

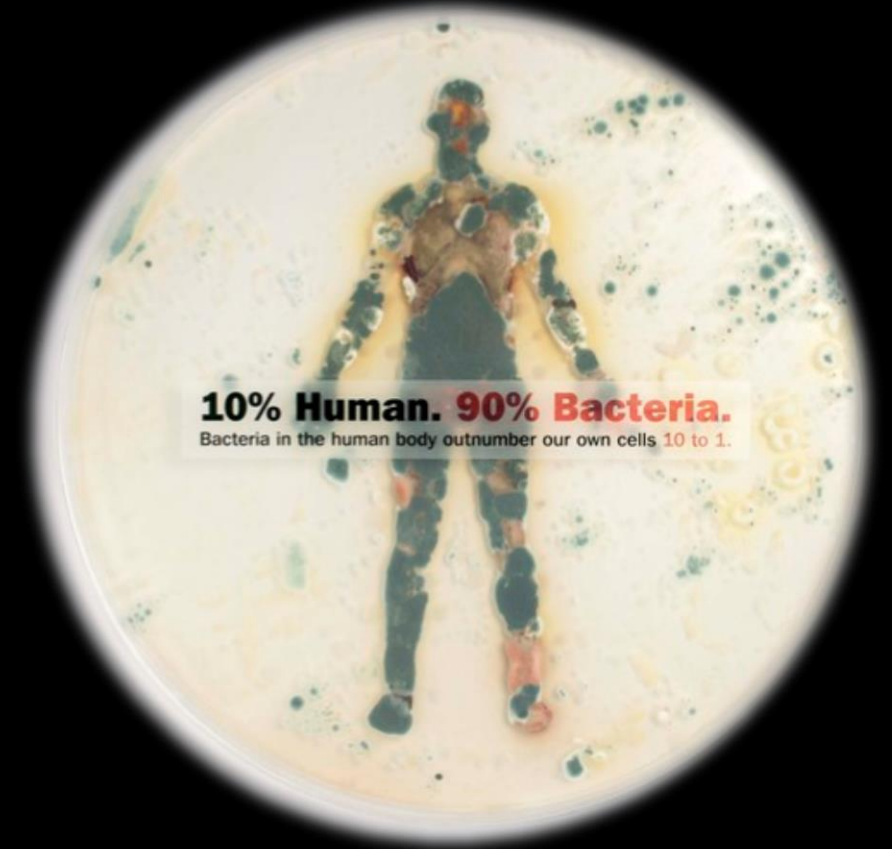
The vital role of
the microbiome
in human health
abandoning hygiene is
not the way to a
healthy microbiome

