The Human Microbial Environment

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Environment and Health Summer School

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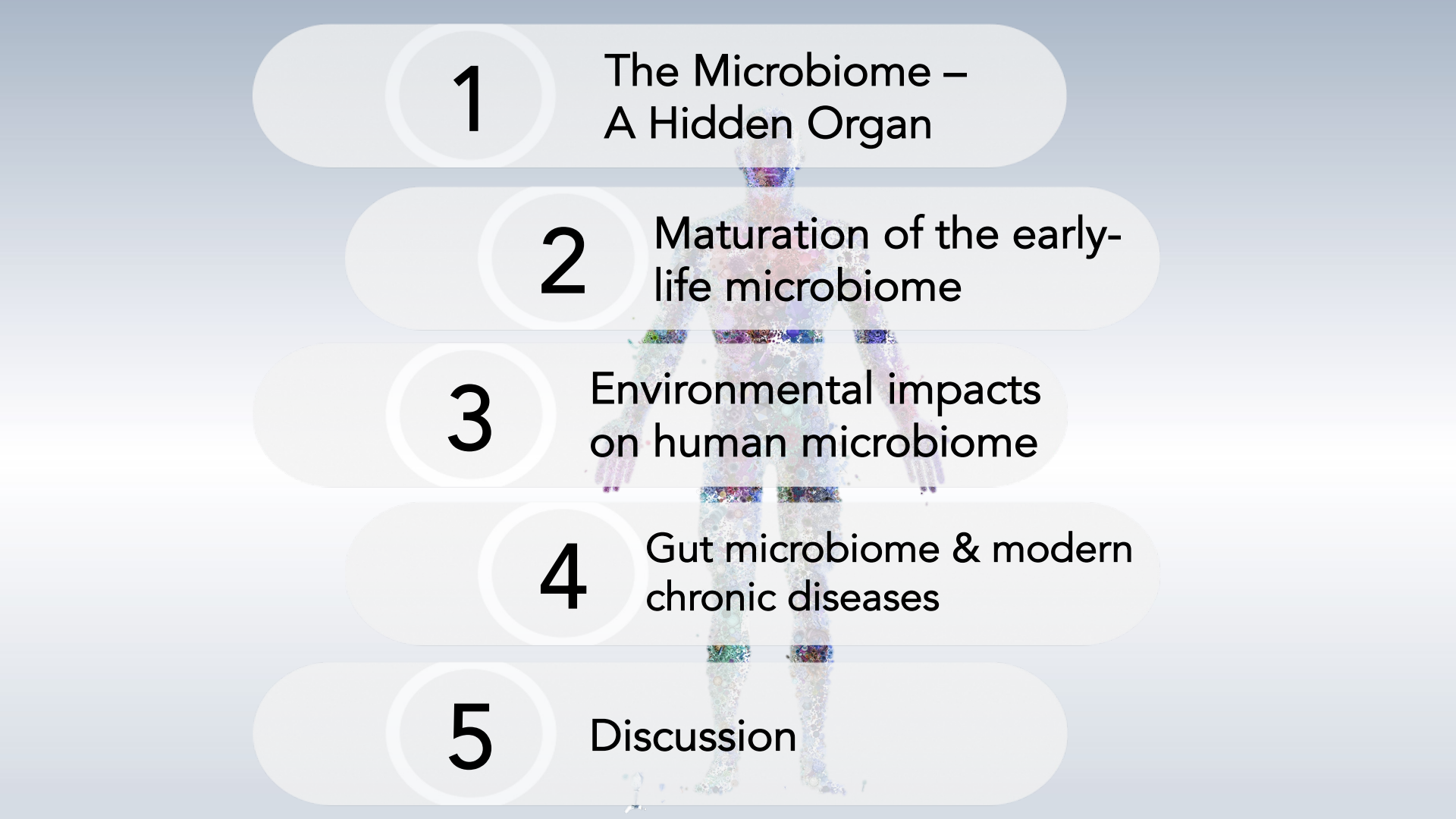


1 The Microbiome – A Hidden Organ

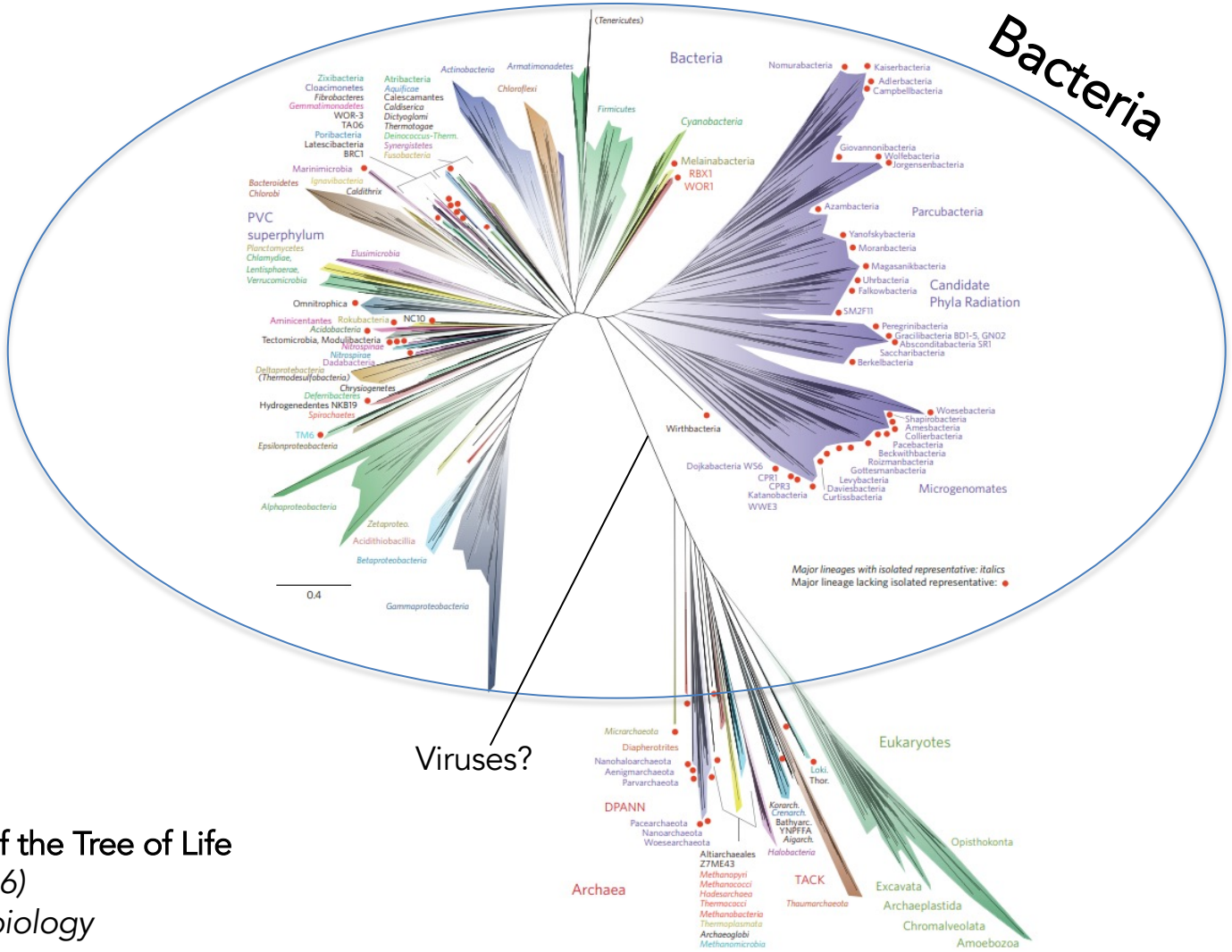
2 Maturation of the early-life microbiome

3 Environmental impacts on human microbiome

4 Gut microbiome & modern chronic diseases

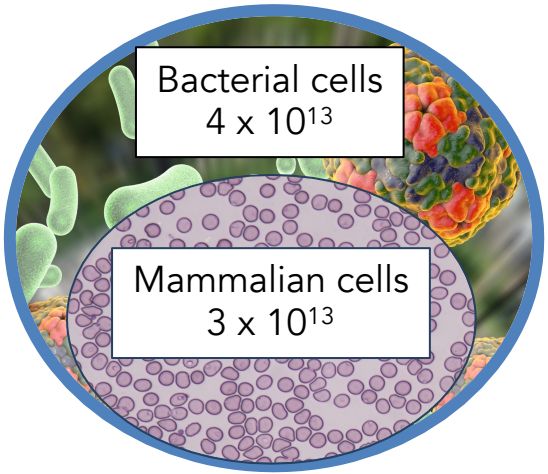
5 Discussion

1 The Gut Microbiome – A Hidden Organ

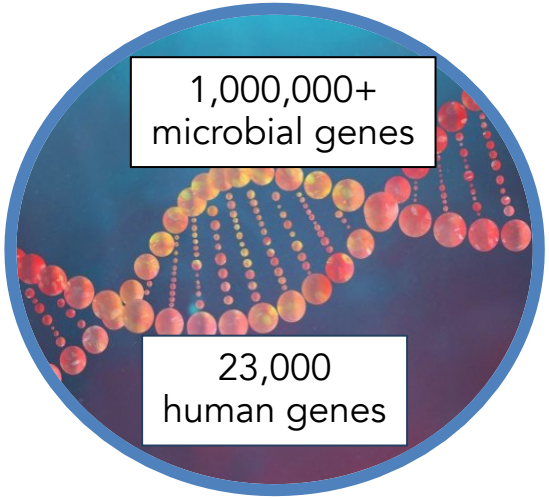


A New View of the Tree of Life
Hug et al (2016)
Nature Microbiology

The Human Microbiome



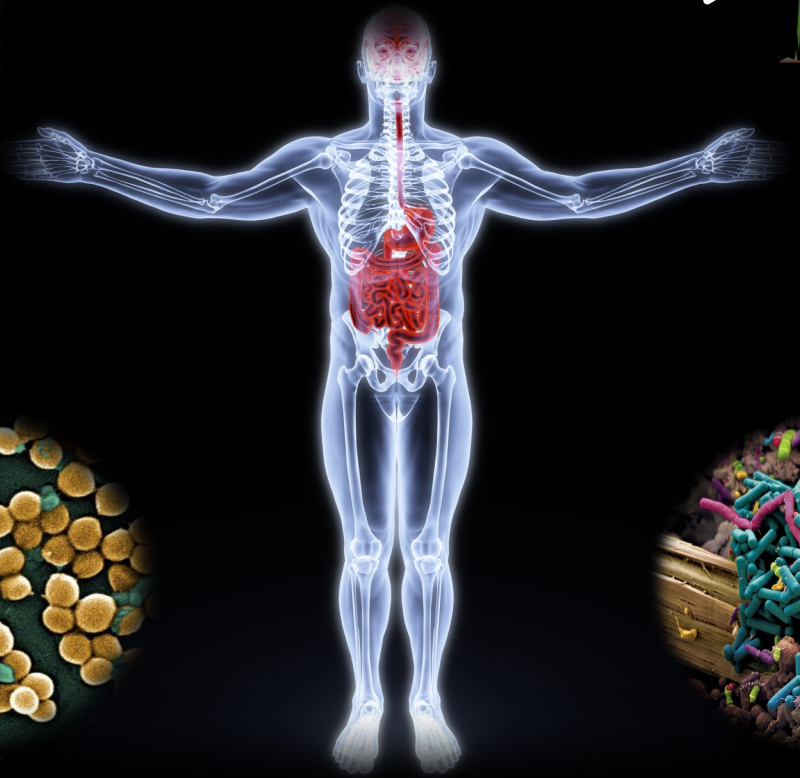
Microbiota

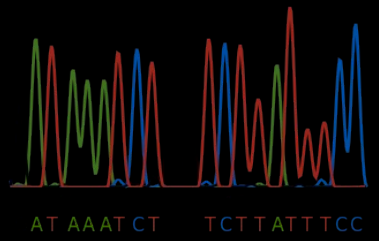


Microbiome

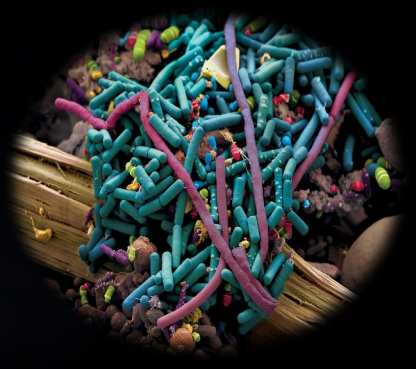
Technological advances = Evolution of microbiome understanding

