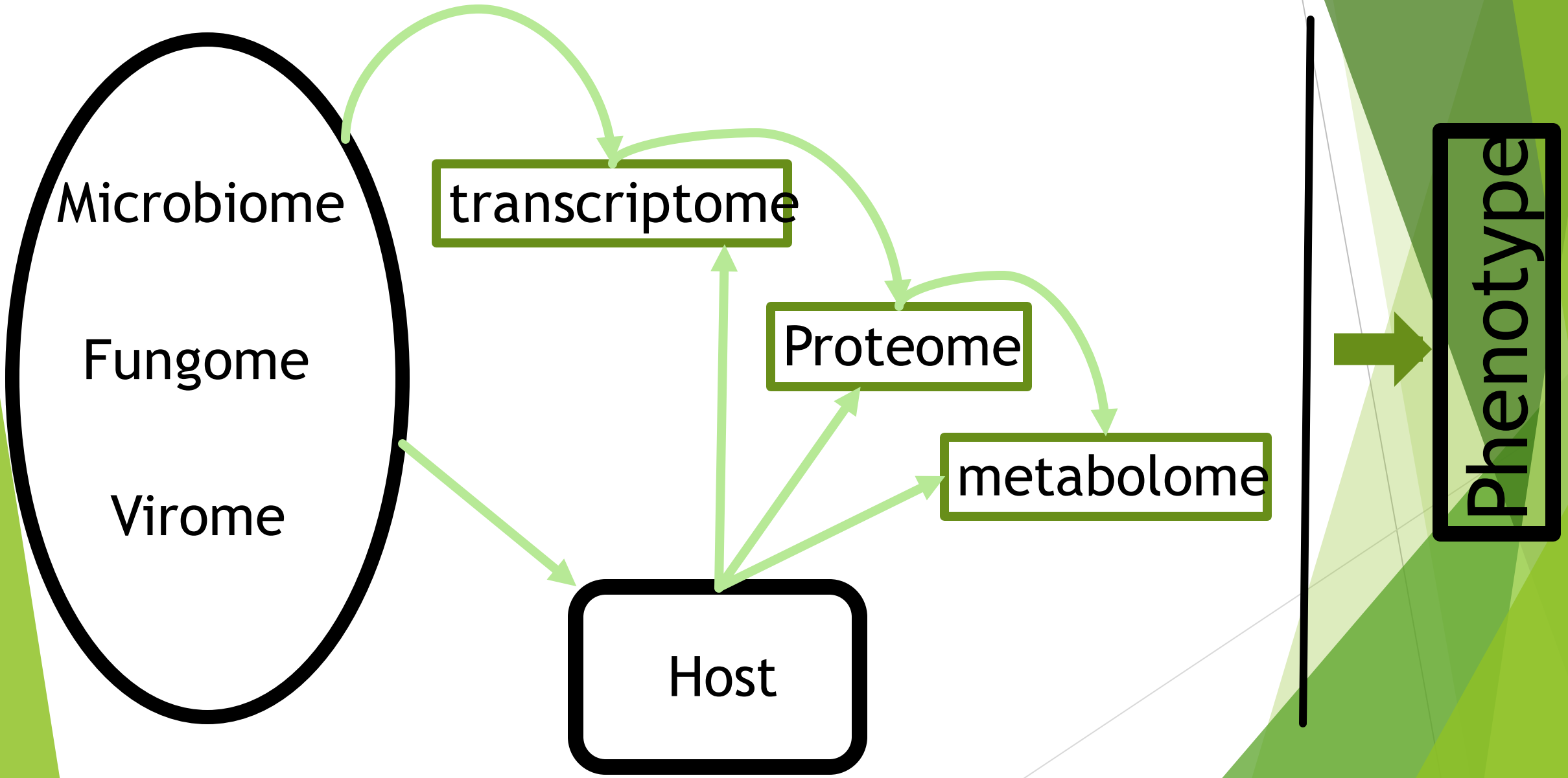
A CLINICIANS GUIDE TO THE MICROBIOME

Community state type

Diversity

Operational Taxonomic Unit

Microbiome –not the only ‘ome’



Caesarean Delivery and Chronic Disease

- Observational Evidence
  - Type 1 DM
  - Asthma
  - Obesity
- But the absolute rates of the increases low
  - Eg Asthma for SVD 7.9% vs 9.5% C/S
- Multiple attempts to manage confounders

- Non-twin sibling studies
  - Don't show the same association

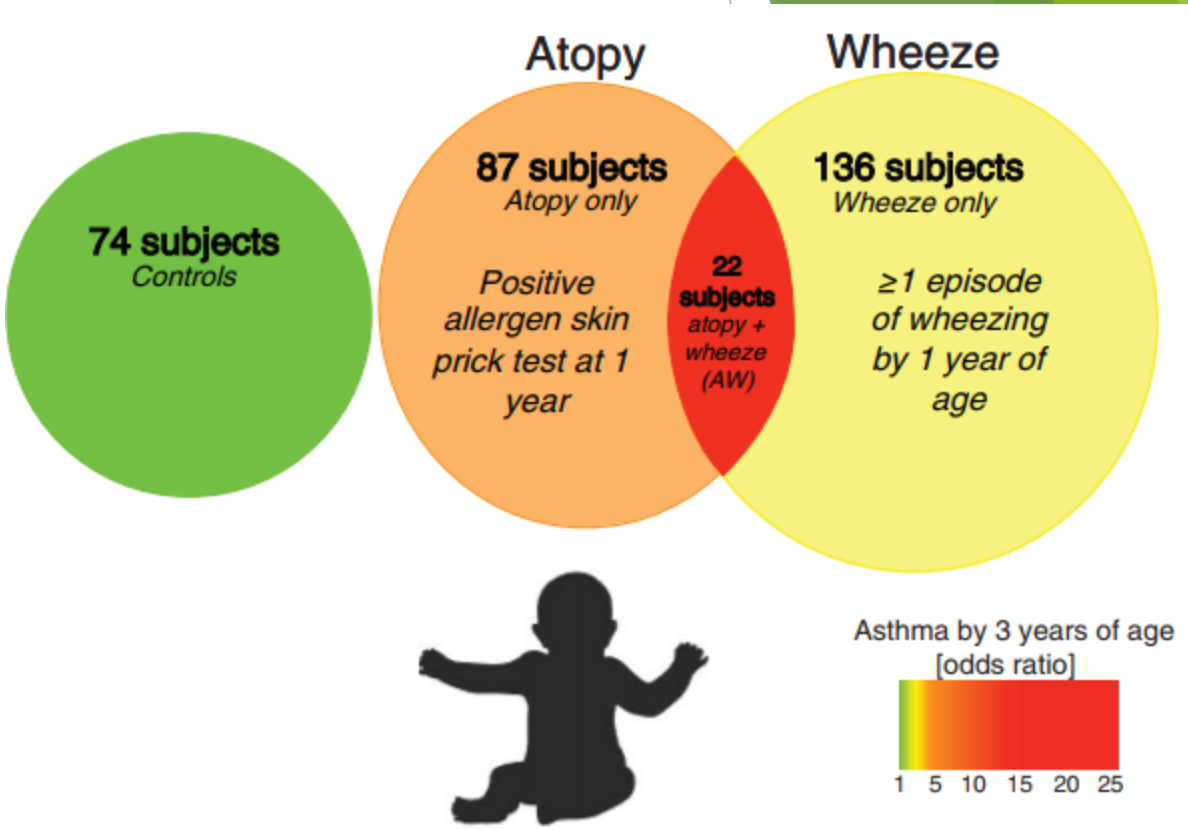
- Term Breech Trial one of the few randomized trials
  - More "medical problems", 20.8 vs 14.8% at 2 years
  - upper respiratory, gastrointestinal, ear, skin, allergic, or other problems by parental report

Blustein et al, Arrieta et al, Rushing et al, Stinson et

Does the microbiome influence long term outcomes?