Colin Hill

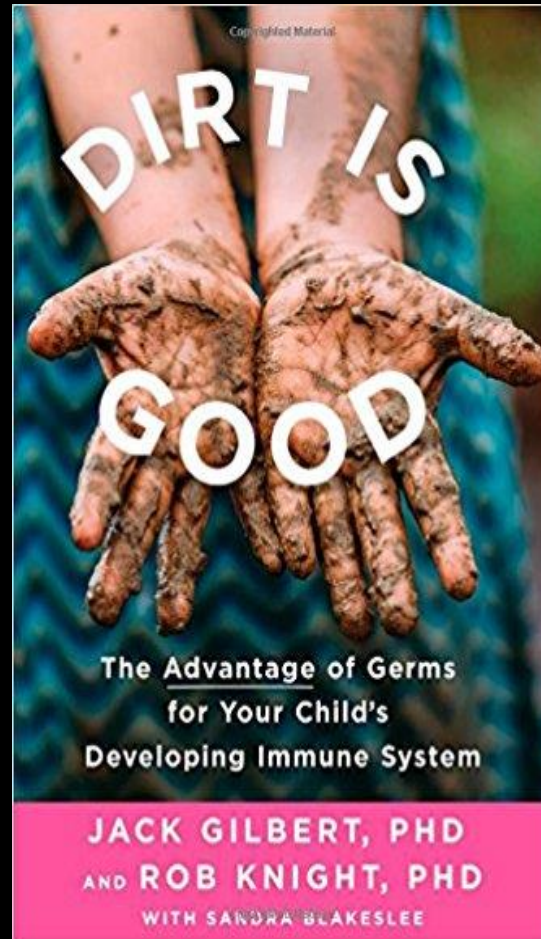
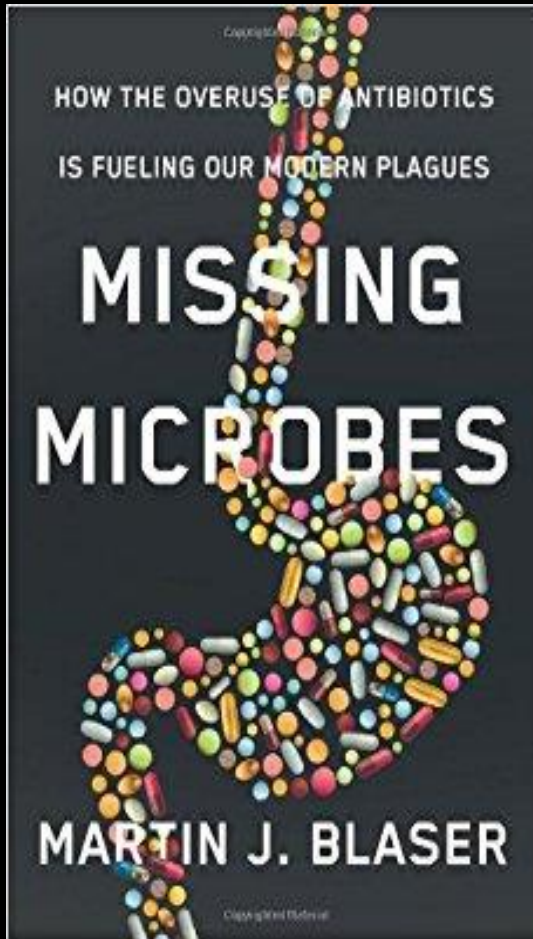
APC Microbiome Institute

University College Cork

@colinhillucc

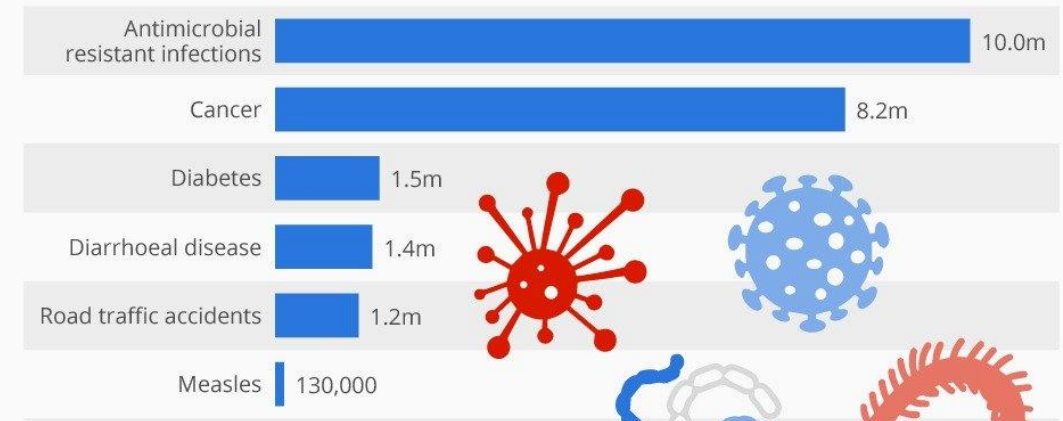


Mixed messages?