Culture





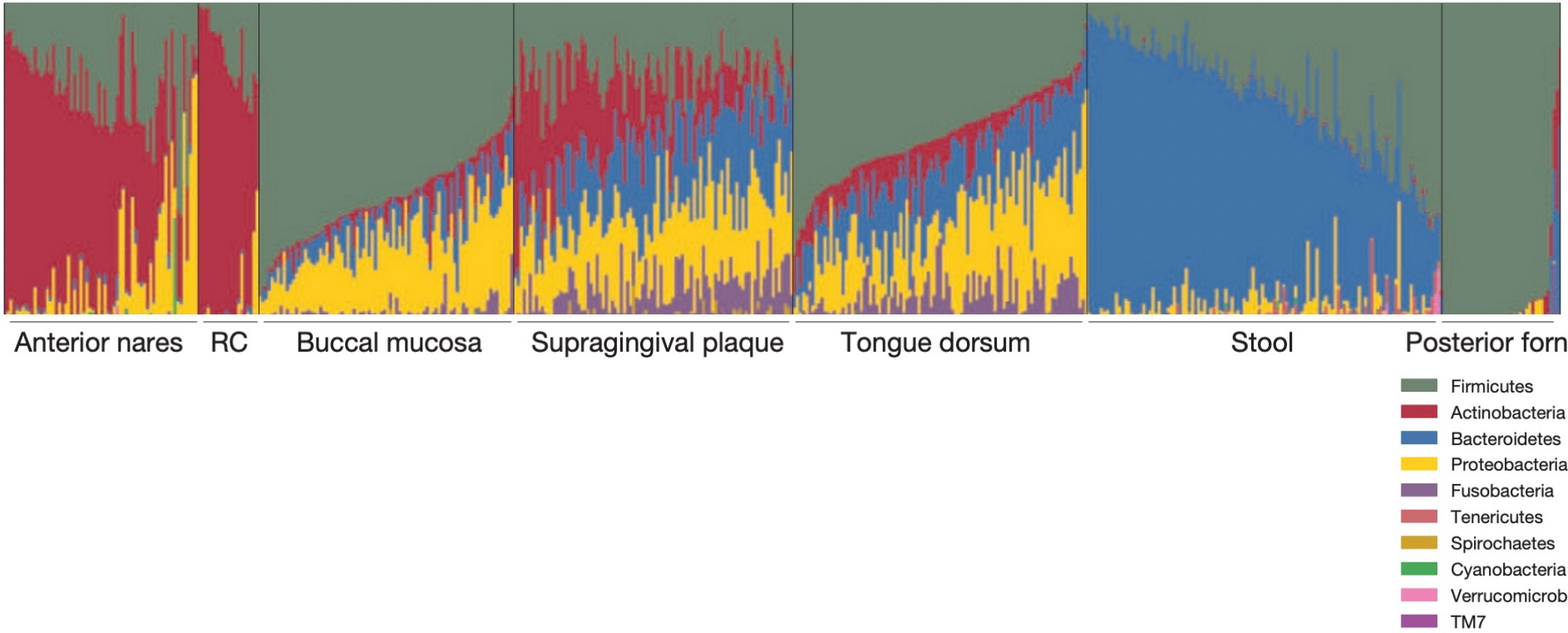
Sequencing



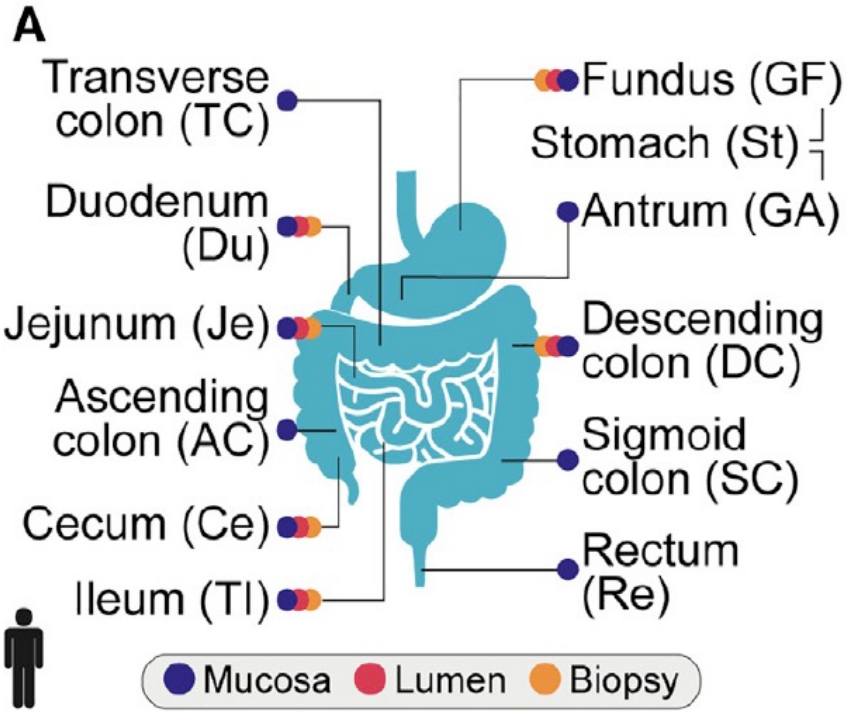
The Human Microbiome

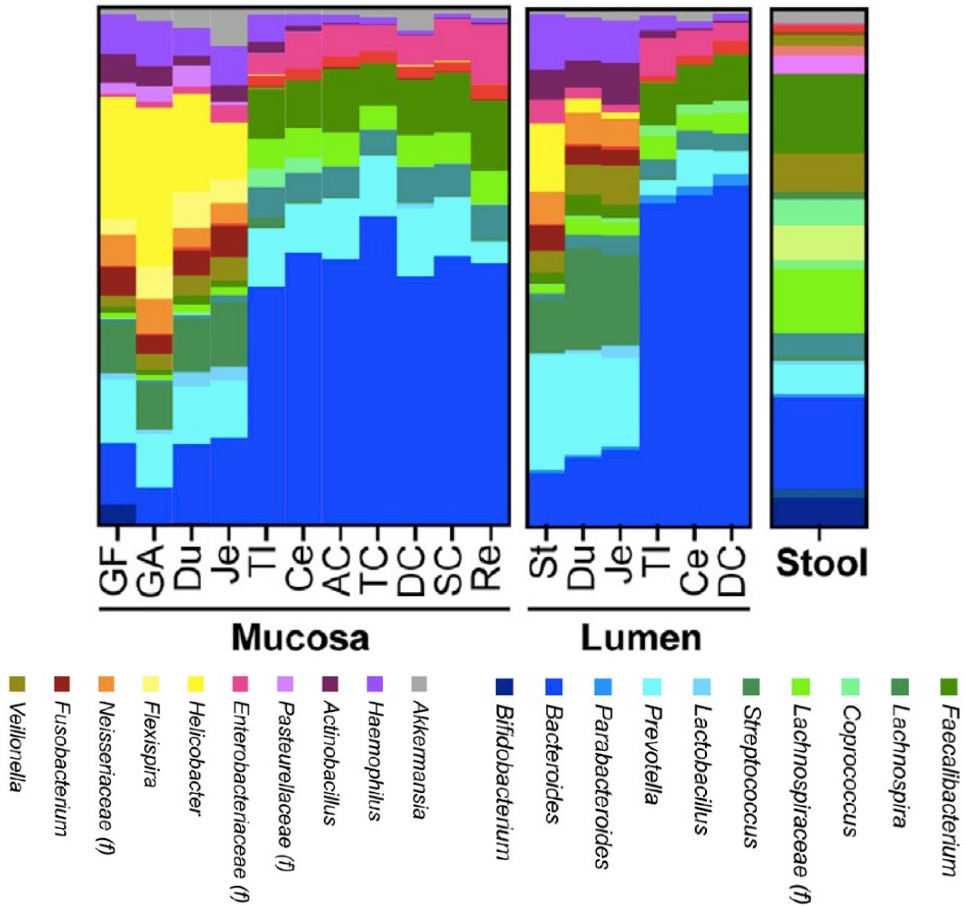
- >1000 different bacterial species
- Viruses, archaea, fungi
- Bacteria weight ~200g
- Huge proportion unknown
- Each individual microbiome as unique as fingerprint

Microbes differ in different body sites

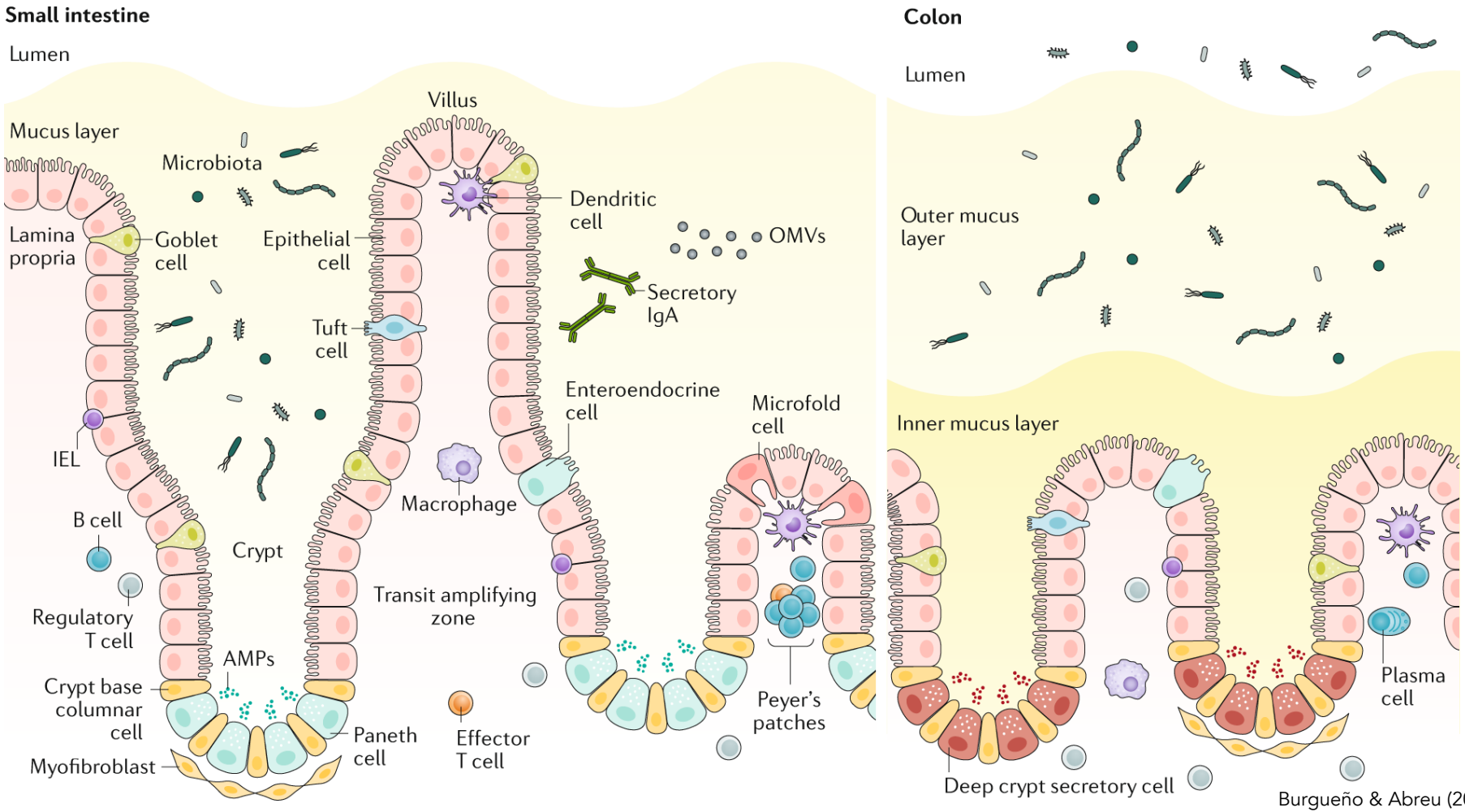


The gut microbiota differs throughout the intestinal tract



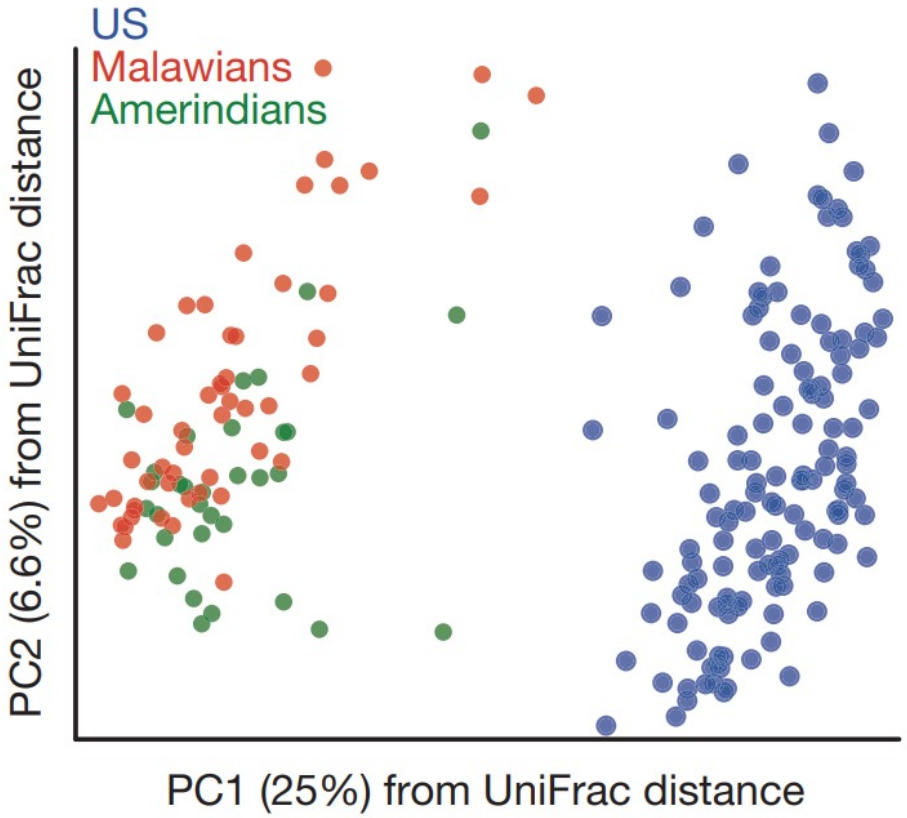


Zmora et al. *Cell* (2018)

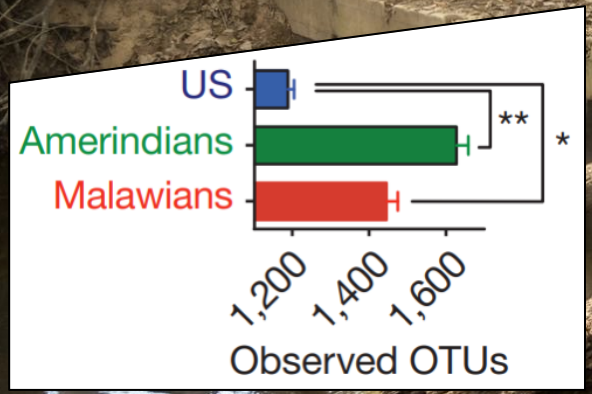


Burgueño & Abreu (2019)
Nat Rev Gastro Hep

What is a ‘normal’ microbiota?



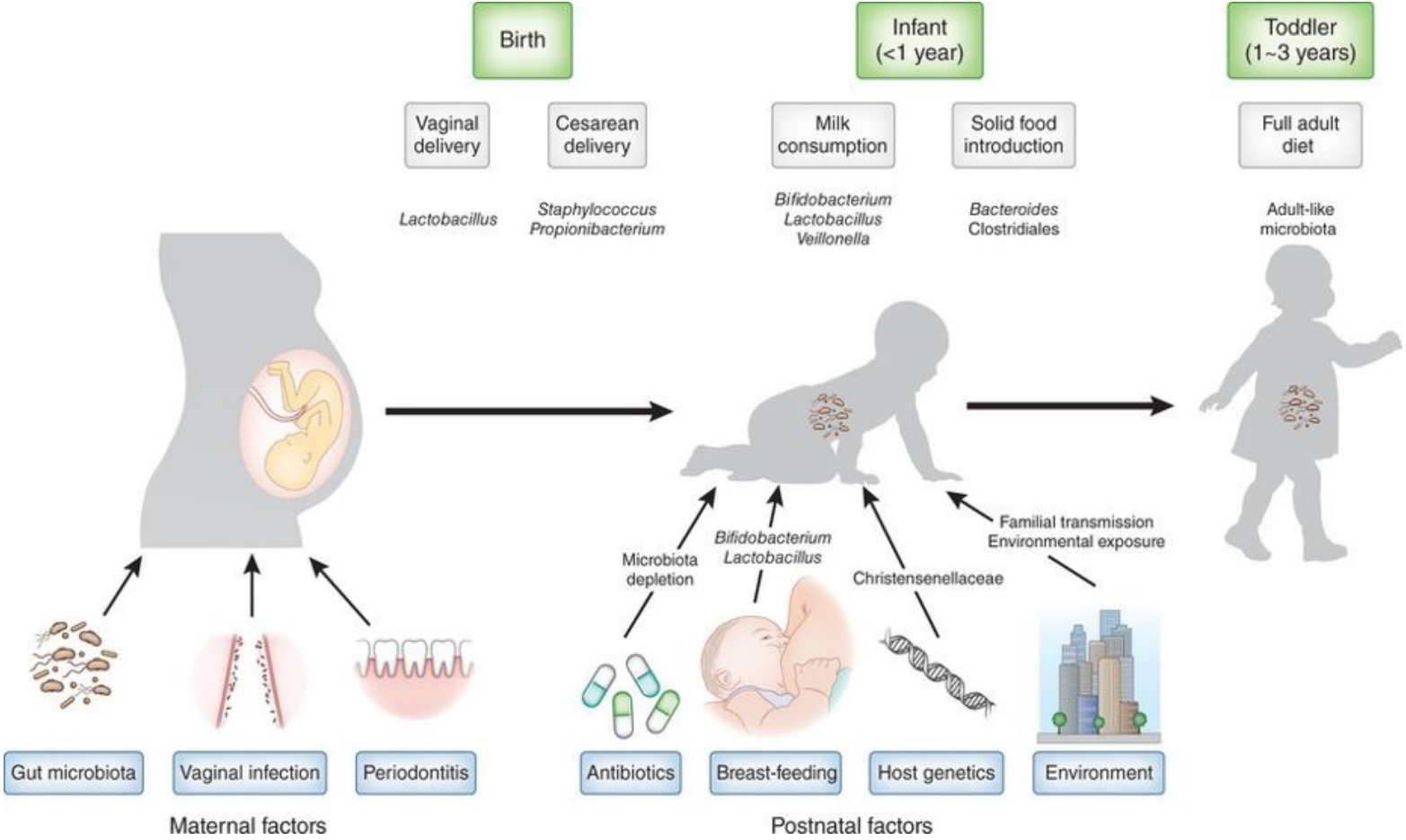
Yatsunenko (2012)
Nature



Yatsunenko (2012) *Nature*

2 Maturation of the early-life microbiome

What influences the gut microbiome?