- Children with Atopy and wheeze had lower abundances of the genera *Faecalibacterium*, *Lachnospira*, *Rothia*, *and Veillonella*, exclusively at 3 months

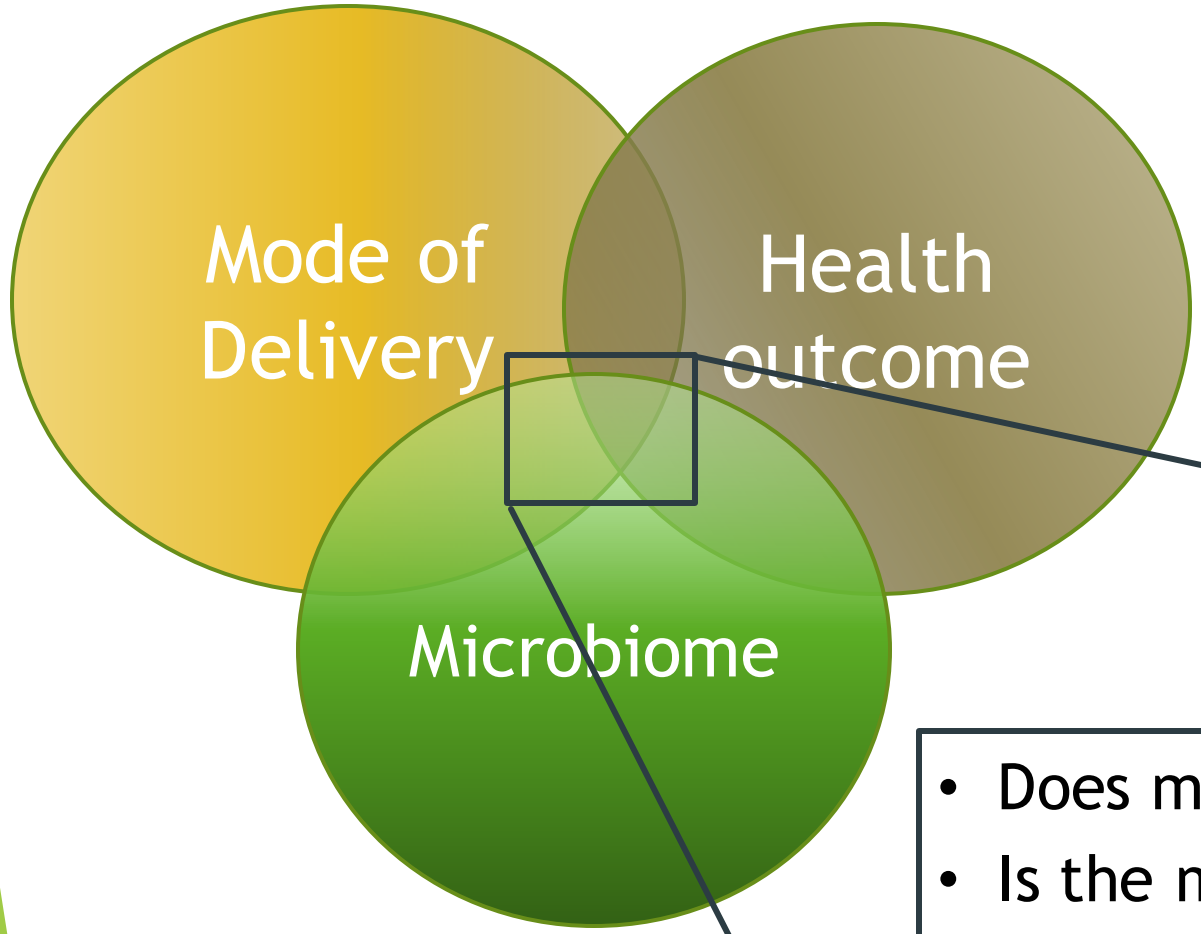
- Show that infants at risk of asthma exhibited transient gut microbial dysbiosis during the first 100 days of life
- Association of antibiotic use with atopy and wheeze, but no association with Caesarean birth or formula feeding



ASTHMA

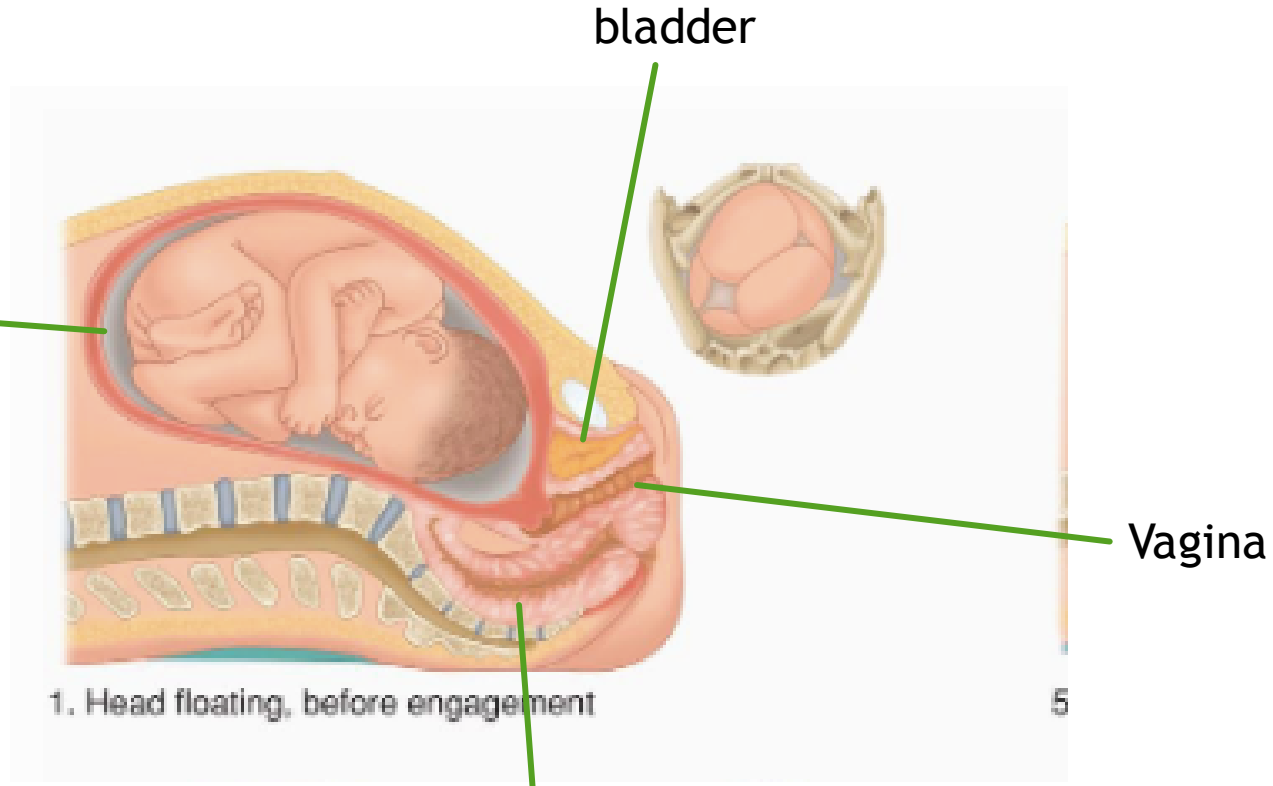
Early infancy microbial and metabolic alterations affect risk of childhood asthma

Marie-Claire Arrieta,[1,2]* Leah T. Stiemsma,[2,3]* Pedro A. Dimitriu,[2] Lisa Thorson,[1] Shannon Russell,[1,2] Sophie Yurist-Doutsch,[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 Finlay[1,2,12‡§]



- Does mode of delivery affect health outcomes?
- Is the microbiome related to health outcomes?
- Does mode of delivery influence infant microbiomes?
- What if anything can and should be done about this??

Does mode of delivery influence microbiomes?