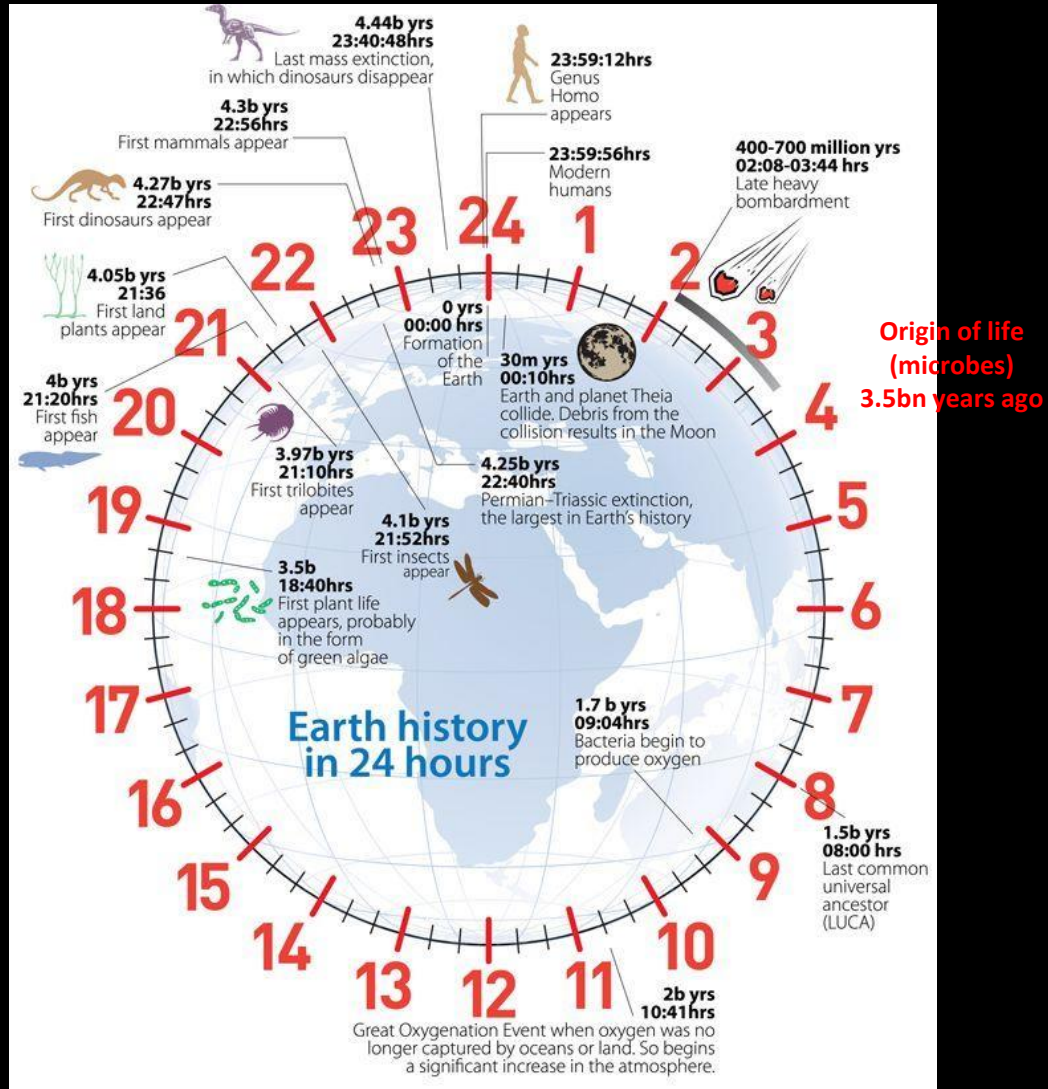


Deaths From Drug-Resistant Infections Set To Skyrocket

Deaths from antimicrobial resistant infections and other causes in 2050



We live in a microbial world



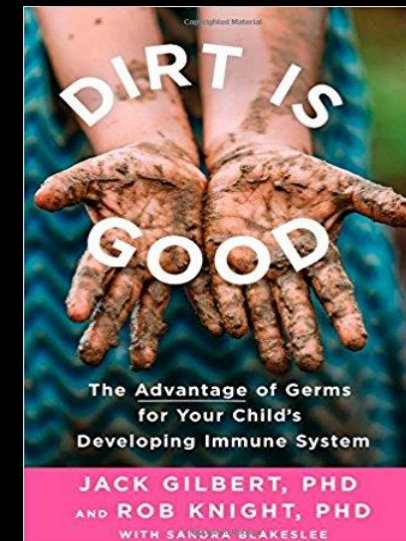
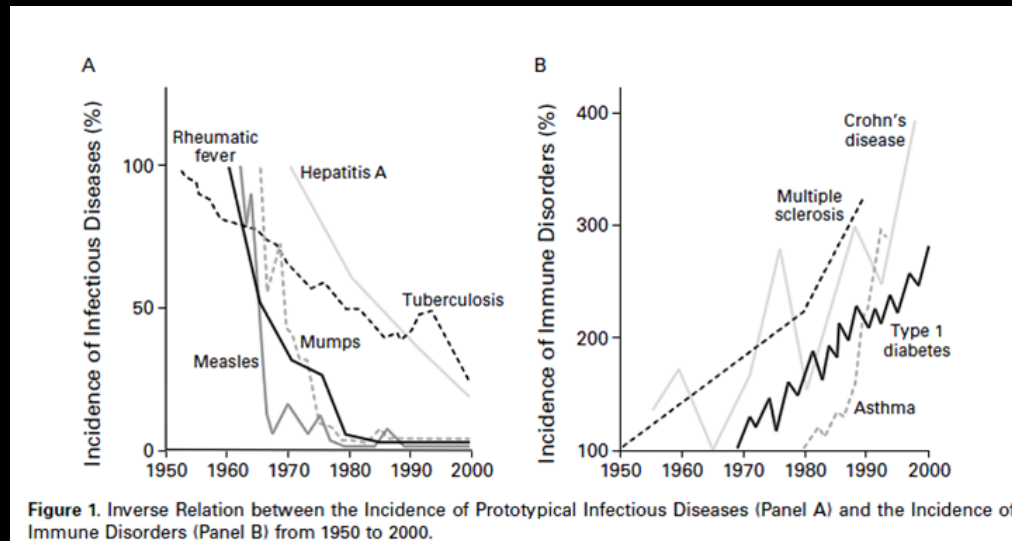
We (and every other animal) only exist because we have evolved to deal with microbes

The vast majority of microbes are beneficial (essential) to the planet

Very few are pathogenic (cause disease) and a few more cause spoilage of food

Hygiene hypothesis (David Strachan)

- We have become too clean
- Lack of exposure to infectious microbes in early childhood increases the likelihood of allergic diseases
- We should expose children to more 'risk' of infection

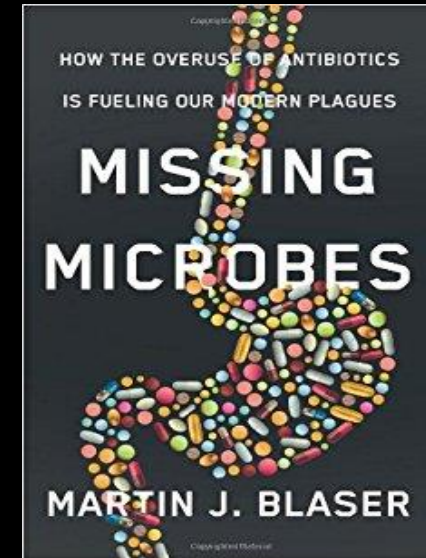


'Old friends' hypothesis (Graham Rook)

In our evolutionary past we built a relationship with microbes that is/was beneficial to our health