The first 1000 days

From conception to 2 years of age

-9 to 0 months
Pregnancy

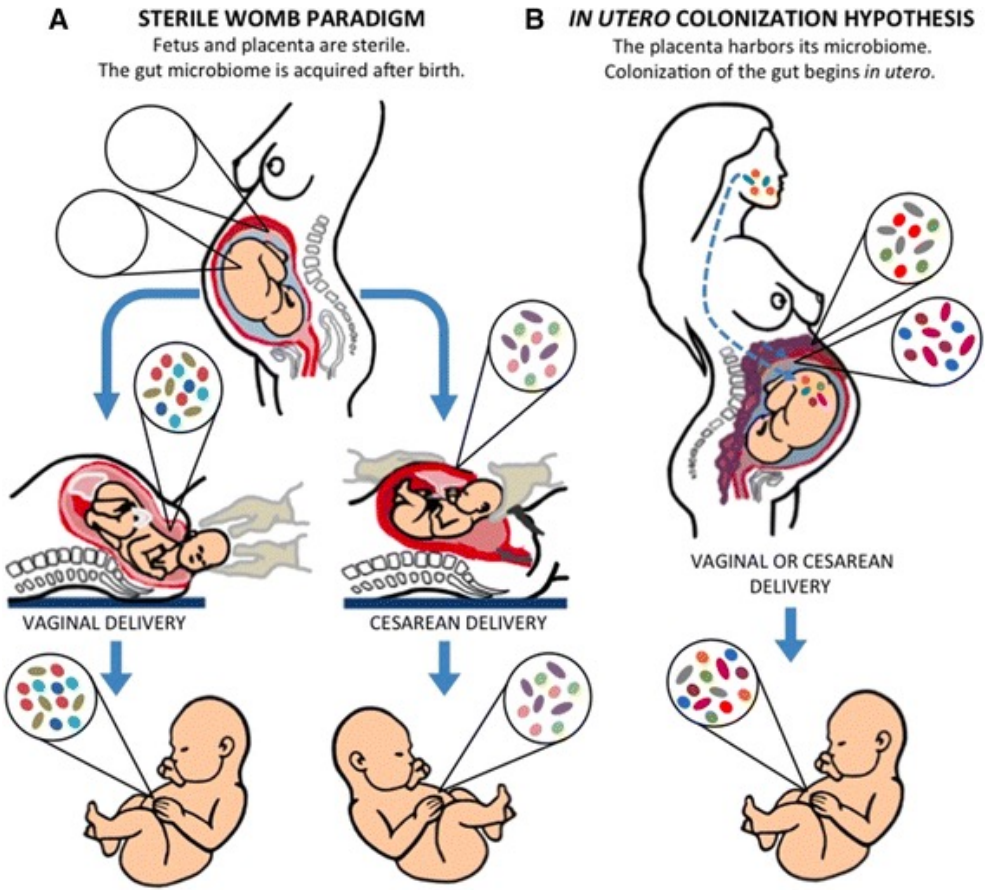
0 to 6 months
Breastfeeding

6 to 12 months
Solid food Introduction

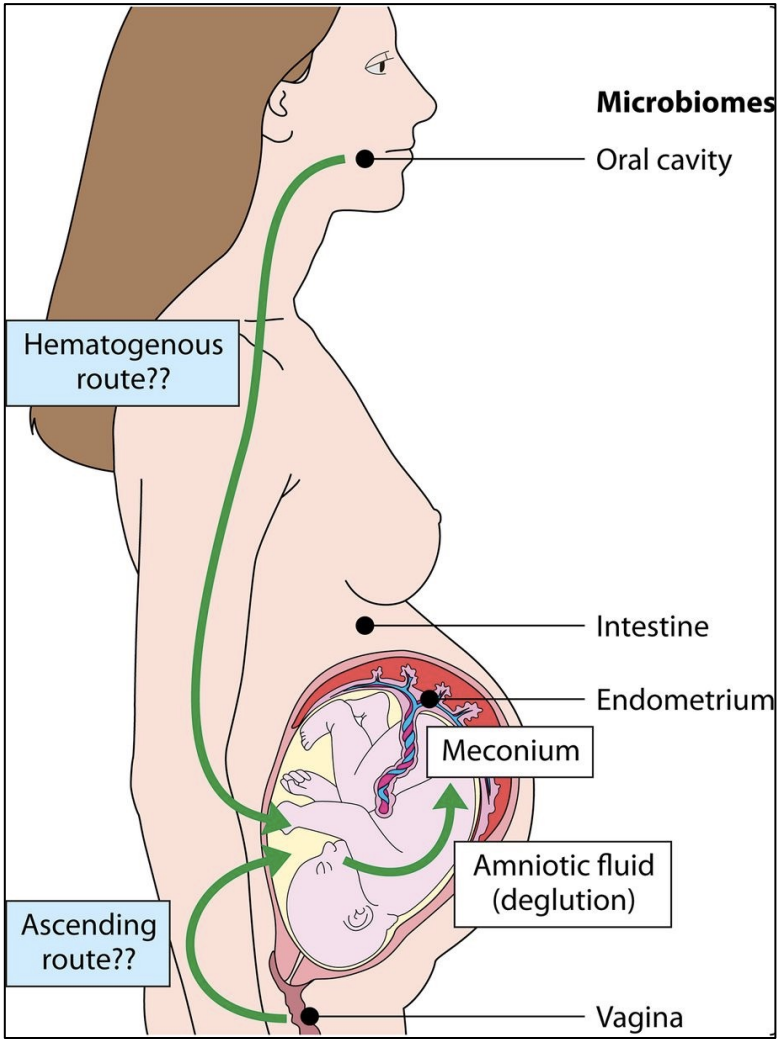
> 12 months
Transition To family diet

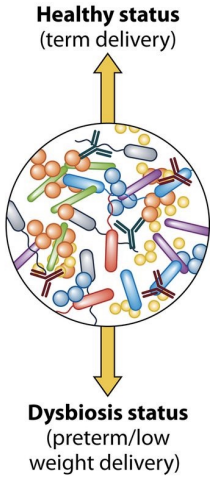
Day 0 – 270: Pregnancy

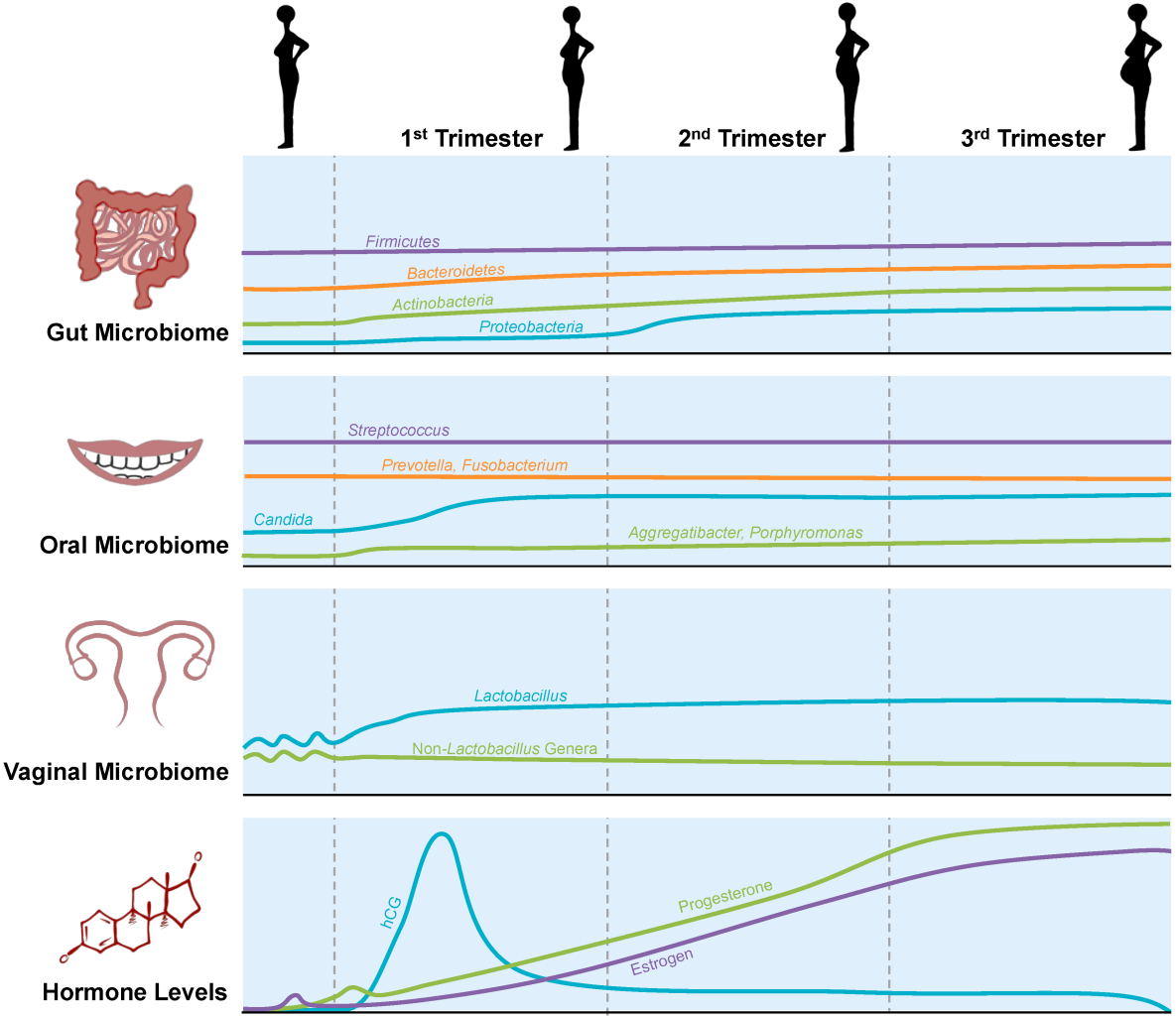
Is the fetus sterile?



Perez-Munoz (2017)
Microbiome

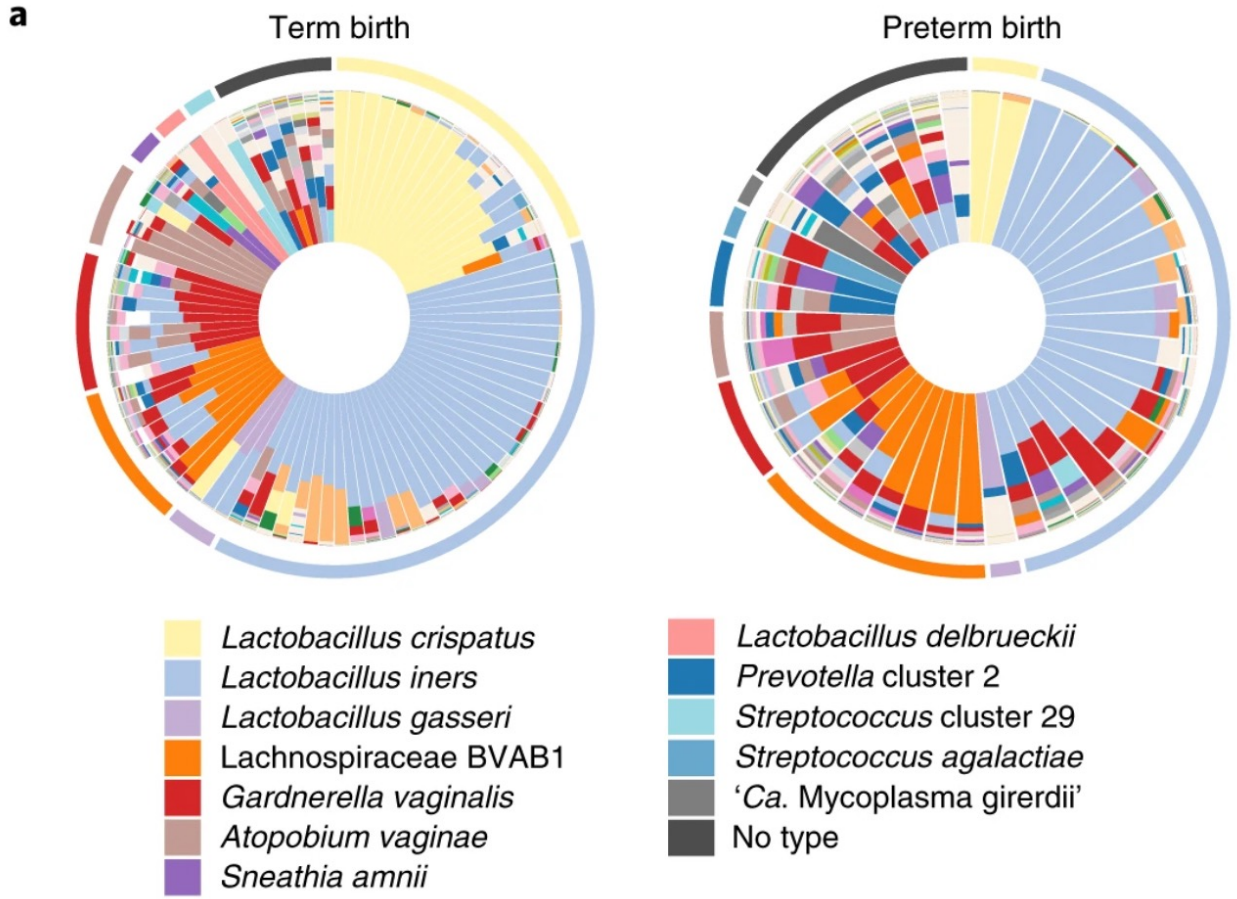

Microbiomes
Oral cavity
Hematogenous route??
Intestine
Endometrium
Meconium
Amniotic fluid (deglution)
Ascending route??
Vagina


Healthy status
(term delivery)
Dysbiosis status
(preterm/low weight delivery)