Maturation of the infant microbiome community structure and function across multiple body sites and in relation to mode of delivery

Derrick M Chu[1–3], Jun Ma[1], Amanda L Prince[1], Kathleen M Antony[1], Maxim D Seferovic[1] & Kjersti M Aagaard[1–5]

PROSPECTIVE COHORT Study N-82 plus

Second cross-sectional cohort were enrolled to detect difference by mode of delivery at time of delivery n=82

- **Powered to a 32% C/S rate to detect a difference in the taxonomic composition by mode of delivery at 6weeks**

Eligibility

-age >18

-28w G.A.

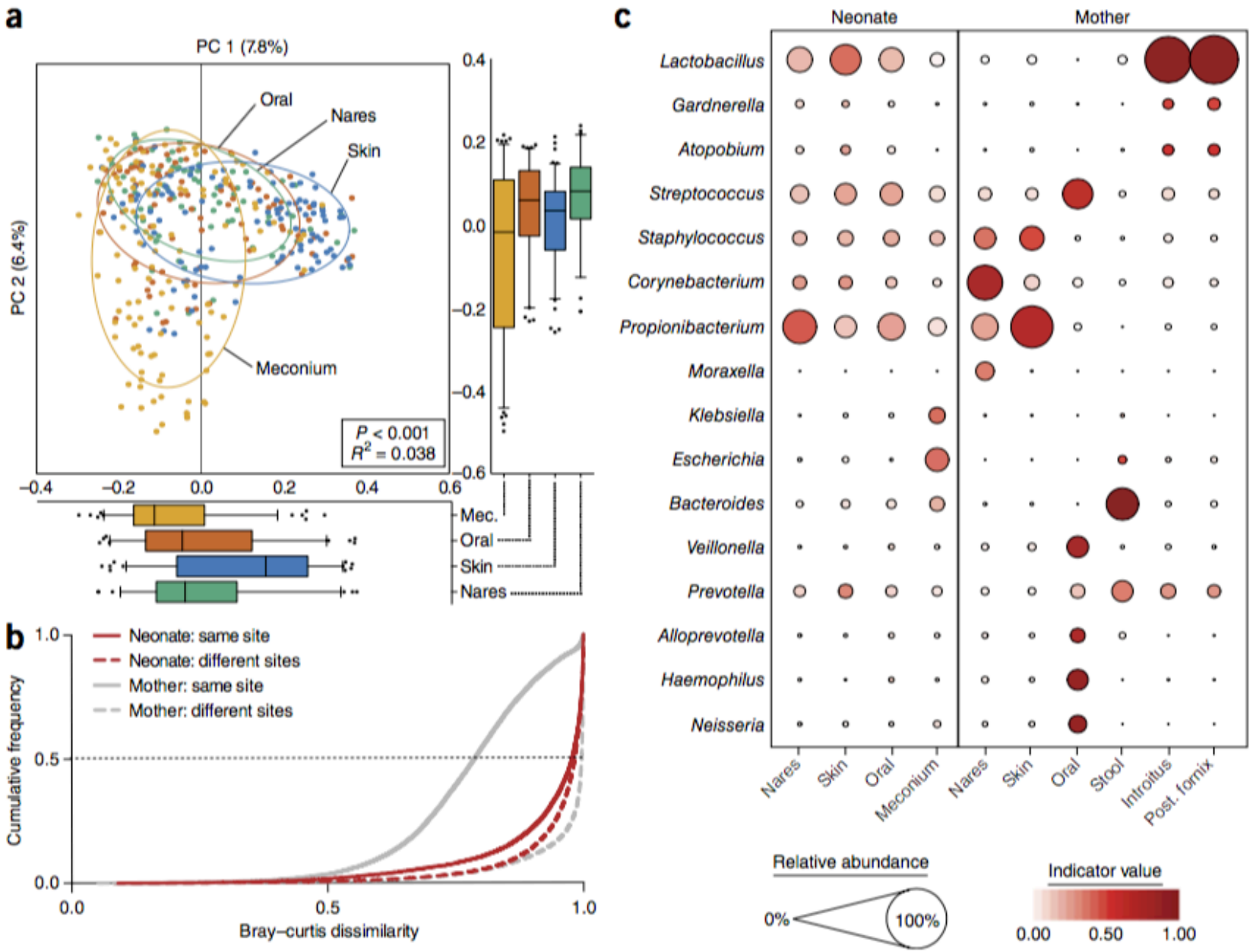
Exclusion

HIV or hepatitis C infection, known immunosuppressive disease, known use of cytokines or immunosuppressive agents within the last 6 months,

a history of cancer (except for squamous or basal cell carcinoma of the skin that could be managed by local excision),

treatment of suspicion of ever having had toxic shock syndrome

major surgery of the gastro-intestinal tract (except for cholecystectomy or appendectomy) in the past 5 years.



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Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns

Maria G. Dominguez-Bello[a,1,2], Elizabeth K. Costello[b,1,3], Monica Contreras[c], Magda Magris[d], Glida Hidalgo[d], Noah Fierer[e,f], and Rob Knight[b,g]

[a]Department of Biology, University of Puerto Rico, San Juan, Puerto Rico 00931; [b]Department of Chemistry and Biochemistry, [e]Department of Ecology and Evolutionary Biology, and [f]Cooperative Institute for Research in Environmental Sciences, University of Colorado, Boulder, CO 80305; [c]Center of Biophysics and Biochemistry, Venezuelan Institute for Scientific Research, Caracas 1020A, Venezuela; [d]Amazonic Center for Research and Control of Tropical Diseases, Puerto Ayacucho 7101, Amazonas, Venezuela; and [g]The Howard Hughes Medical Institute, University of Colorado, Boulder, CO 80305