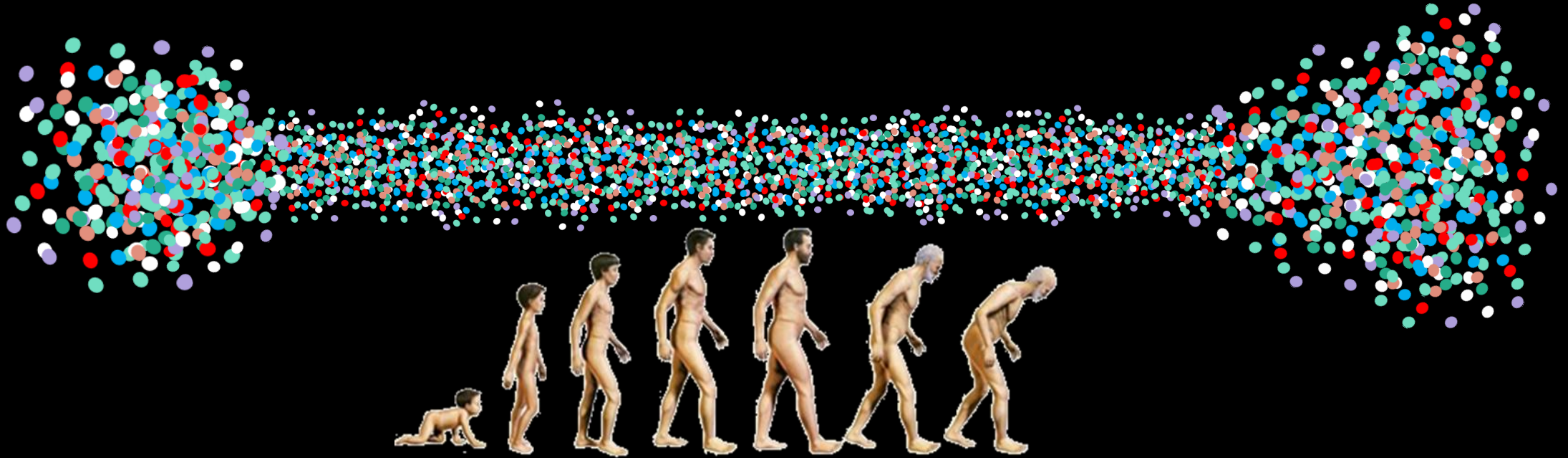
Due to modern living conditions (including hygiene & antibiotics) we have 'lost' some of these 'old friends'

This does NOT mean we need to expose ourselves to more microbes by practicing a 'dirtier' lifestyle (**not** part of Rook hypothesis).



The human microbiome

Microbiome/microbiota = collection of microbes on/in any particular environment



A stable microbiome assembles in the first years of life and, barring major insults, remains relatively stable until old age

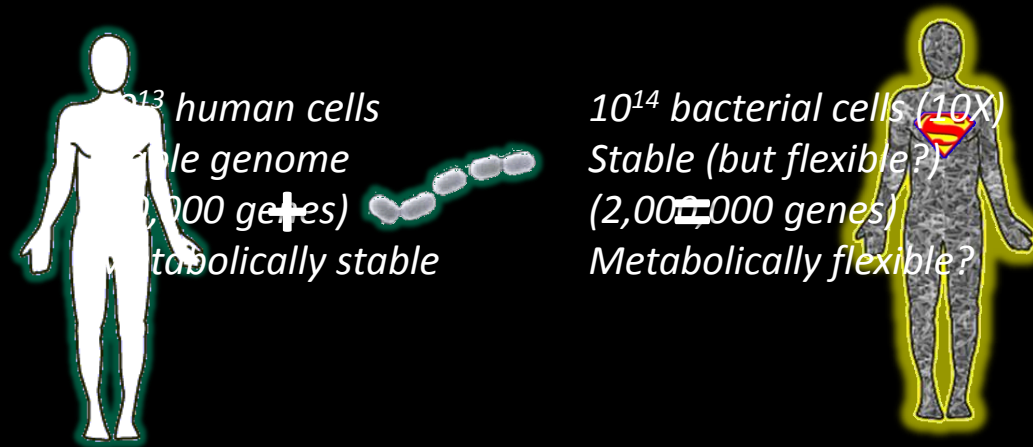
Loss of diversity and stability in old age are associated with deteriorating health indexes