Amir et al (2020)
Microorganisms

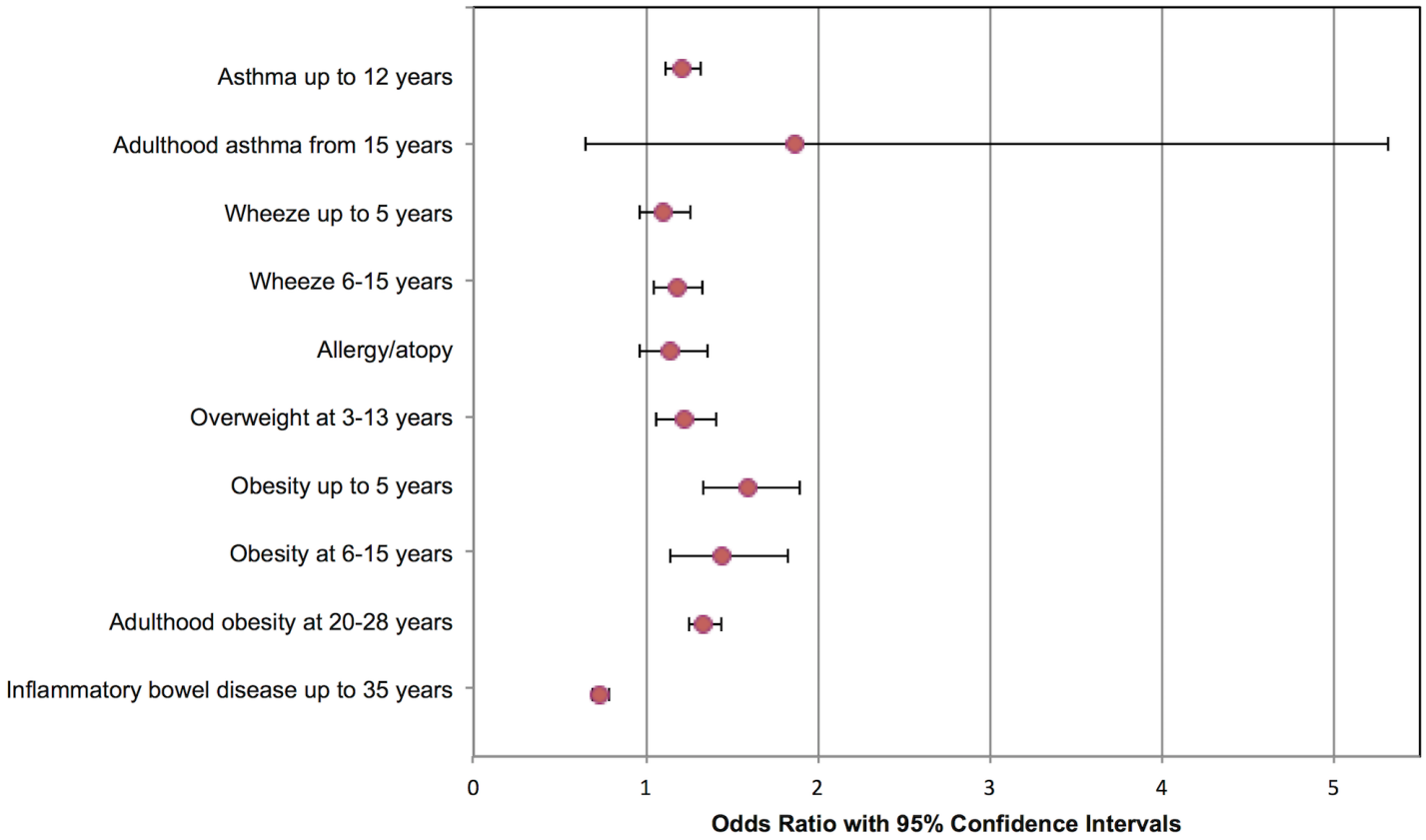
Vaginal microbiome and preterm birth



Fettweiss et al (2019)
Nat Micro

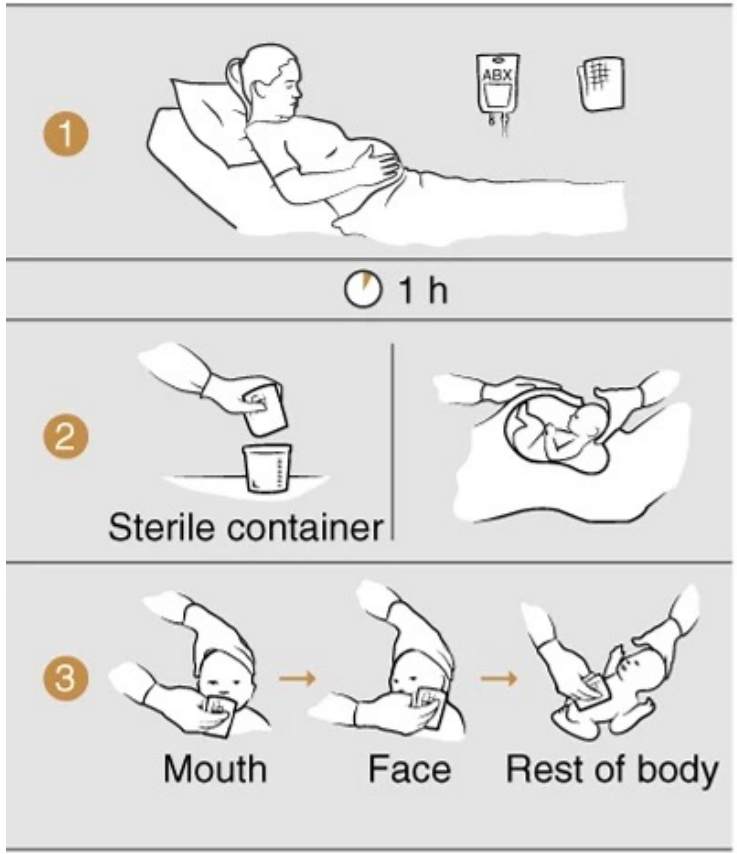
Day 270:
Birth

Long-term associations with C-section birth



Keag et al (2018)
Plos Medicine

Vaginal Seeding



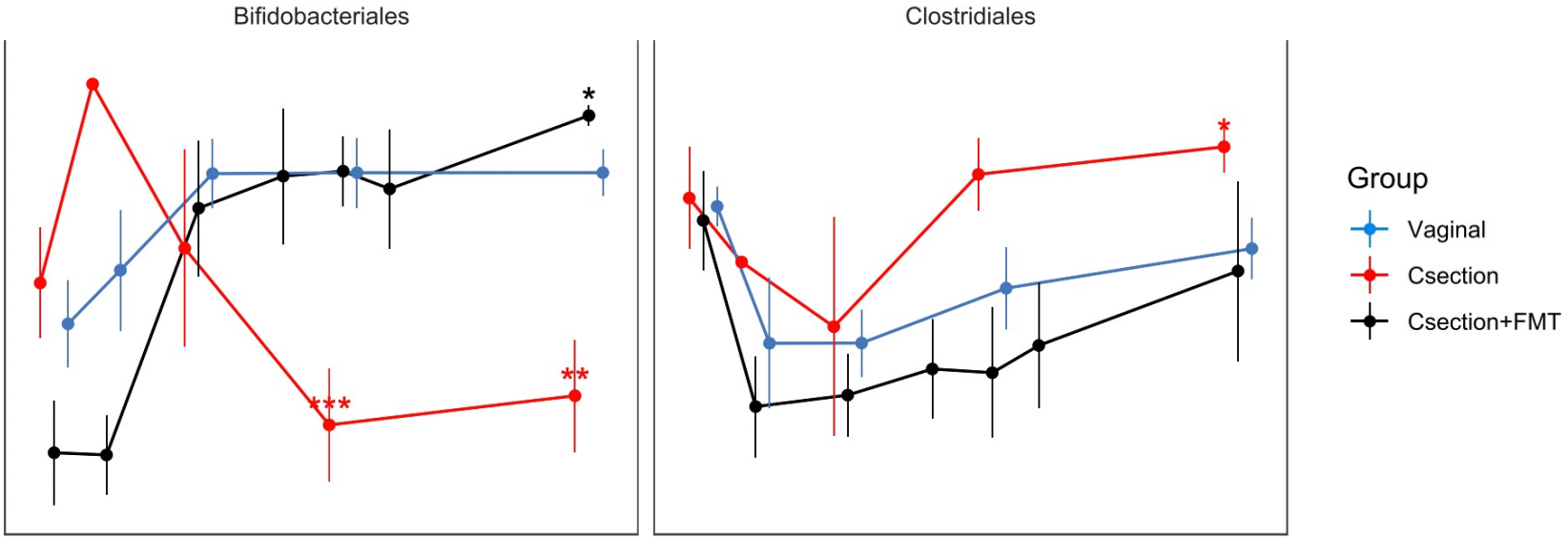
Vaginal Seeding

Standard vaginal delivery

C-section delivery

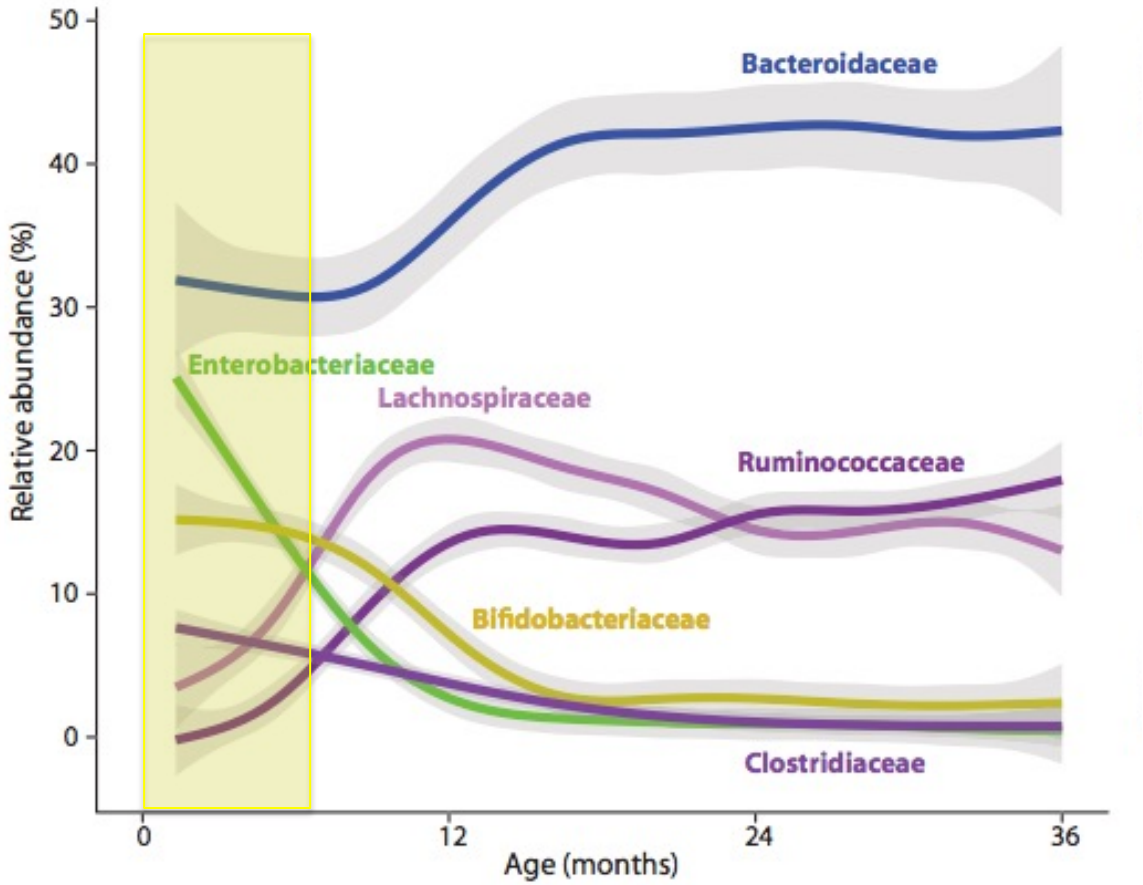
Vaginal ‘seeding’