- Infant gut microbiome evolves over time

C/S
Elective CS
Emergency CS

SVD

0

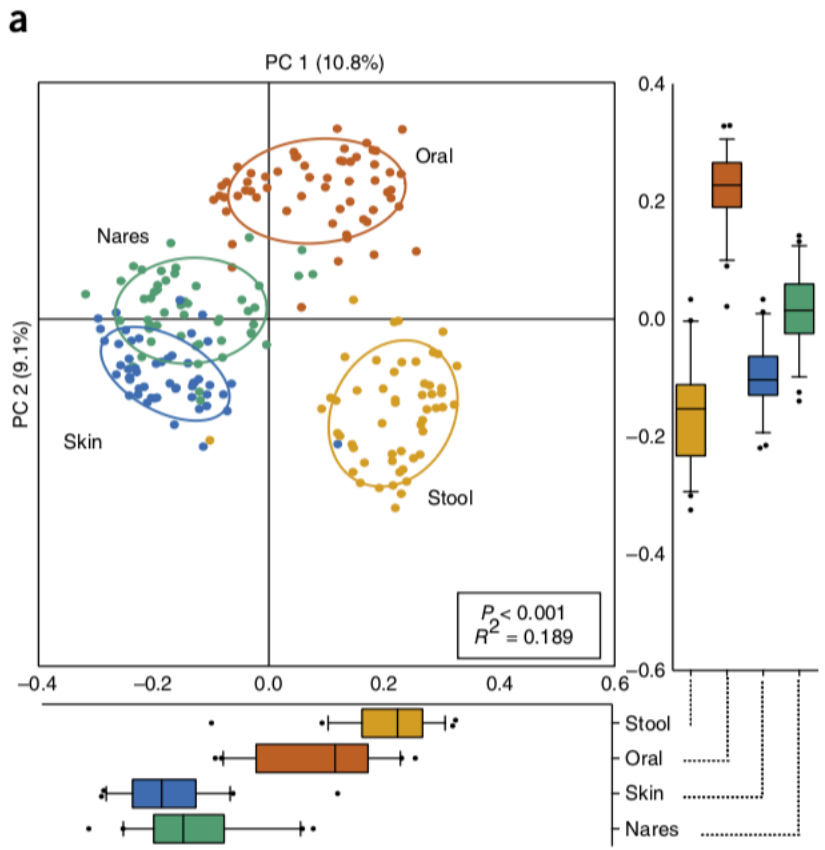
2-3years

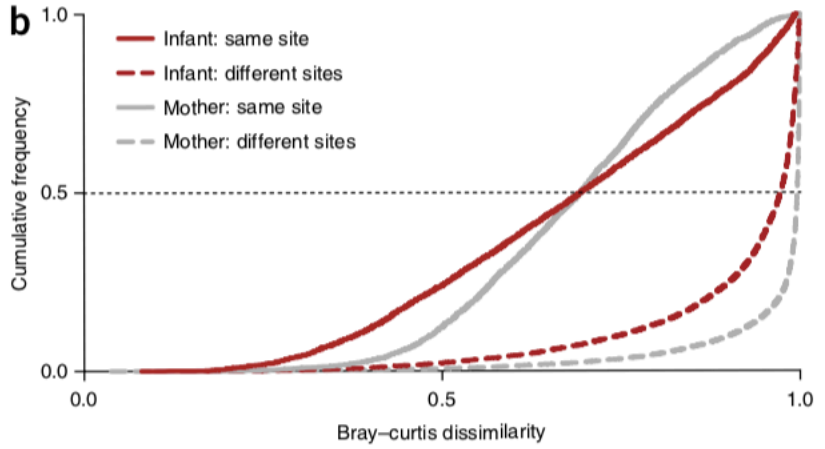
Asthma

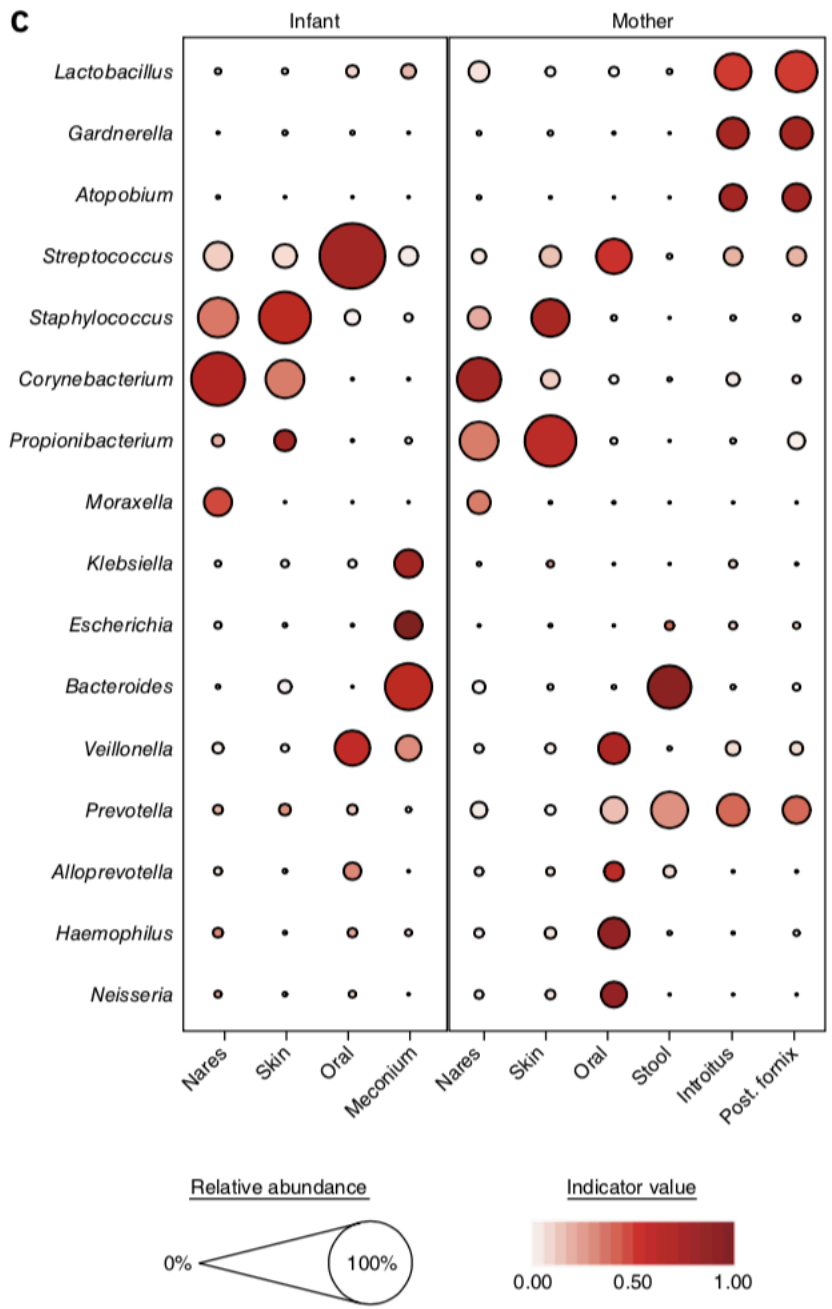
6 weeks post delivery

Body site specific maturation

Were no longer colonized by maternal vaginal flora



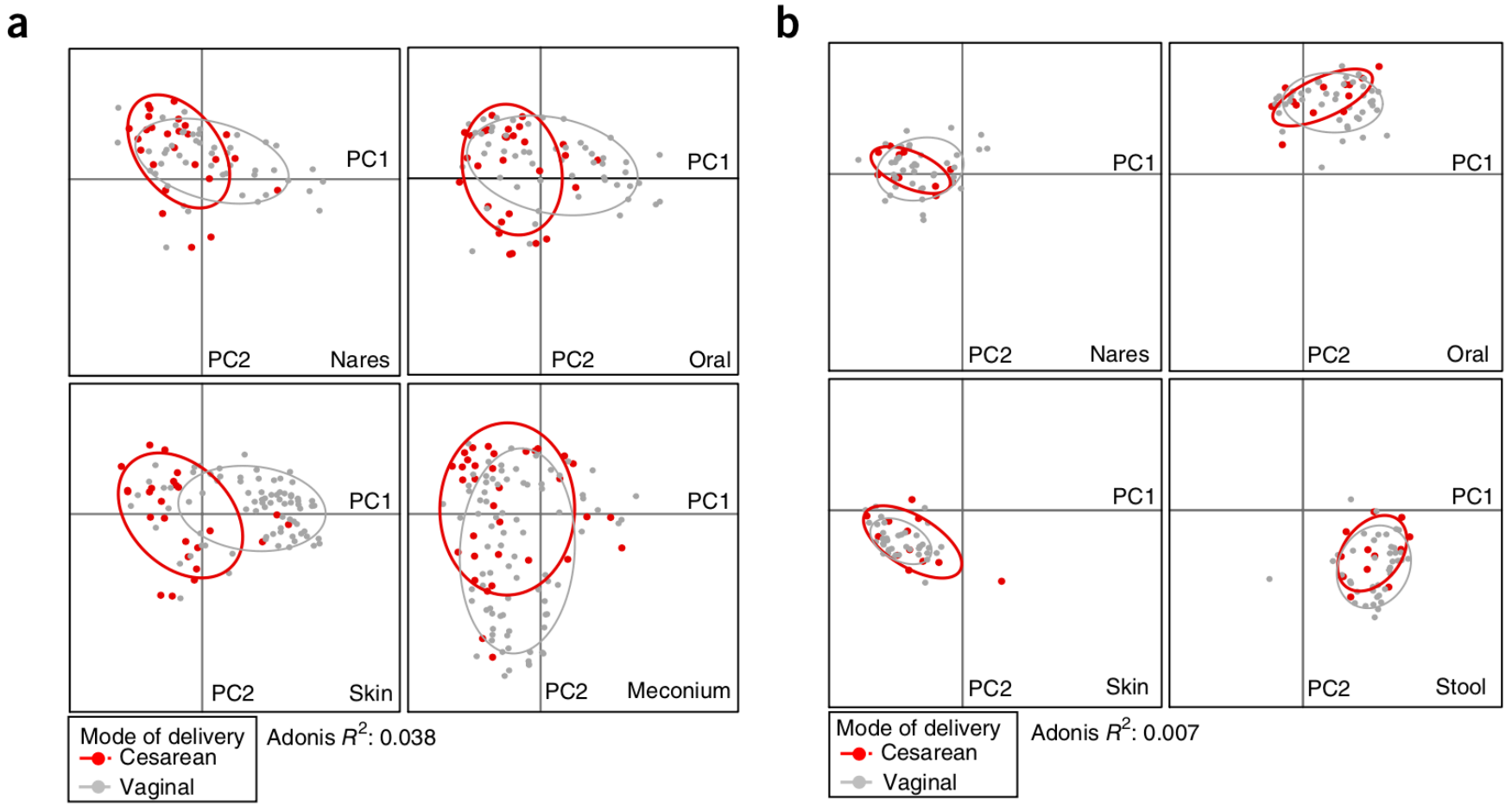




Mode of Delivery and PC2

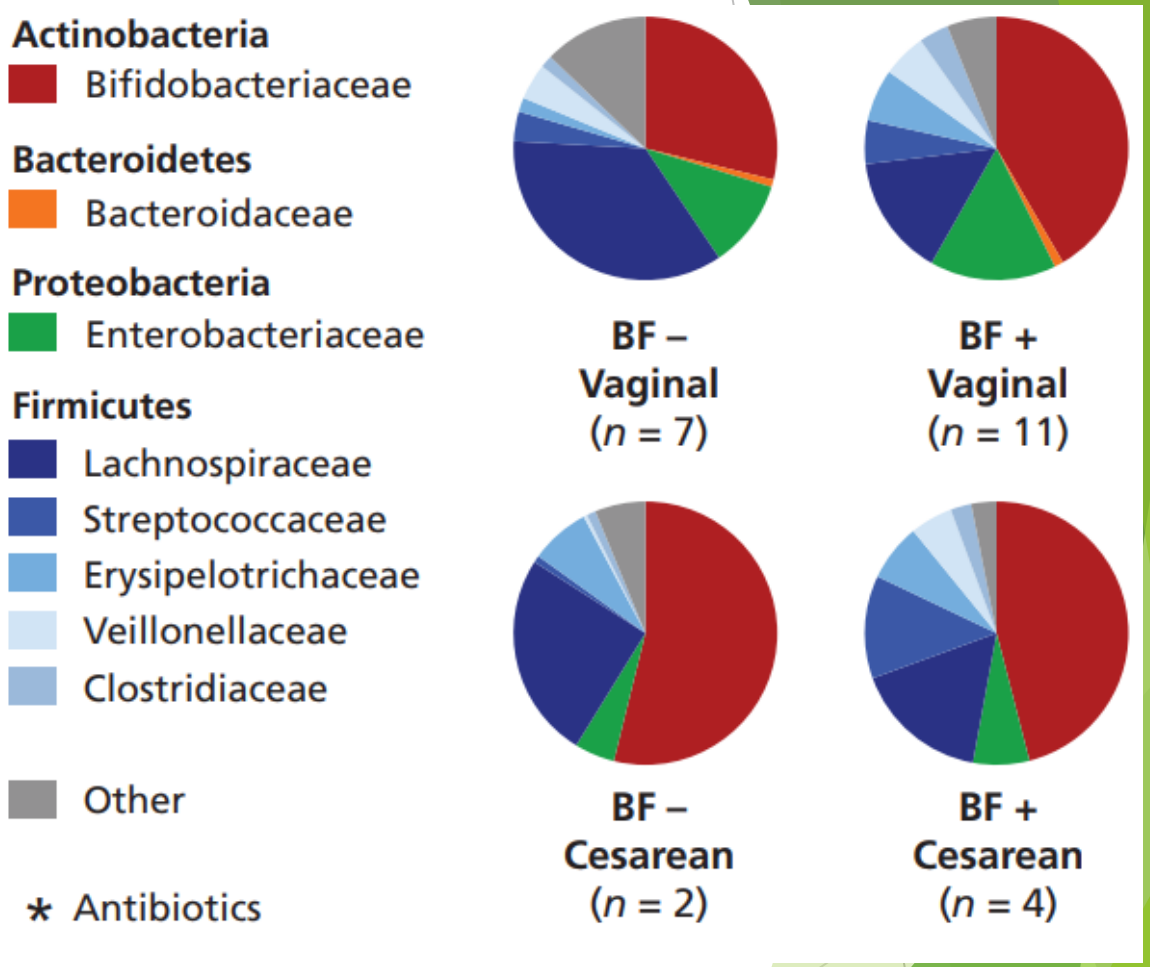
Infants clustered according to mode of delivery initially

At 6 weeks mode of delivery did not influence clustering



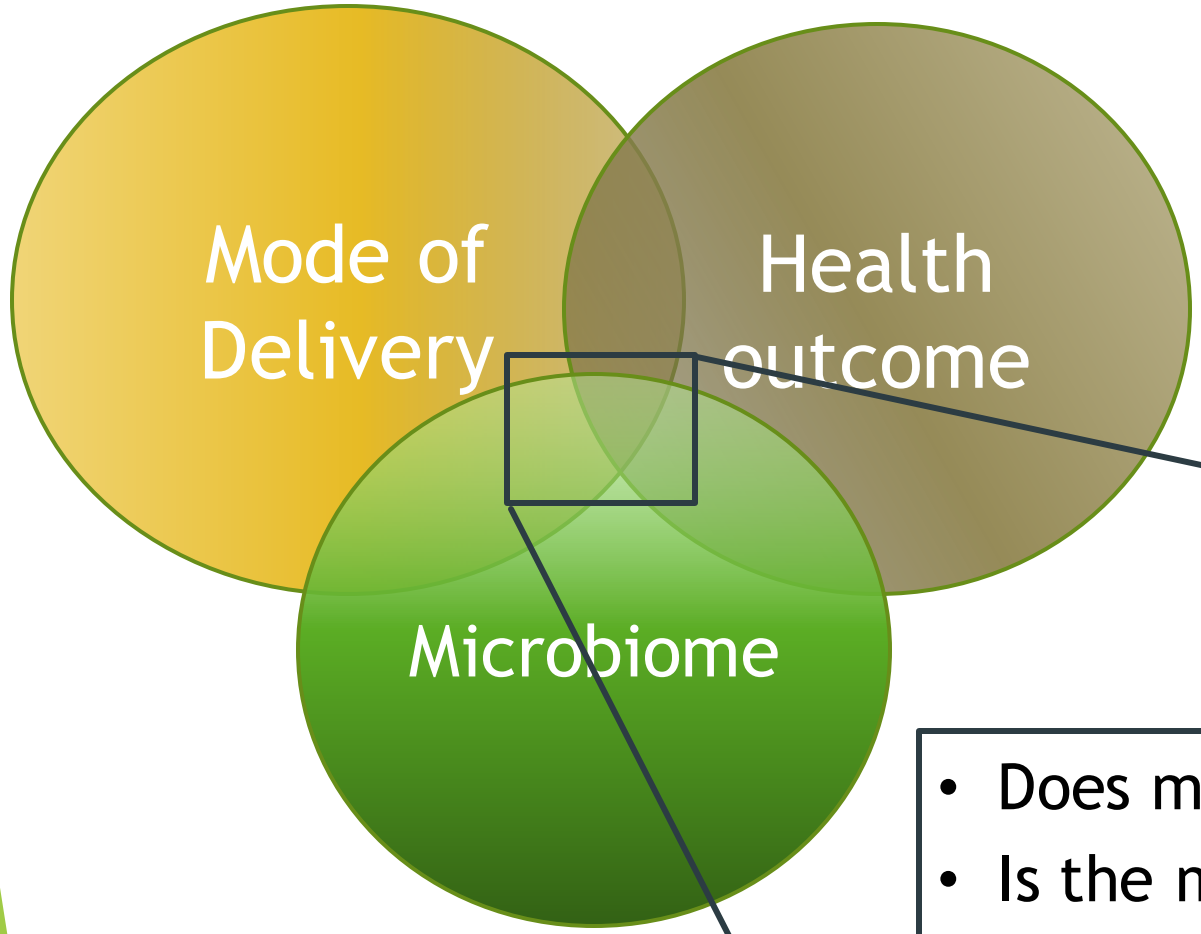
0-12 months

- Increased Enterobacteriaceae and bacteriodes with C/S
- Formula increased *Clostridium* species and increased richness of diversity