Fecal transplant – C-section

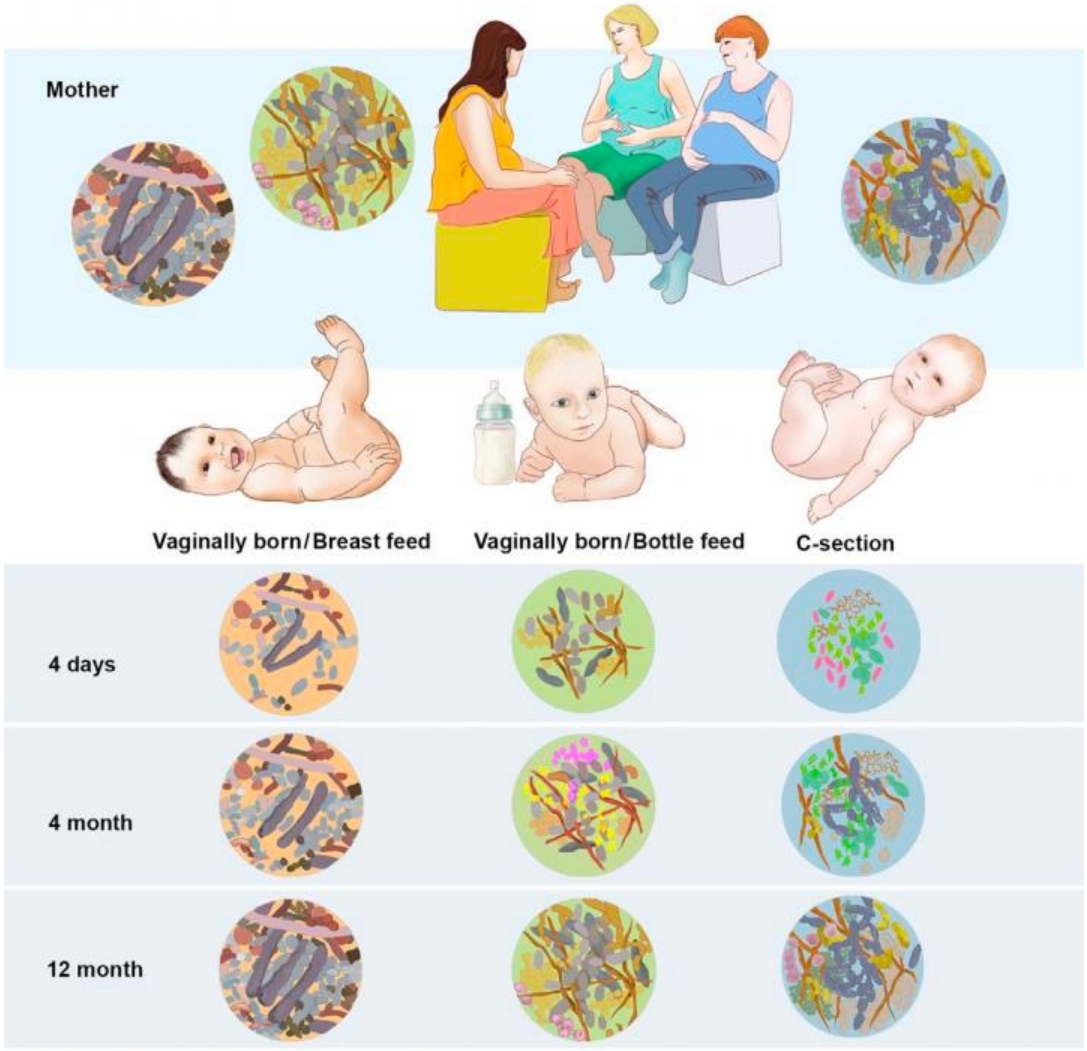


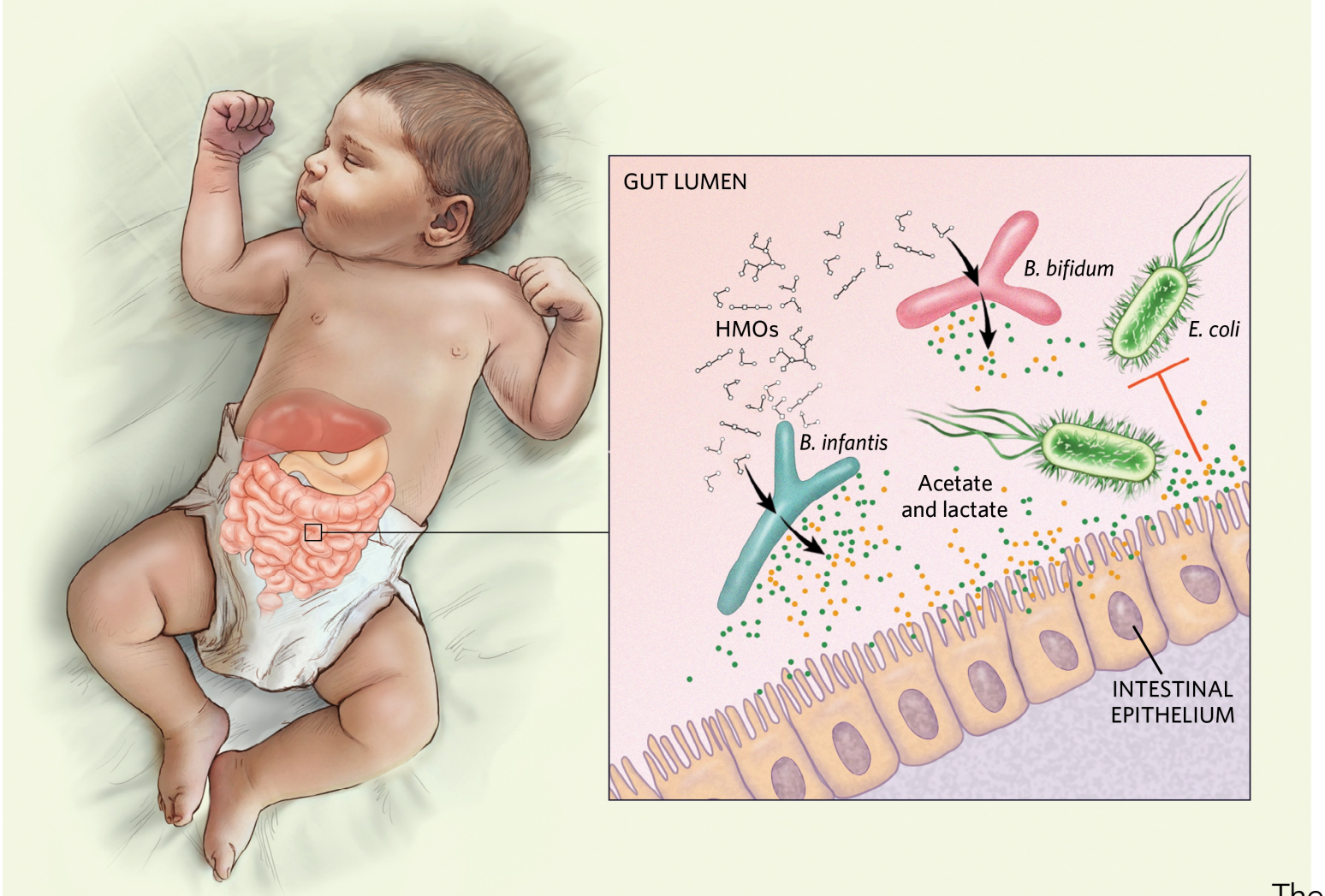
Day 270 - 450
First 6 months

Gut Microbiome in the First 1000 Days

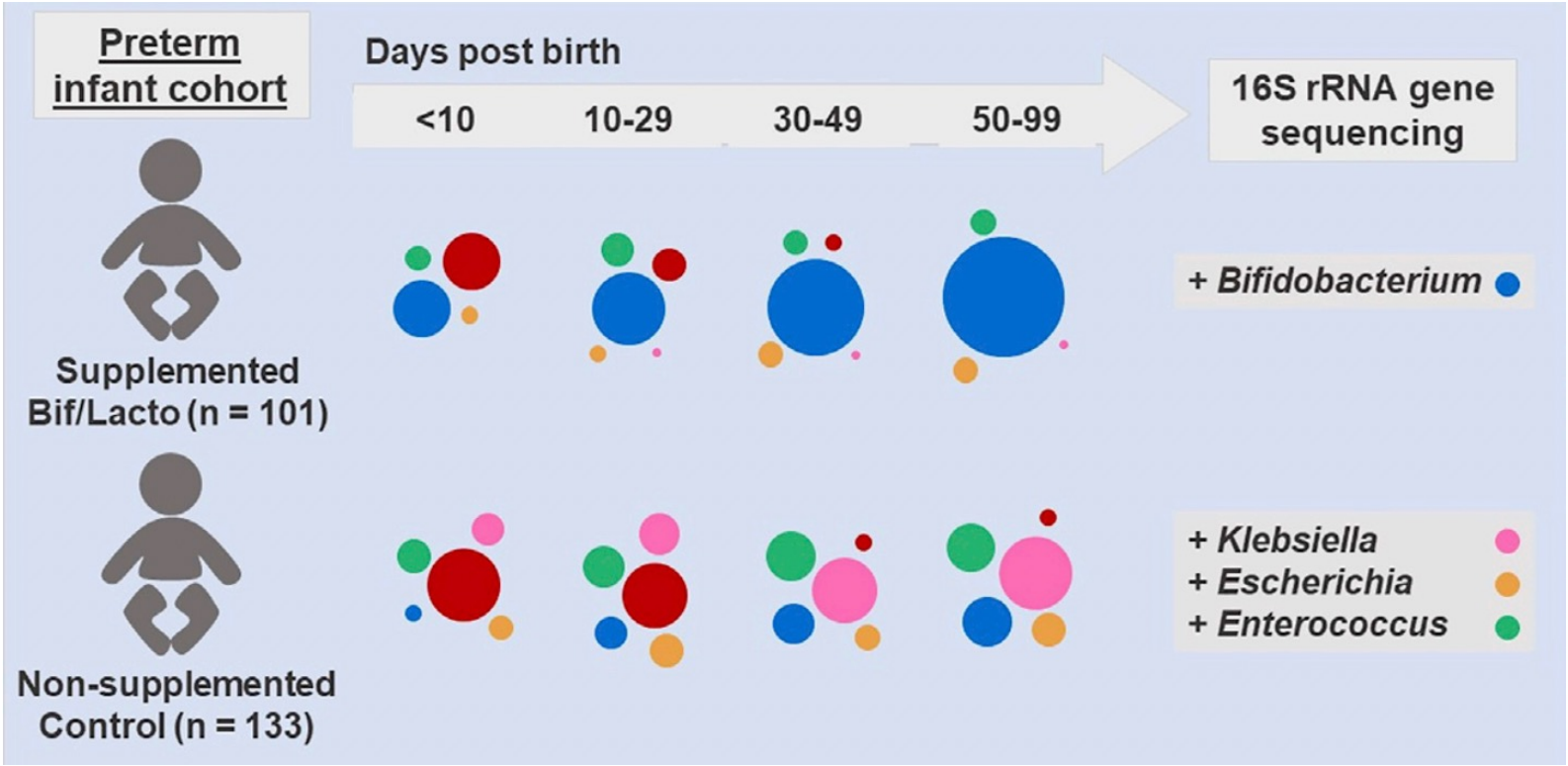


Yassour et al. (2016)
Sci Trans Med


Mother
Vaginally born/Breast feed
Vaginally born/Bottle feed
C-section
4 days
4 month
12 month

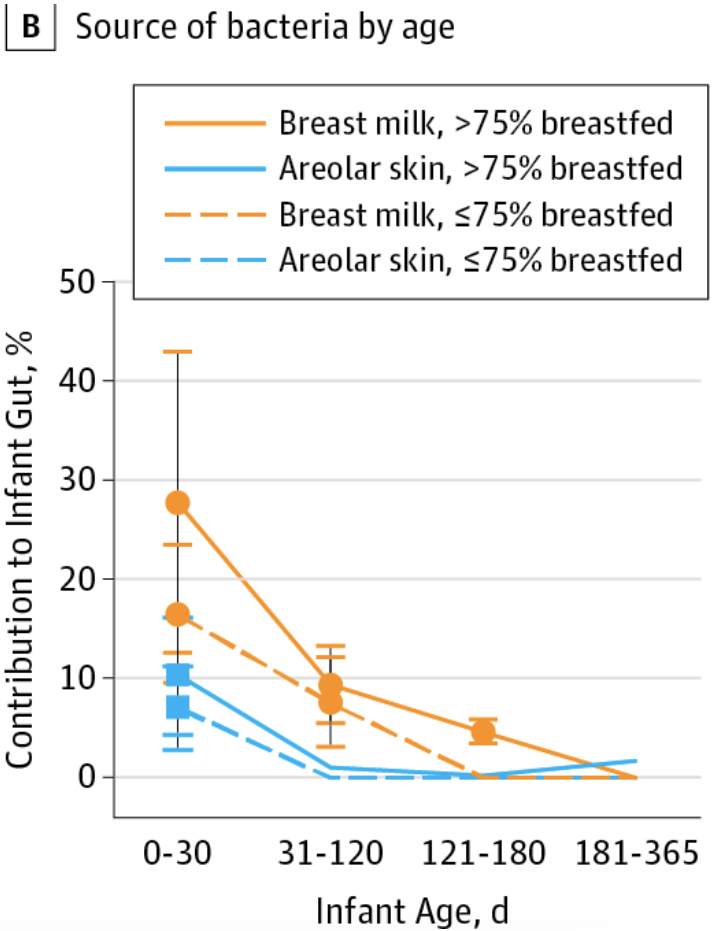

GUT LUMEN
HMOs
B. bifidum
E. coli
B. infantis
Acetate
and lactate
INTESTINAL
EPITHELIUM

Probiotics in preterm birth can reduce risk of sepsis, NEC, death



Alcon-Giner et al (2020)
Cell Rep Med

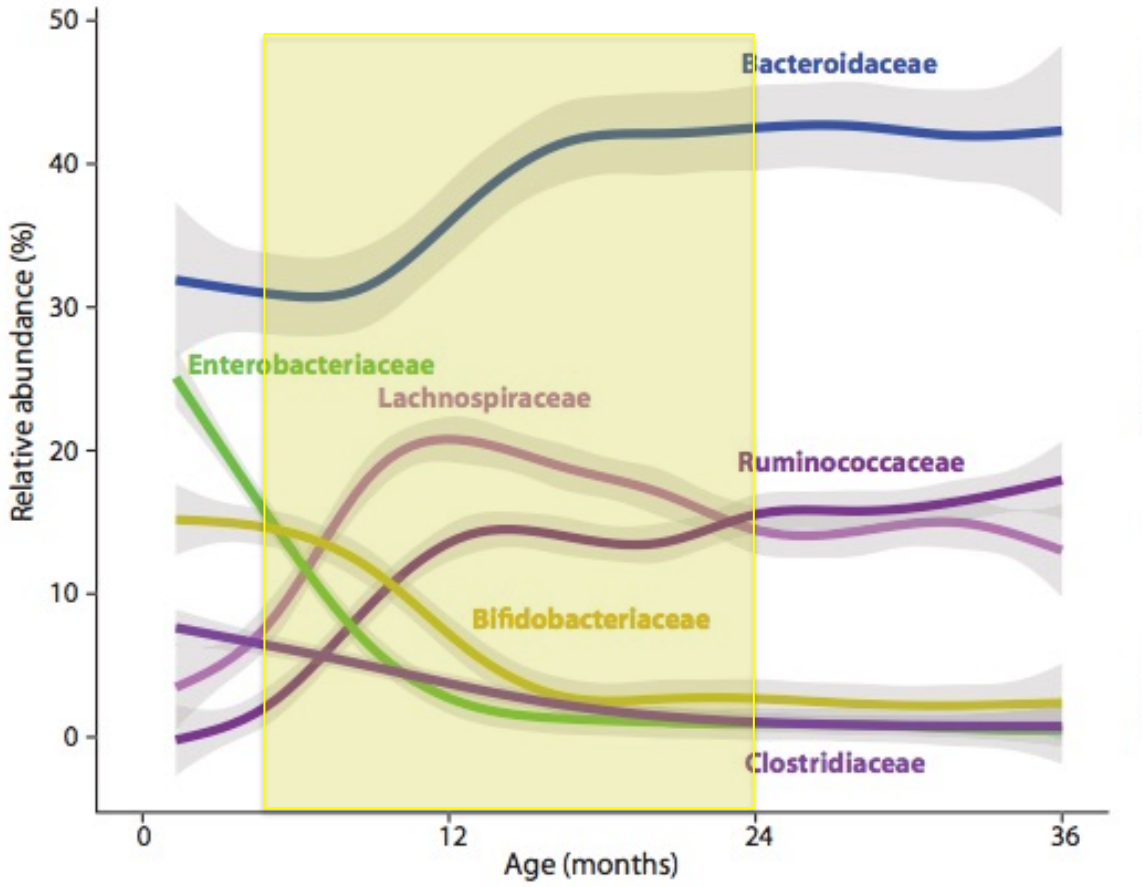
Breastmilk seeds and feeds the infant gut microbiota



Pannaraj et al (2017)
JAMA Paediatrics

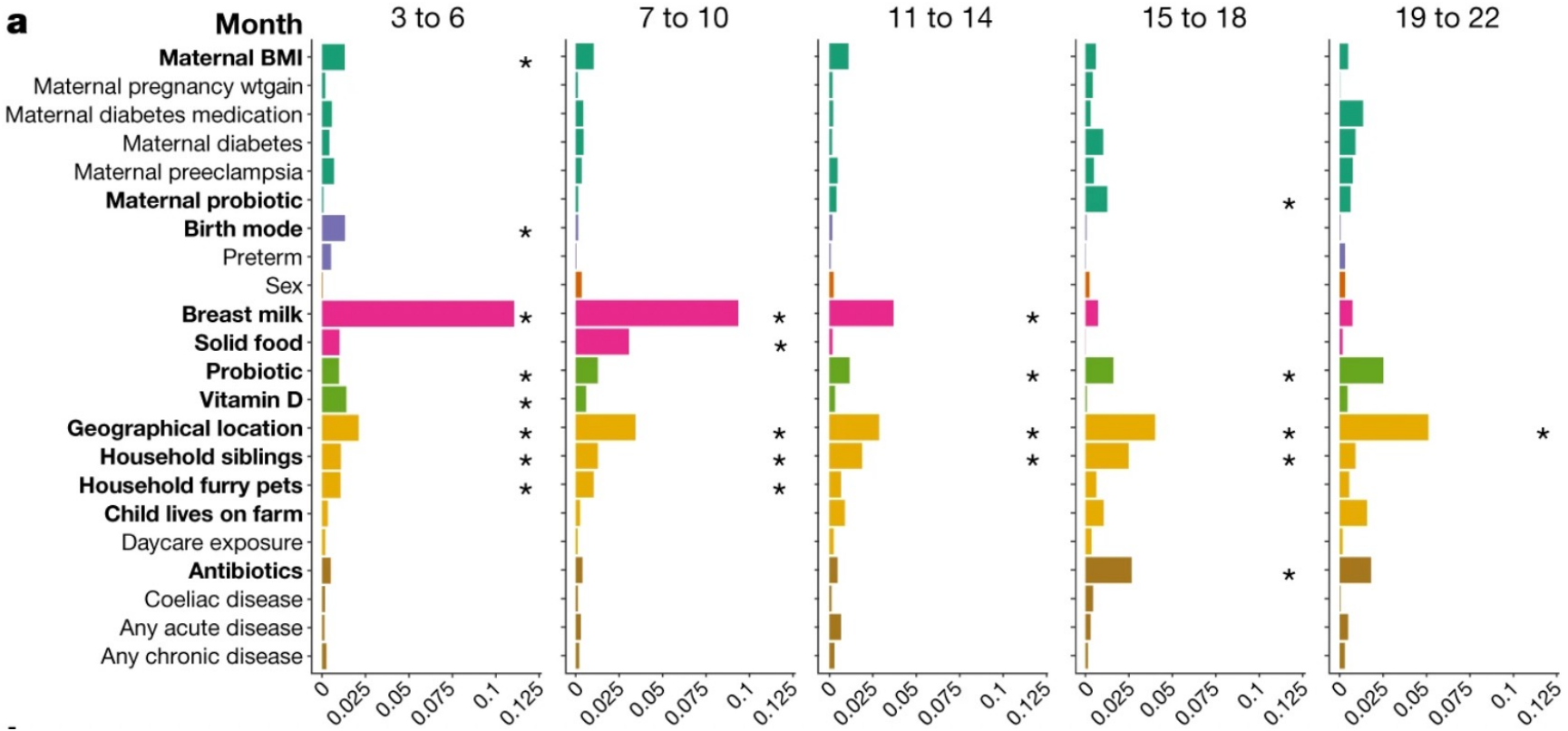
Day 450 - 1000
Up to 2 years

Gut Microbiome in the First 1000 Days



Yassour et al. (2016)
Sci Trans Med

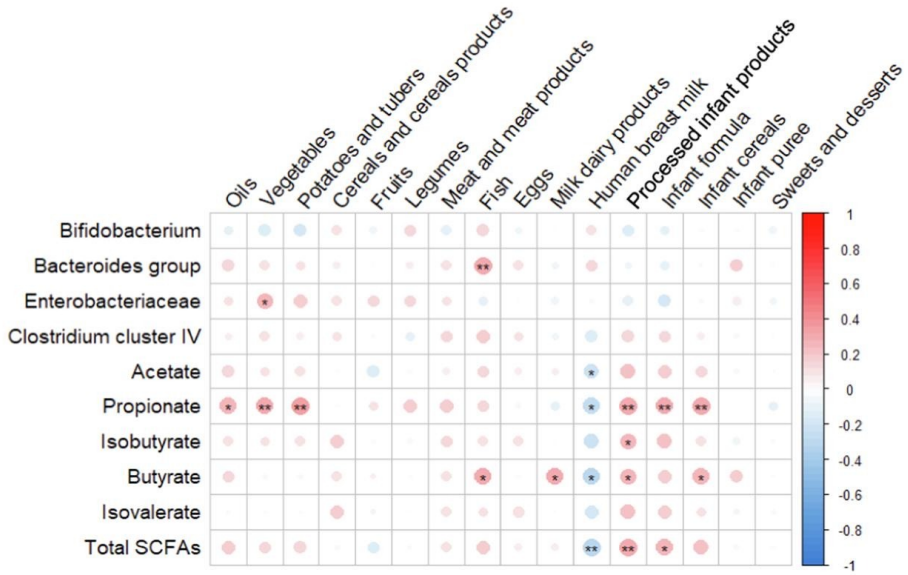
Influences on gut microbiome composition throughout childhood