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



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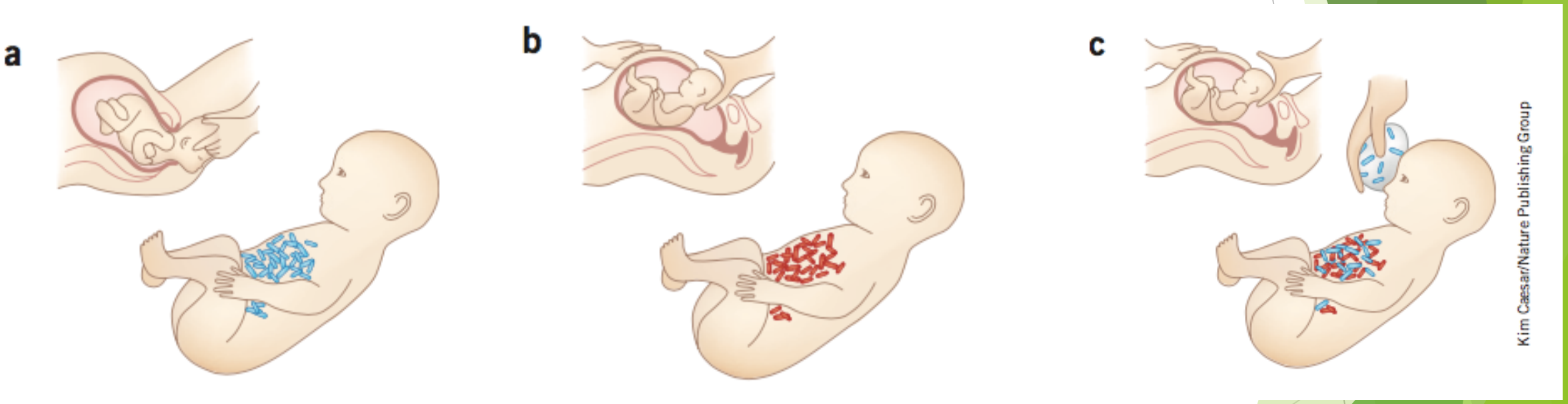
Seeding



Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer

Maria G Dominguez-Bello[1,2], Kassandra M De Jesus-Laboy[2], Nan Shen[3], Laura M Cox[1], Amnon Amir[4], Antonio Gonzalez[4], Nicholas A Bokulich[1], Se Jin Song[4,5], Marina Hoashi[1,6], Juana I Rivera-Vinas[7], Keimari Mendez[7], Rob Knight[4,8] & Jose C Clemente[3,9]

- Sterile gauze is placed in the vagina for 1h
- Infant is swabbed immediately after delivery on the mouth, face and body

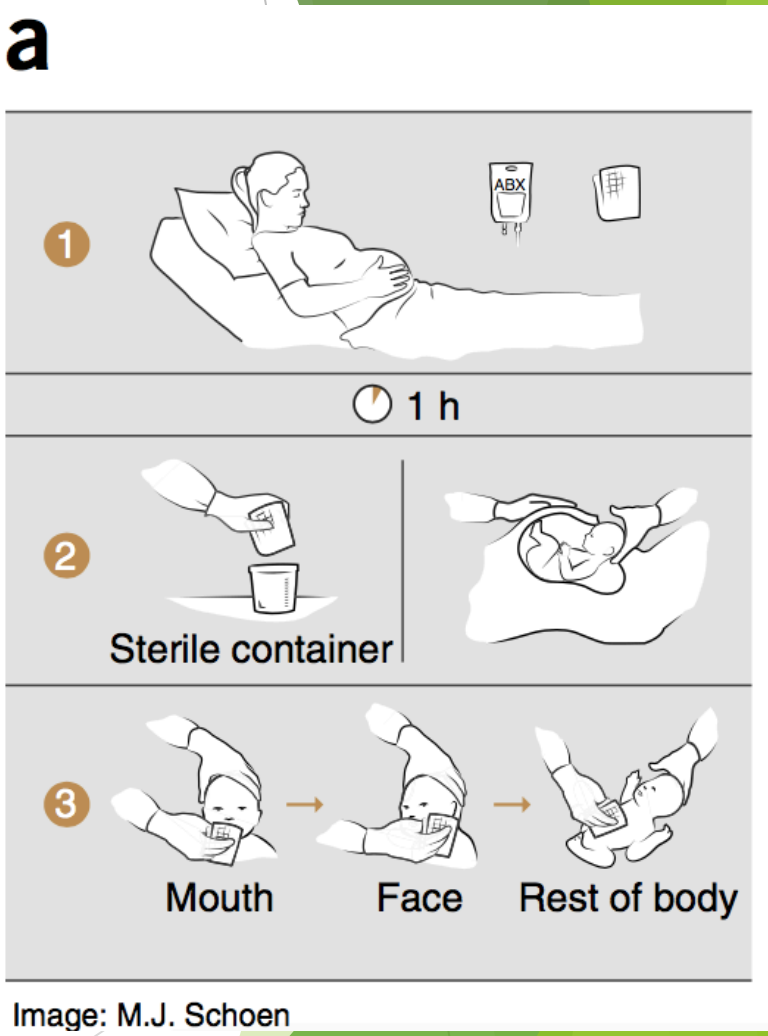


Image: M.J. Schoen

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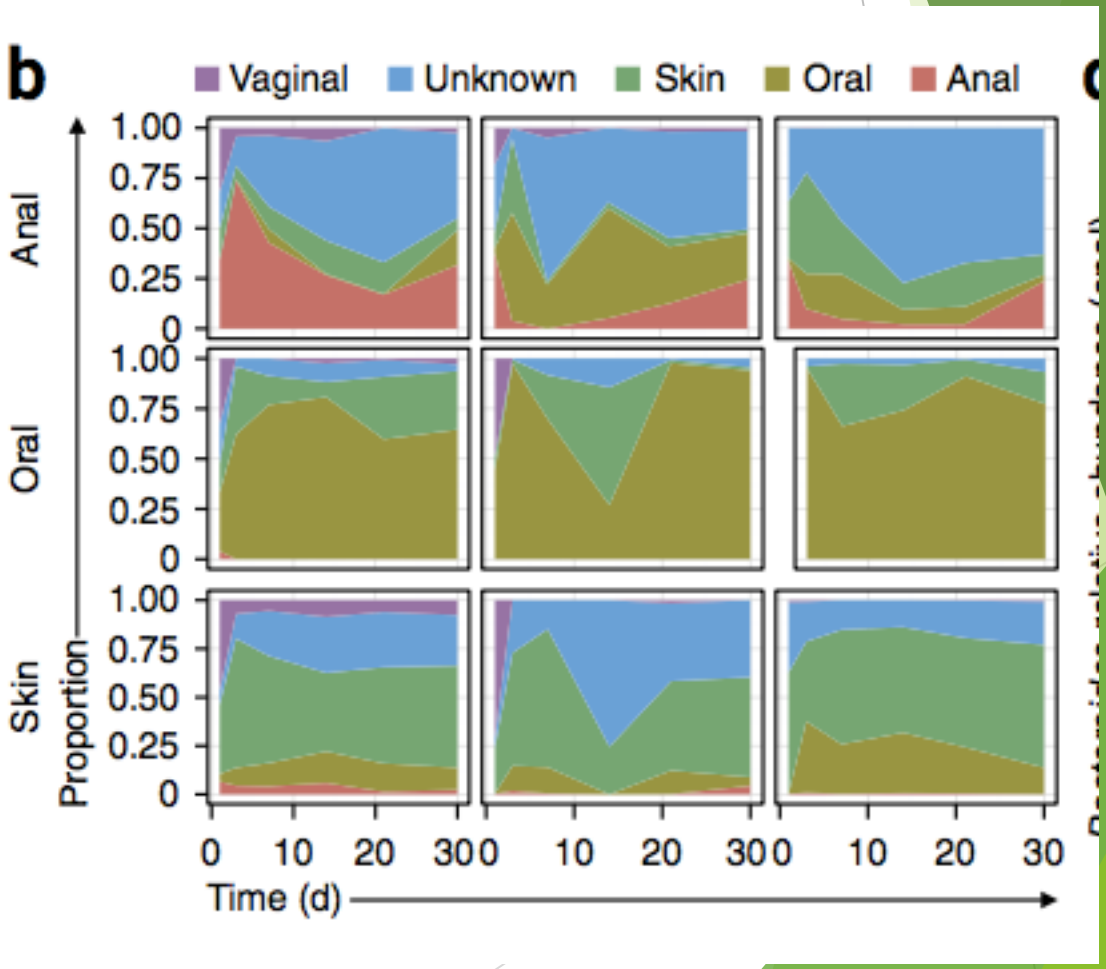
- Similarities between the CS swabbed infants and the Vaginally delivered infants

- ?source tracking at the swab for the source of the gut microbiome

SVD CS+Swab CS



Vaginal Seeding: What are the assumptions

- Maternal vaginal microbiome directly seeds the infant gut
- Vaginal microbiome is THE microbiome that influences outcomes
- This seeding is longitudinal and not transient
- Other factors play a lesser role
  - Antibiotics
  - Breast feeding

What are some of the remaining questions?

- Can the microbiome be transferred from mom to baby via a vaginal swab?
- The assumption is that we are transferring the correct microbiome…which microbiome???
- Is microbiome as a whole is required or single species?
  - Lack of CST data
  - Most of the data focuses on specific species or changes in diversity
- Does this artificial transfer result in a sustainable change that is appropriate?

Are there risks?

- Undetected pathogens
- HSV, GBS, HCV, HPV and others that we cannot detect are being directly inoculated into the infant mouth
- No clear direct evidence of benefit

Practice Advisory: Vaginal Seeding

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

November 8, 2016

J van Schalkwyk, Z Pakzad, D Money
Nov. 6, 2015

WOMEN'S HEALTH RESEARCH INSTITUTE AT BC WOMEN'S

Neonatal oropharyngeal colonization with maternal vaginal discharge following Cesarean delivery

Editorials

"Vaginal seeding" of infants born by caesarean section

BMJ 2016 ; 352 doi: http://dx.doi.org.ezproxy.library.ubc.ca/10.1136/bmj.i227 (Published 23 February 2016)
Cite this as: *BMJ* 2016;352:i227

"VAGINAL SEEDING" AFTER CAESAREAN SECTION

Offering women safer options than "vaginal seeding" for infants born by caesarean section

Clever Banda *consultant paediatrician and senior lecturer*

Placentophagy

http://www.easttennesseeplacentamedicine.com/Services---Pricing.html

A quick word on Placentophagy

- “Traditional Chinese encapsulation process”
- natural, nutrient-rich organ into a simple pill to support your postpartum recovery

What and the why?

What is in the Placenta and How Does it Benefit Me?

- Prolactin: promotes lactation
- Oxytocin: for pain relief and bonding of mother and infant
- Cortisone: combats stress and unlocks energy stores
- Interferon: stimulates the immune system to protect against infections
- Prostaglandins: anti-inflammatory
- Hemoglobin: replenishes iron deficiency and anemia
- Gammaglobulin: immune booster that helps protect against infections
- Thyroid stimulating hormone: boosts energy and aids in recovery from stressful events
- Gonadotrophin: the precursor to estrogen, progesterone and testosterone
- Urokinase inhibiting factor and factor XIII: stops bleeding and enhances wound healing
- Human Placental Lactogen (HPL): stimulates mammary gland function and milk production
- Placental Opioid–Enhancing Factor (POEF): stimulates the production of your body's natural opioids, including endorphins, reduces pain, increases well-being

What are the Benefits of Placentophagy?

- Increased energy levels
- Re-balancing of hormones
- Replenishes depleted iron levels
- Reduces post-natal bleeding (lochia)
- Assists with involution of the uterus
- Enhances healing
- Increases milk production
- Rich nutritional source
- Lower rates of 'baby blues'
- Reduced risk of postpartum depression
- Faster recovery
- Decreased anemia
- Decreased fatigue
- An increased sense of well-being
- A more enjoyable post-natal experience

Methods of Encapsulation:

	RAW	TCM	COMBINATION
Placenta Steamed?	No	Yes	Yes
Capsule Yield	Most	Least	Moderate
Dehydration Temperature	160°F for 2 hours* 115°F for 16-22 hours	140°F for 2 hours 125°F for 10-12 hours	160°F for 2 hours 115°F for 16-20 hours
Time to Dehydrate	18-24 hours	12-14 hours	18-22 hours
Other Considerations	Retains the highest concentration of hormones, vitamins and minerals. Best done within the first 48 hours postpartum.	Steaming with ginger and myrrh infuses warmth and creates a milder capsule.	Perfect combination to infuse some warmth without losing a lot of nutrients.

*Dehydration at 160°F for 2 hours is to meet Food Safety Standards. If you prefer your placenta only be dehydrated at 115°F please let me know.

Is there a biologically plausible mechanism?

What is in the Placenta and How Does it Benefit Me?

- Prolactin: promotes lactation
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Presence and concentration of 17 hormones in human placenta processed for encapsulation and consumption

Sharon M. Young [a, *], Laura K. Gryder [a, b], David Zava [c], David W. Kimball [c], Daniel C. Benyshek [a]

11-Deoxycortisol	28
17-hydroxyprogesterone	28
7-ketodehydroepiandrosterone	28
Aldosterone	28
Allopregnanolone[b]	28
Androstenedione	28
Corticosterone	28
Cortisol	28
Cortisone	28
Dehydroepiandrosterone	28
Dihydrotestosterone	0
Estradiol[b]	28
Estriol	28
Estrone	28
Melatonin	9
Progesterone[b]	28
Testosterone	28

<DL: Below detectable limit

estradiol, progesterone, and allopregnanolone could theoretically reach physiologic thresholds

What is the evidence?

Table 1. Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care

Quality of evidence assessment*	Classification of recommendations†
I: Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2: Evidence from well–designed cohort (prospective or retrospective) or case–control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category	D. There is fair evidence to recommend against the clinical preventive action
	E. There is good evidence to recommend against the clinical preventive action
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.[56]

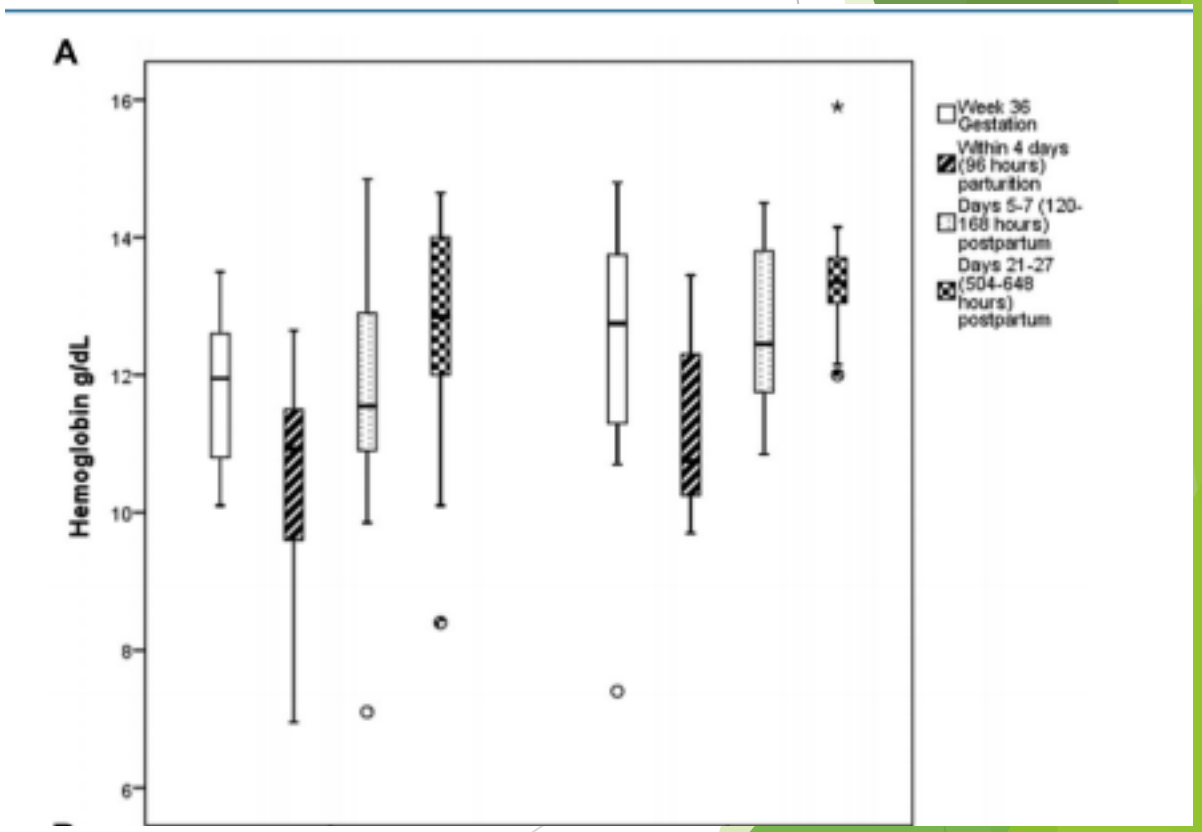
†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.[56]