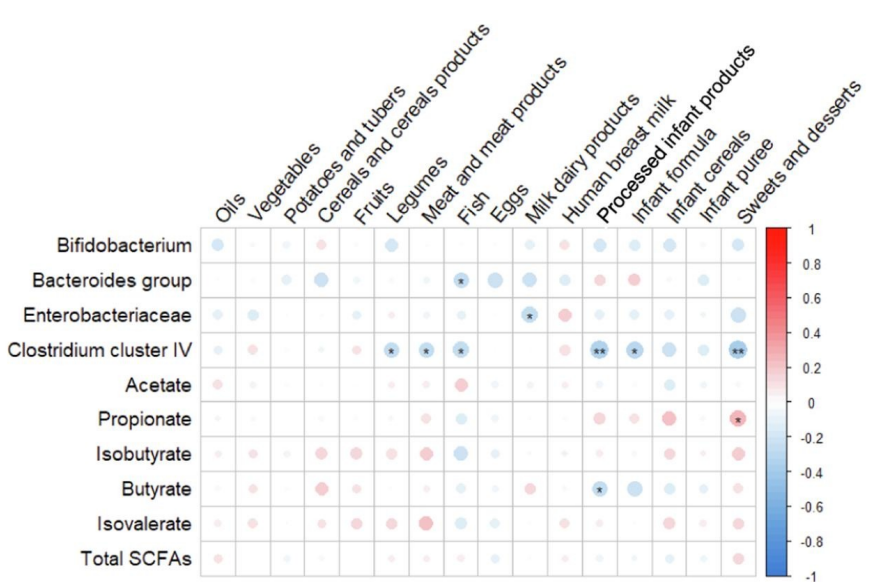
Stewart et al (2018)
Nature

Complementary foods affect gut microbiome maturation during weaning

6 months

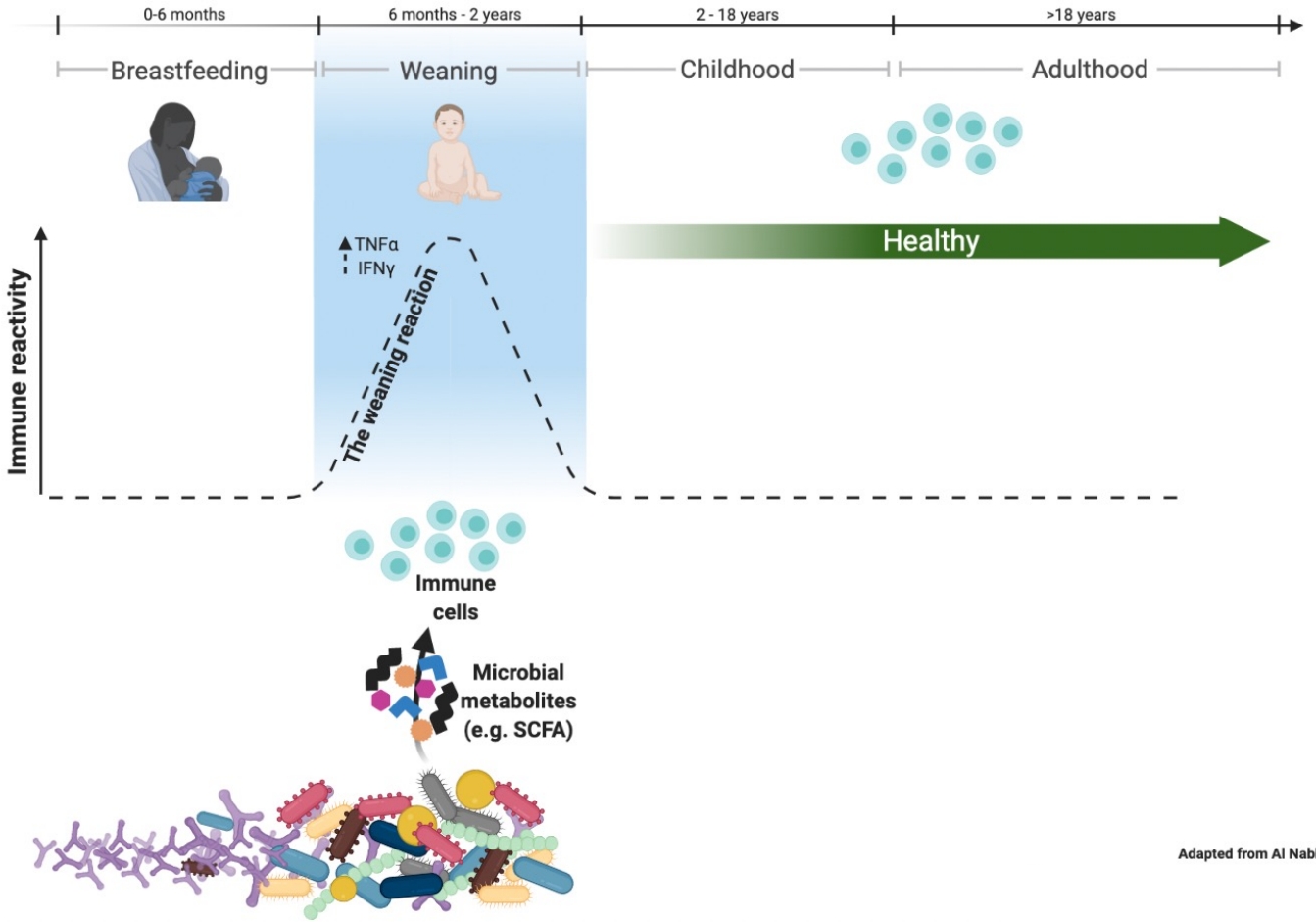


12 months



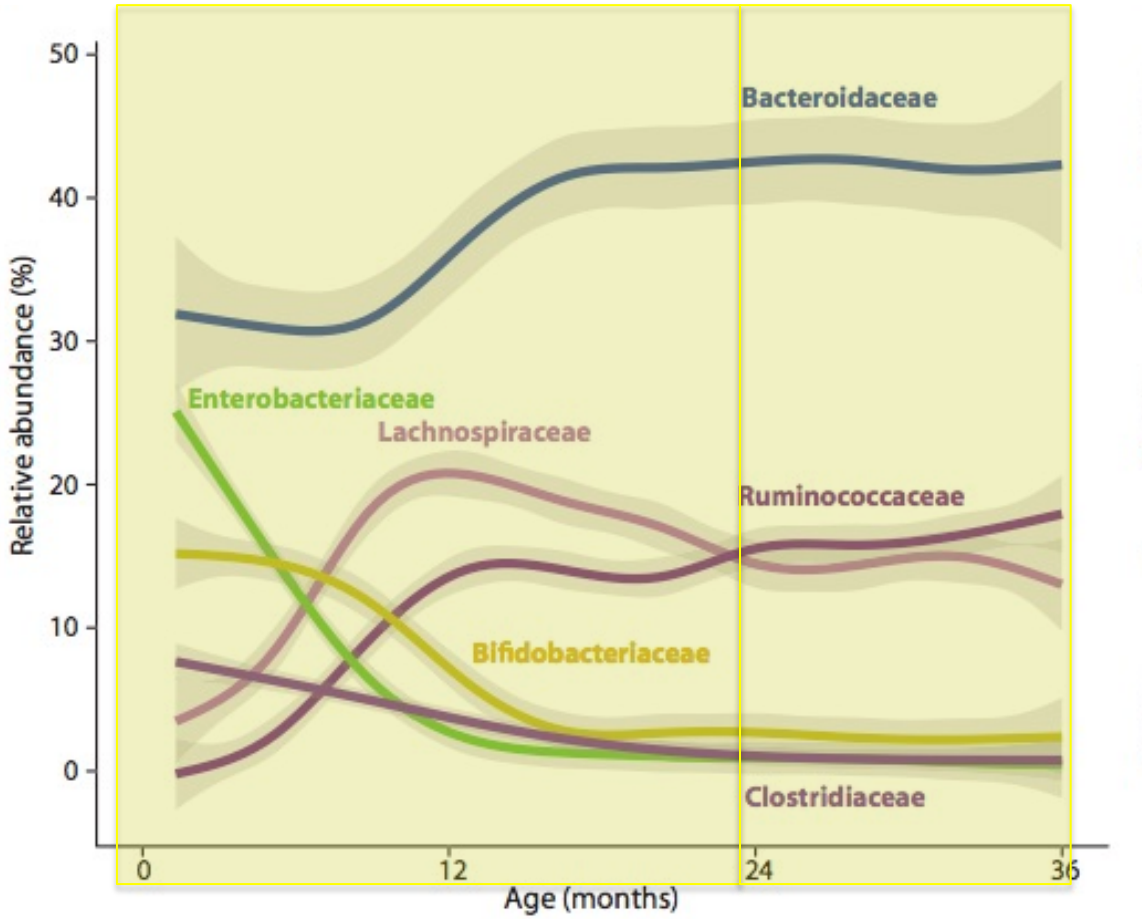
Gomez-Martín et al (2022)
Food Res Int

The weaning microbiome drives immune maturity



Adapted from Al Nabhani et al. *Immunity* (2019)

Gut Microbiome in the First 1000 Days



Yassour et al. (2016)
Sci Trans Med

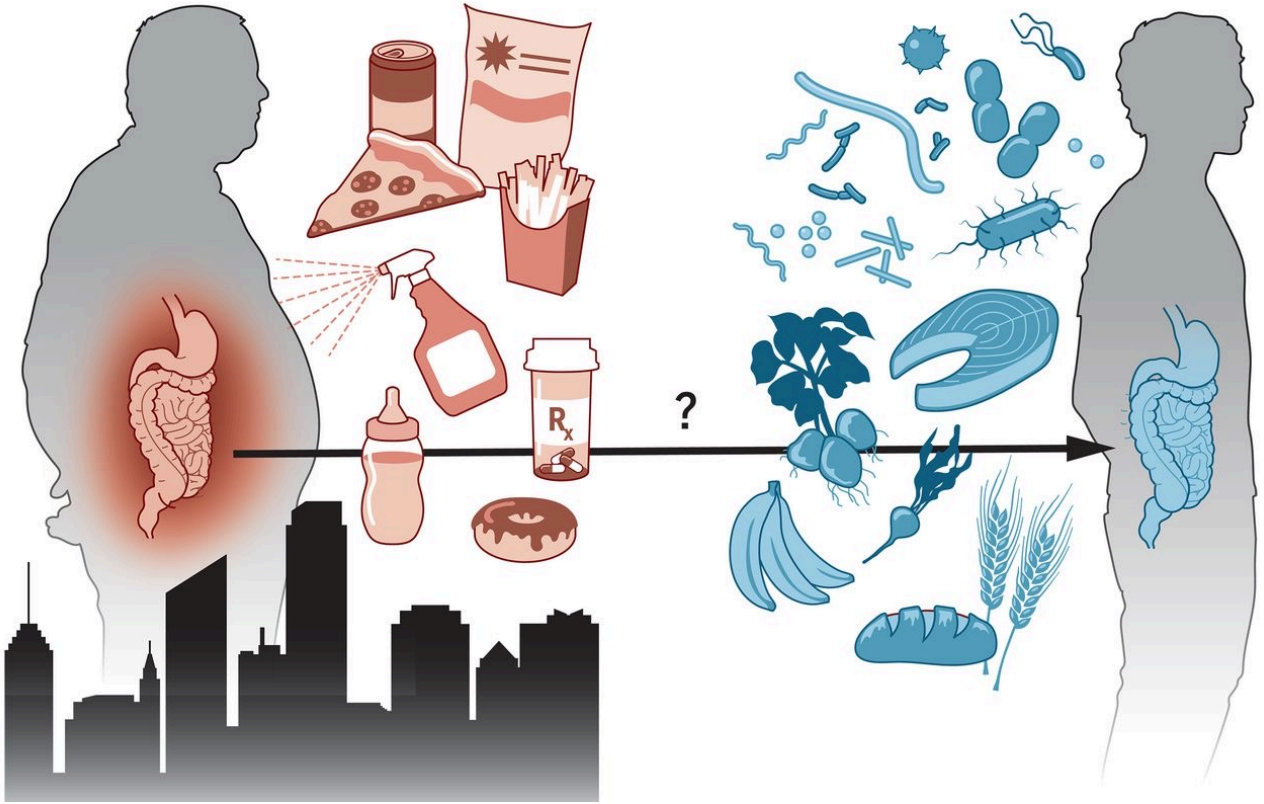
Questions?

Break

3 Environmental impacts on human microbiome

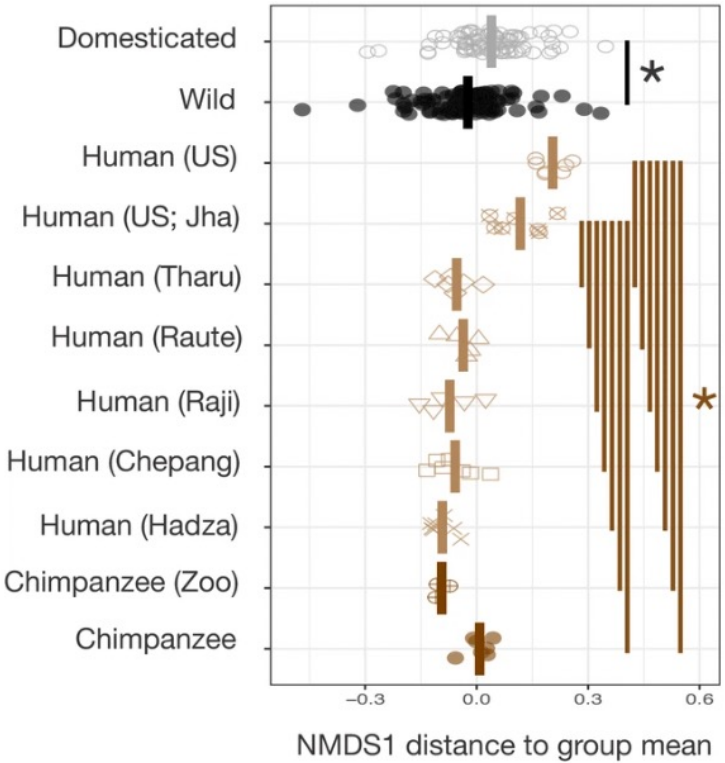
Our microbiomes are shaped by our environments

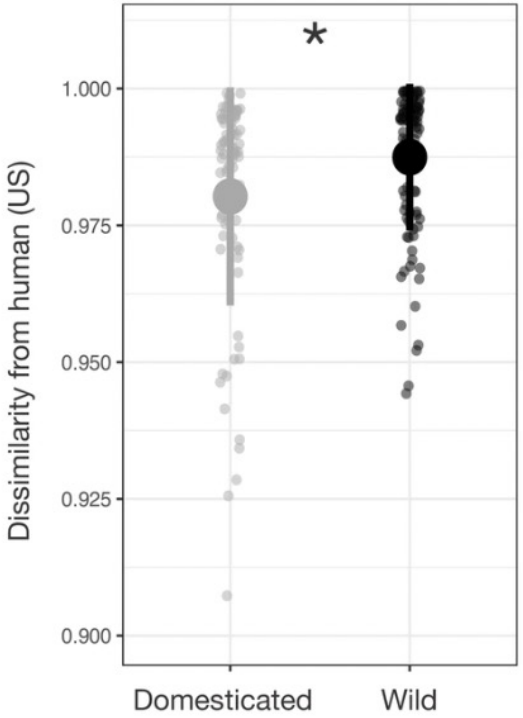
Industrialization changes the microbes that colonize humans



Sonnenburg et al (2019)
Science

Domestication of wild animals mirrors human industrialization of gut microbiome

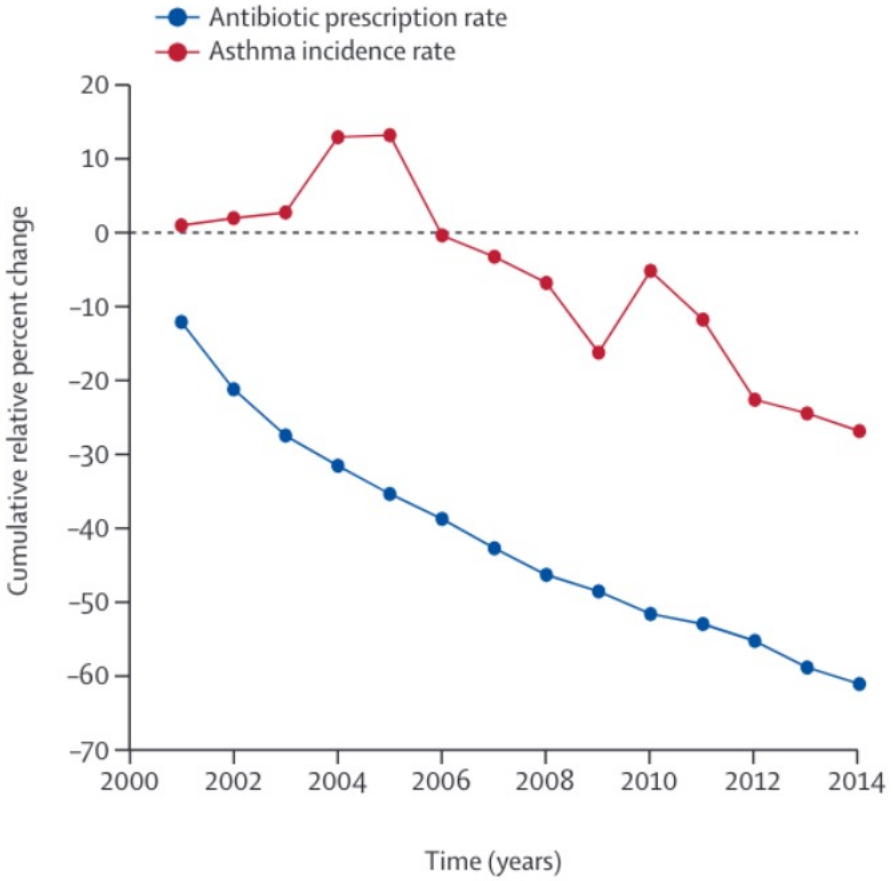




Reese et al (2021)
eLife

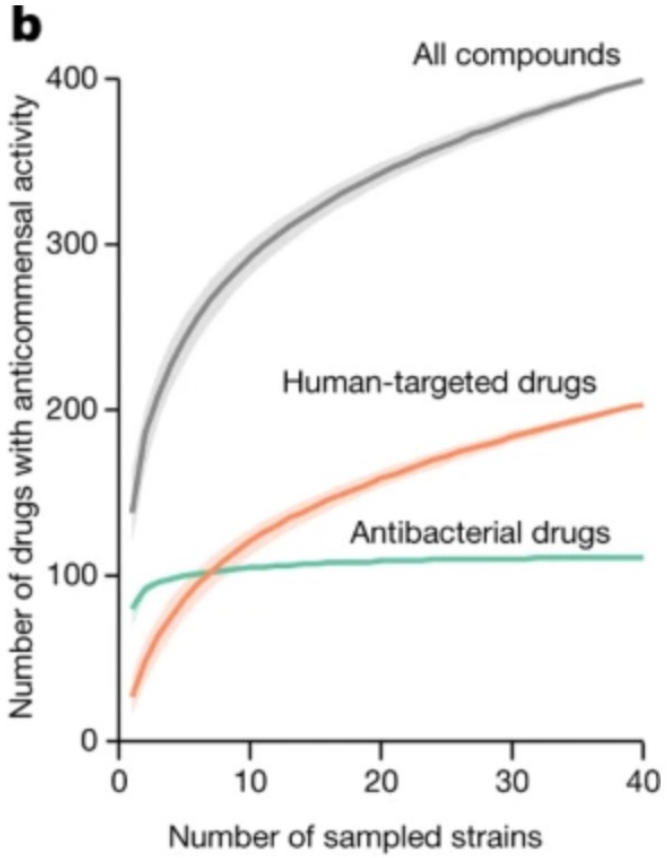
Antibiotics disturb maturation of the early-life gut microbiome