Effects of Human Maternal Placentophagy on Maternal Postpartum Iron Status: A Randomized, Double-Blind, Placebo-Controlled Pilot Study

Laura K. Gryder, MA, Sharon M. Young, PhD, David Zava, PhD, Wendy Norris, BS, Chad L. Cross, PhD, PStat(R), Daniel C. Benyshek, PhD

Grade 1 Evidence

- N=23
- Double blind randomized placebo controlled trial
- Encapsulated placenta vs dehydrate beef
- No difference was shown



CONFLICT OF INTEREST

This study was made possible, in part, by the collaboration between the study authors and Placenta Benefits LTD, a hu-

Human Maternal Placentophagy: A Survey of Self-Reported Motivations and Experiences Associated with Placenta Consumption

Jodi Selander , Allison Cantor , Sharon M. Young & Daniel C. Benyshek

Grade ??

- 189 women were recruited via Facebook, twitter an online messaging boards
- surveyed who consumed their placenta after the birth of at least one child
- No controls
- Questionnaire was not validated

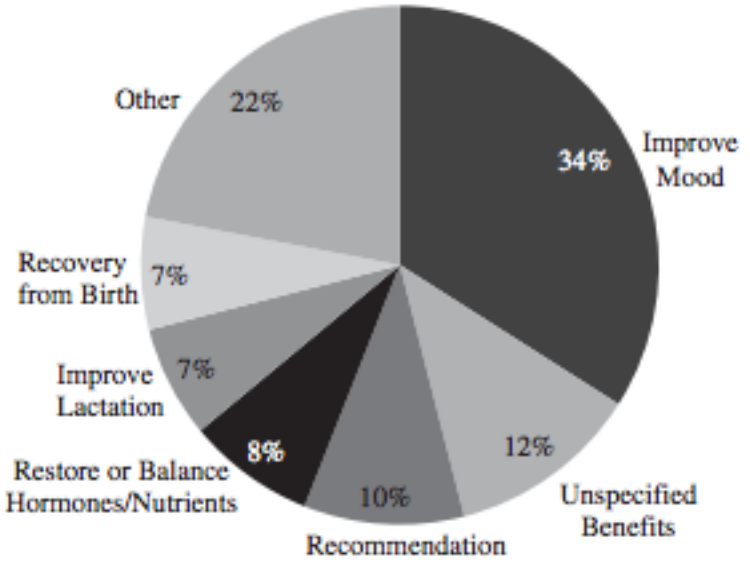


FIGURE 2 Motivation for engaging in placentophagy.

Motivations and Experiences with Maternal Placentophagy

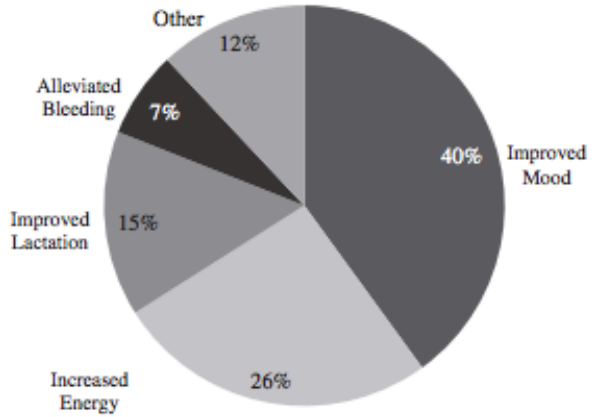


FIGURE 4 Reported positive effects of placentophagy.

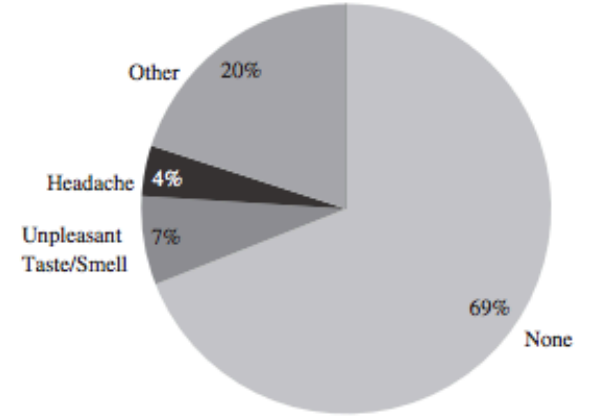


FIGURE 5 Reported negative effects of placentophagy.

Human placentophagy: a review

Alex Farr, MD, PhD; Frank A. Chervenak, MD; Laurence B. McCullough, PhD; Rebecca N. Baergen, MD; Amos Grünebaum, MD

- “To date, there is no scientific evidence for any clinical benefit of human placentophagy. Positive influences on mood, iron status, lactation, and general energy that have been claimed by the supporters of placentophagy have never been proven in clinical studies”

Harm

- GBS BC positive sepsis shortly after birth
  - Treated with 11d of ampicillin
- Returned 5 days later with BC positive GBS sepsis
- Blood culture isolate and placental capsule isolate were identical
  - Same strain on pulse field gel electrophoresis and whole genome sequencing

Buser GL, Mató S, Zhang AY, Metcalf BJ, Beall B, Thomas AR. *Notes from the Field:* Late-Onset Infant Group B Streptococcus Infection Associated with Maternal Consumption of Capsules Containing Dehydrated Placenta — Oregon, 2016. MMWR Morb Mortal Wkly Rep 2017;66:677–678.
DOI: http://dx.doi.org/10.15585/mmwr.mm6625a4

PHAC

- December 6th 2017

- Health Canada advises that placenta encapsulation services are in fact regulated, at the federal level. They fit the definition of a drug and the process is considered to be manufacturing.

- Therefore, claims that the ingestion of these products can prevent a disease or abnormal physical state (such as postpartum depression) or modify organic functions (such as the increased production of breast milk) would be grounds for regulation as a biologic drug under the Food and Drug Regulations, subject to Divisions 1, 1A, 2, 4, 5, and 8.

Conclusions vaginal seeding and placentophagy

- There is a profound knowledge gap between evidence and implementation of a clinical practice in both cases
- Further study is required before an evidence based practice can be recommended for vaginal seeding or placentophagy

Connect With Us!

Maternal Microbiome Legacy Project

Connect & Participate:

Ways to reach us:

604-875-2000 ext 6379

MaternalLegacy@cw.bc.ca

Scan here to have us contact you:

More ways to connect:

whri.org/maternal-microbiome-legacy-project/

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WOMEN'S HEALTH RESEARCH INSTITUTE AT BC WOMEN'S

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

Study Coordinator:
Zahra Pakzad
zahra.pakzad@cw.bc.ca

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Seeding

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Placentophagy

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