Antibiotics associated with asthma and allergies



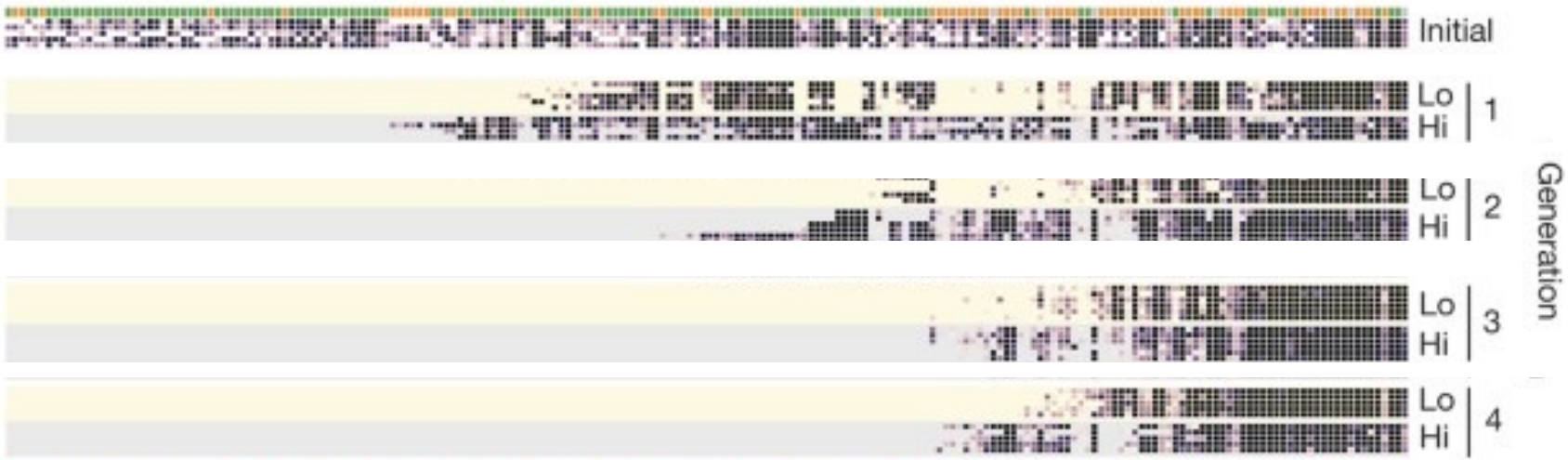
Patrick et al (2020)
Lancet Resp Med

Non-antibiotic drugs have large impact on gut microbiome

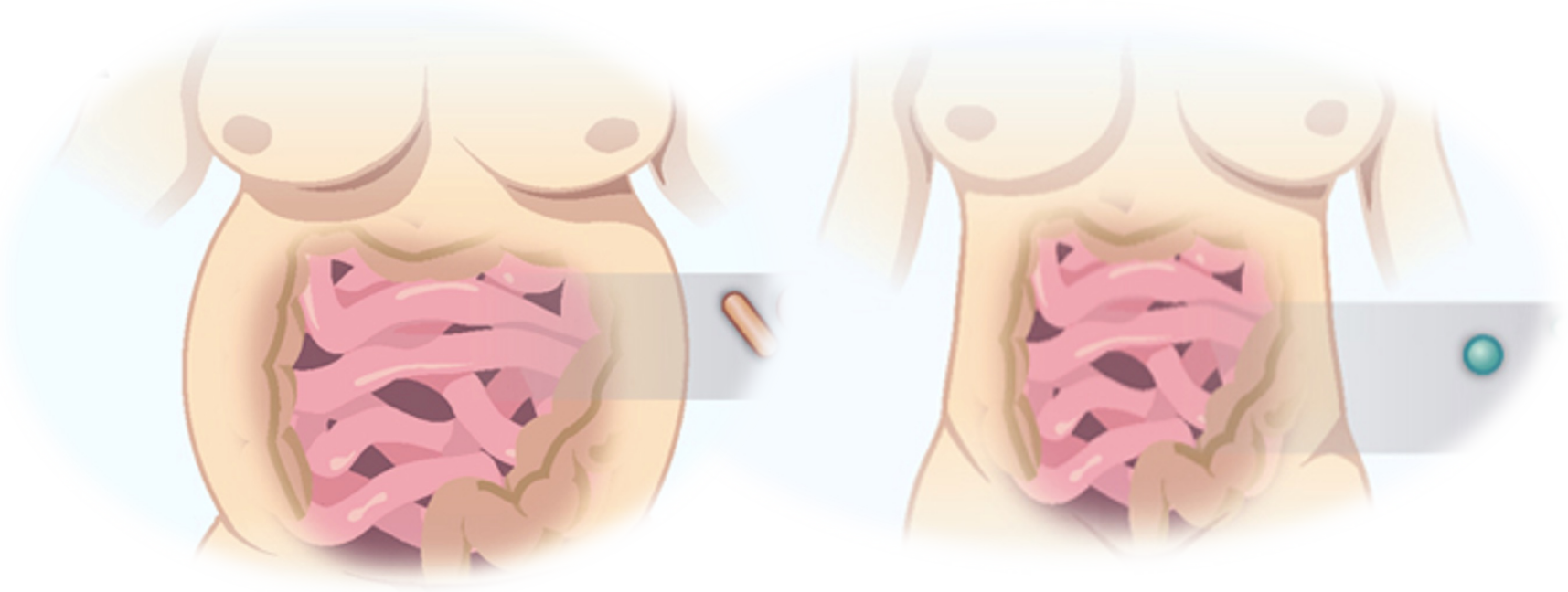


Maier et al (2018)
Nature

Low fiber diets reduce microbiome diversity across generations



Sonnenburg et al (2016)
Nature



4 Gut microbiome & modern chronic diseases

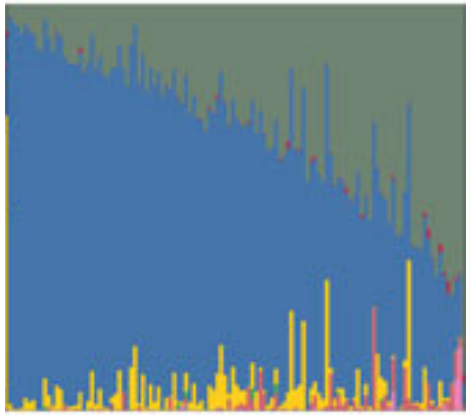
What is a ‘healthy’ microbiome?

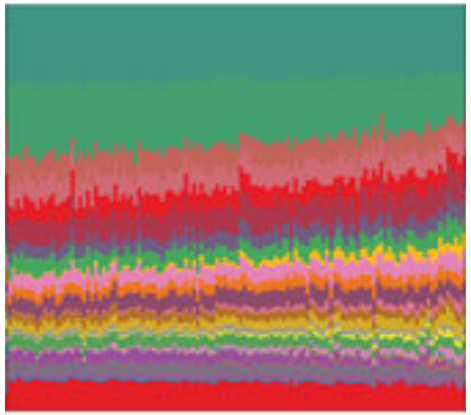
‘Healthy’ human microbiome

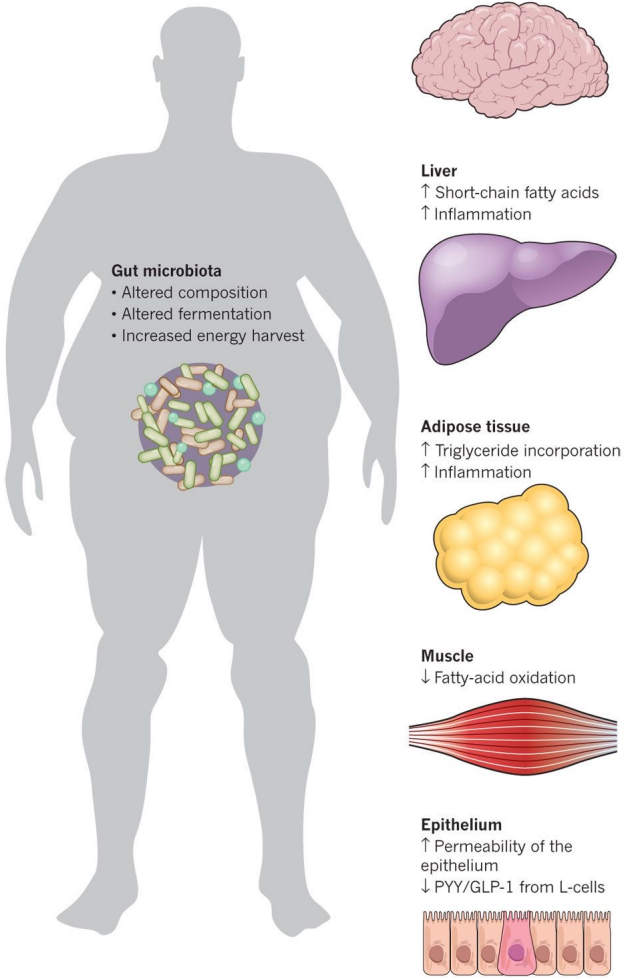
- **Diversity** the only consistent marker of ‘healthy’ gut microbiome

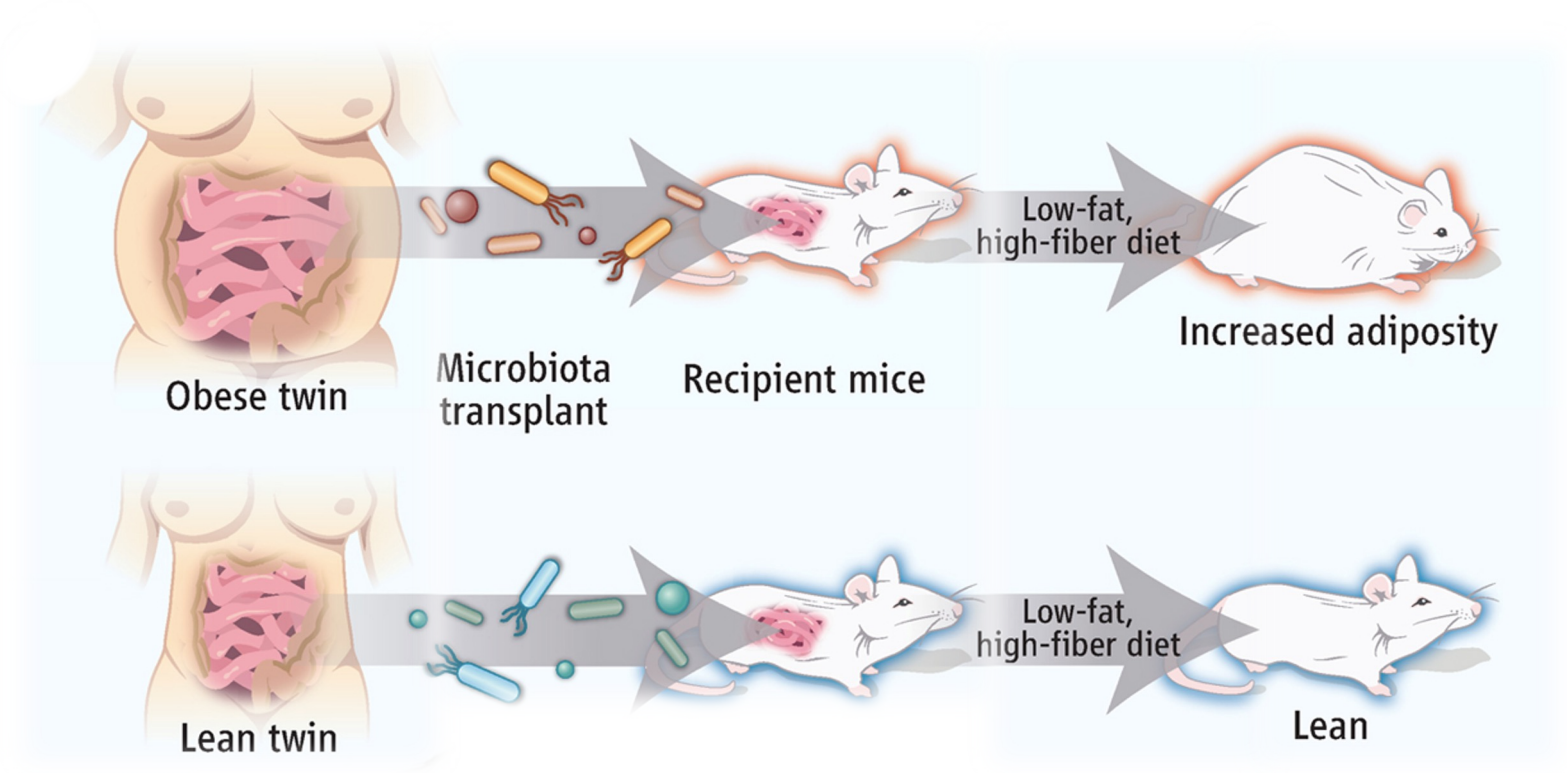
- Gut microbiome ‘enterotypes’ associated with BMI/metabolic health in Western cohorts
  - **Bacteroides** -> high BMI
  - **Ruminococcaceae** -> normal BMI

- Gut microbiome **function** (genes/metabolites) better indicator of health outcomes

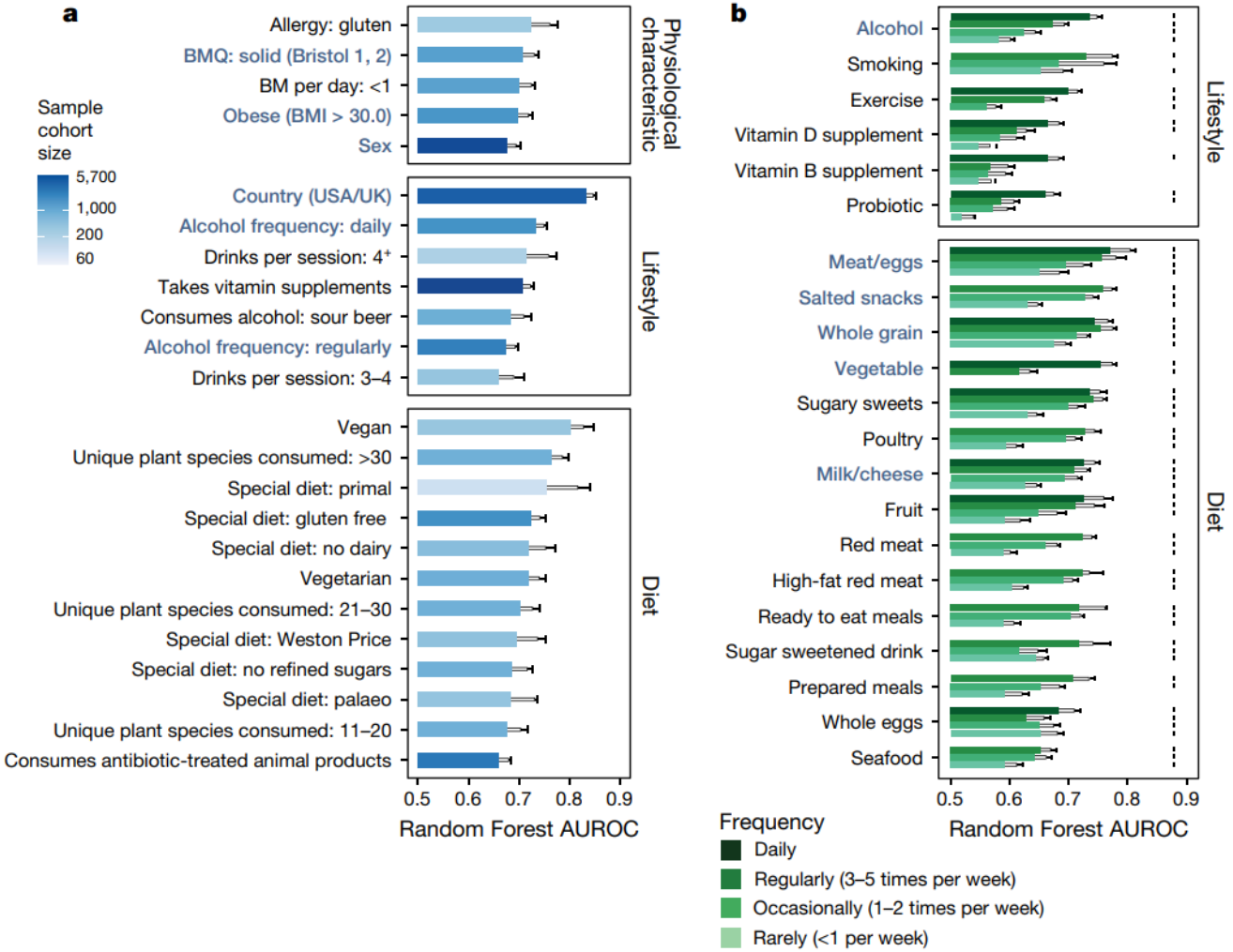





Gut microbiota
• Altered composition
• Altered fermentation
• Increased energy harvest
Brain
↓ Satiety
Liver
↑ Short-chain fatty acids
↑ Inflammation
Adipose tissue
↑ Triglyceride incorporation
↑ Inflammation
Muscle
↓ Fatty-acid oxidation
Epithelium
↑ Permeability of the epithelium
↓ PYY/GLP-1 from L-cells

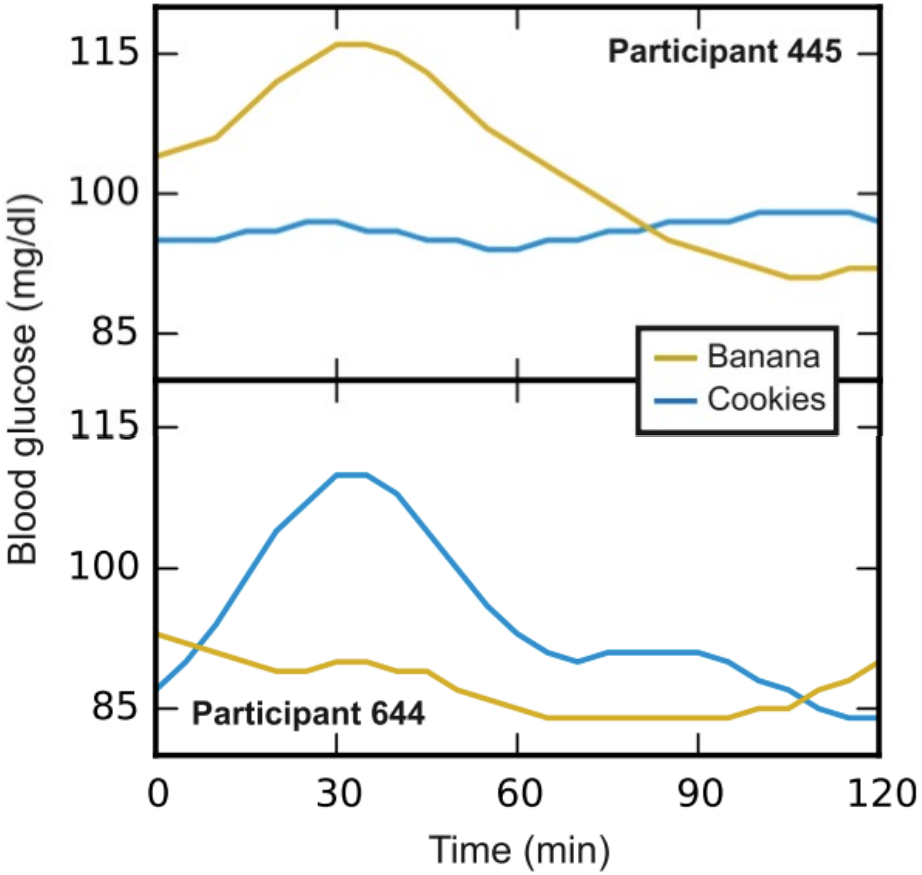


Ridaura et al. (2013) *Science*

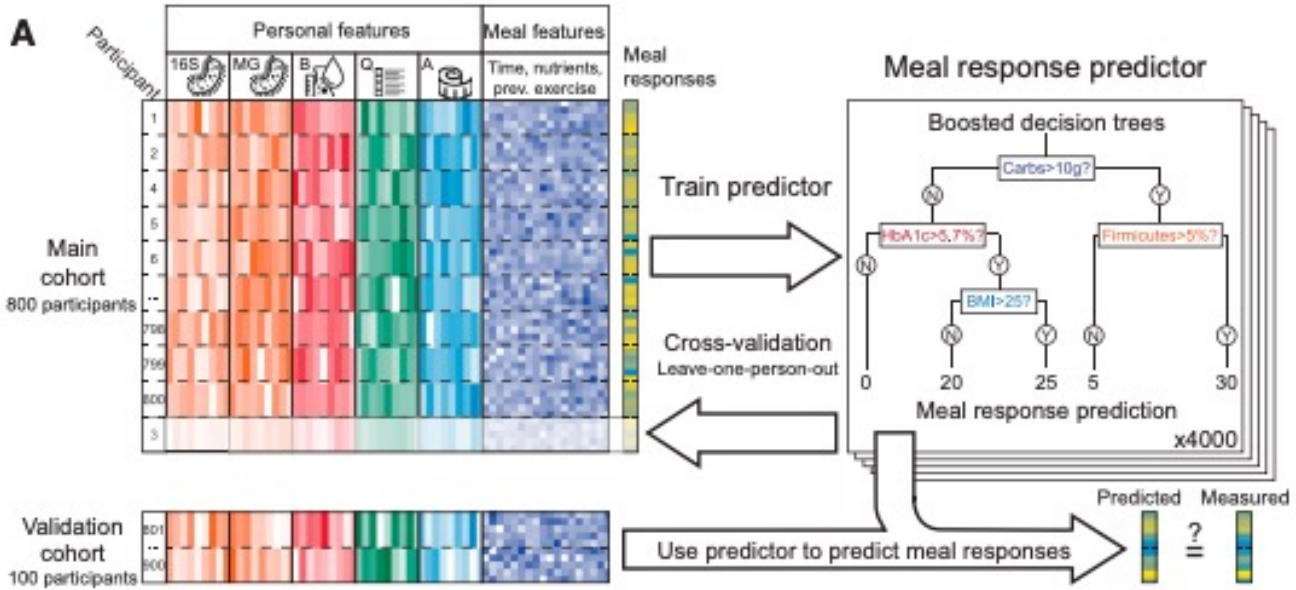


Vujkovic-Cvijin (2020)
Nature

Microbiomes are personalized

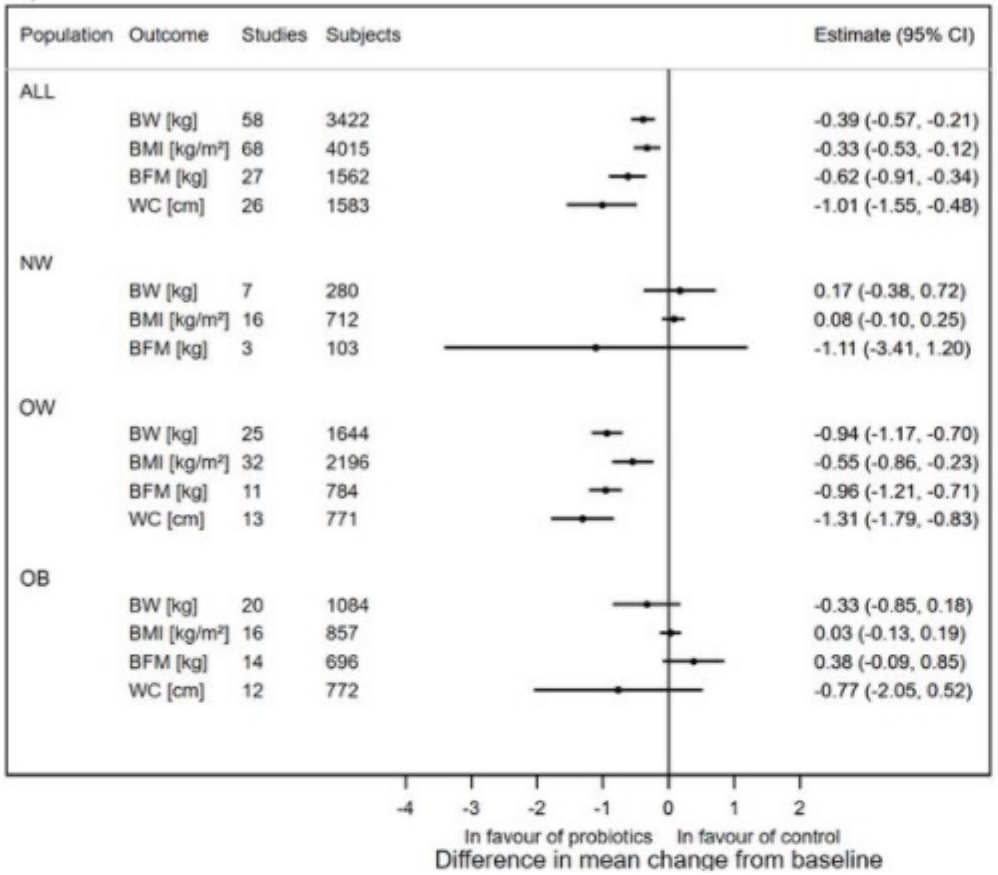


Zeevi et al. (2015)
Cell



Personalized probiotics, diets, treatments

Microbiome-targeted treatments

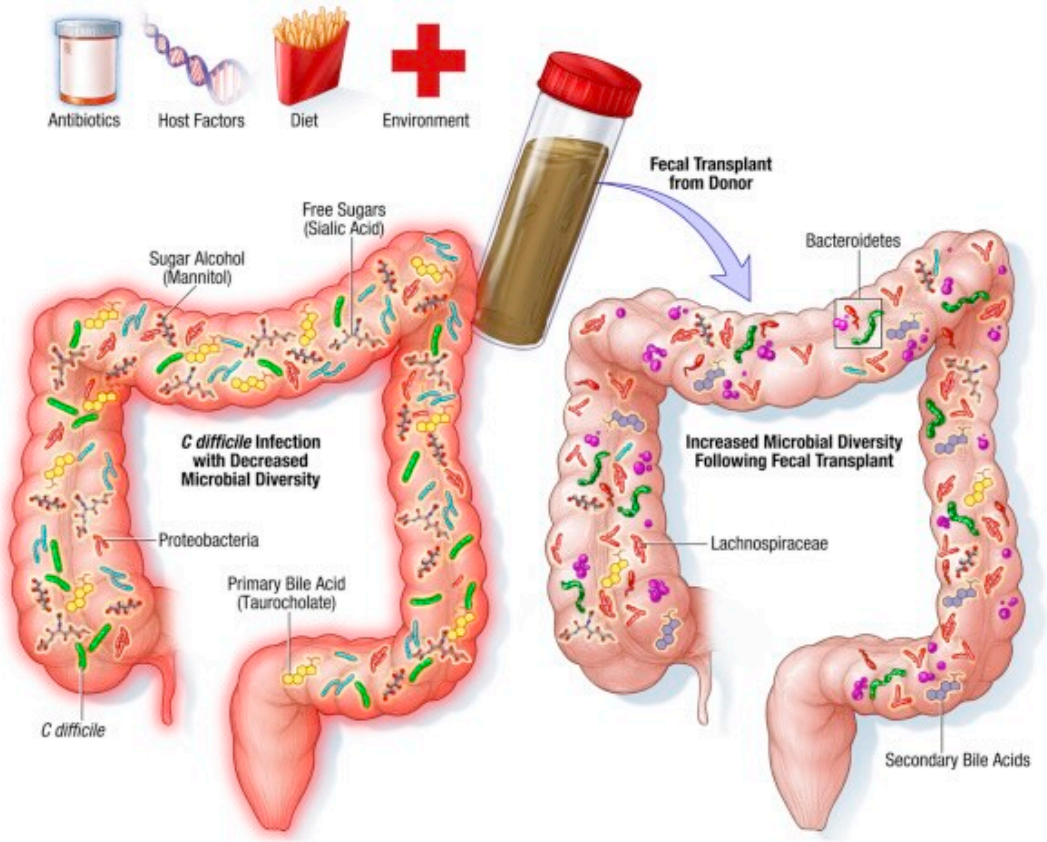


Probiotics and weight loss

- High heterogeneity
- 0.94kg over 8-12 weeks

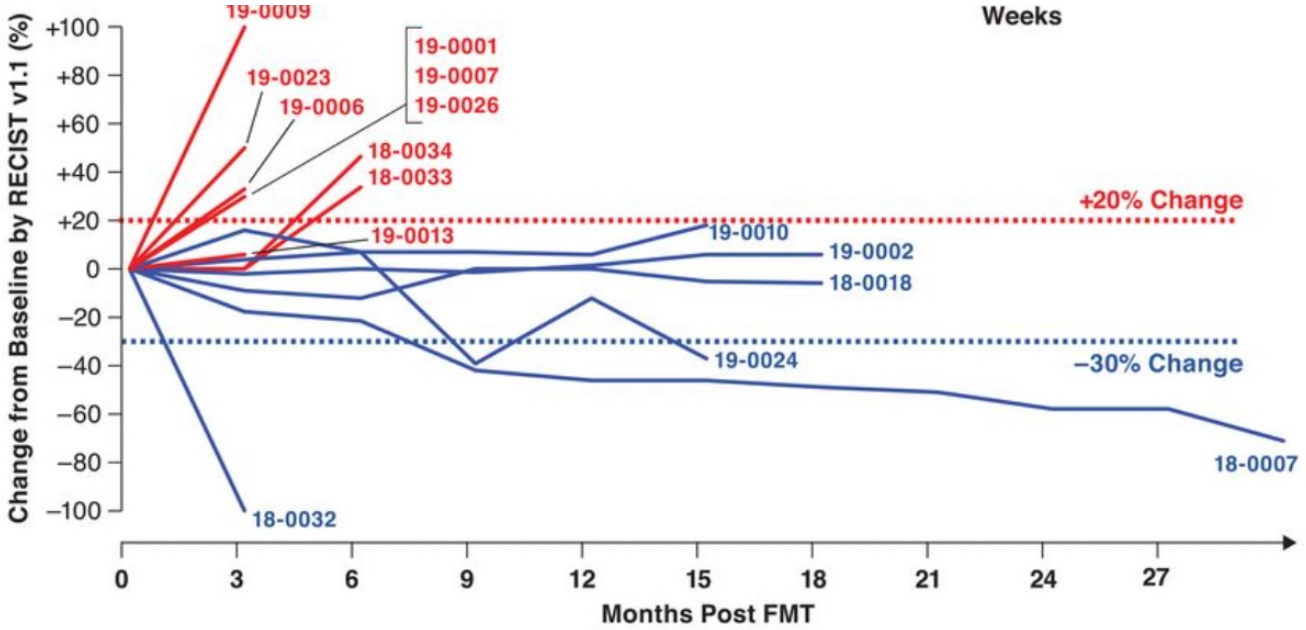
Koutnikova (2019)
BMJ Open

Fecal microbiome transplants (FMT) successfully treat recurrent Clostridium Difficile infection



Kelly (2015)
Gastroenterology

Fecal microbiota transplant overcomes resistance to anti–PD-1 therapy in melanoma patients



Davar (2021)
Science

Thank you