The human microbiome

Microbiome/microbiota = collection of microbes on/in any particular environment

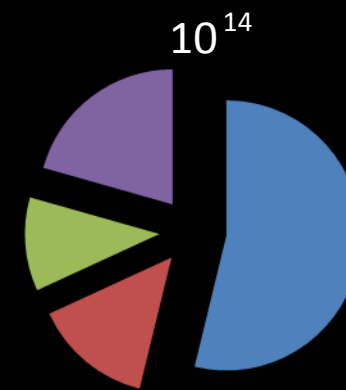
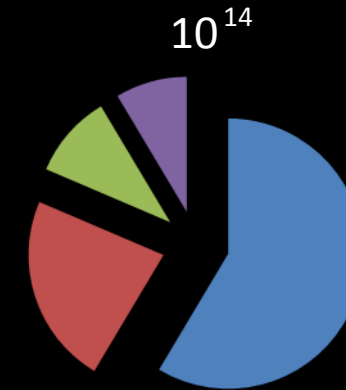
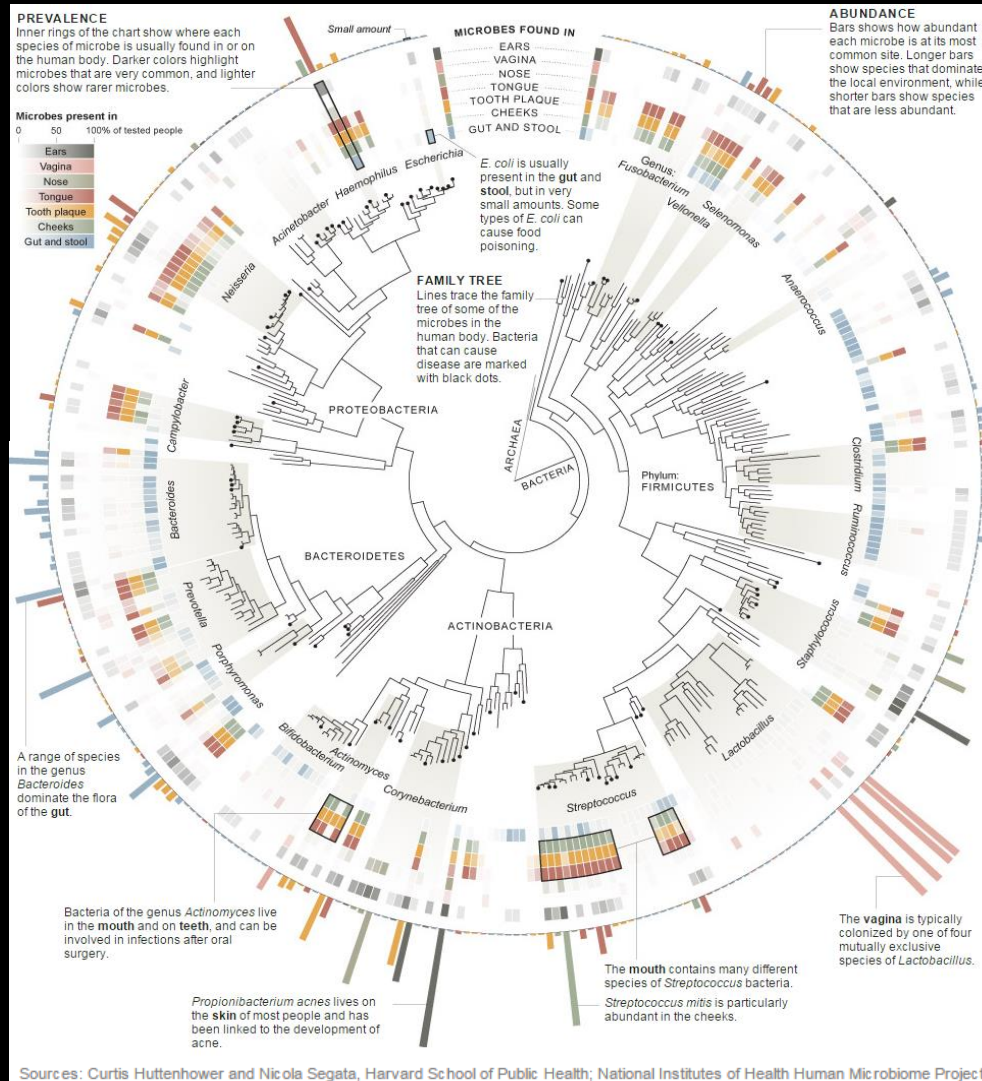
*humans are **superorganisms** whose metabolism represents an amalgamation of microbial and human attributes*

Gill et al. Science 2006



The human microbiome

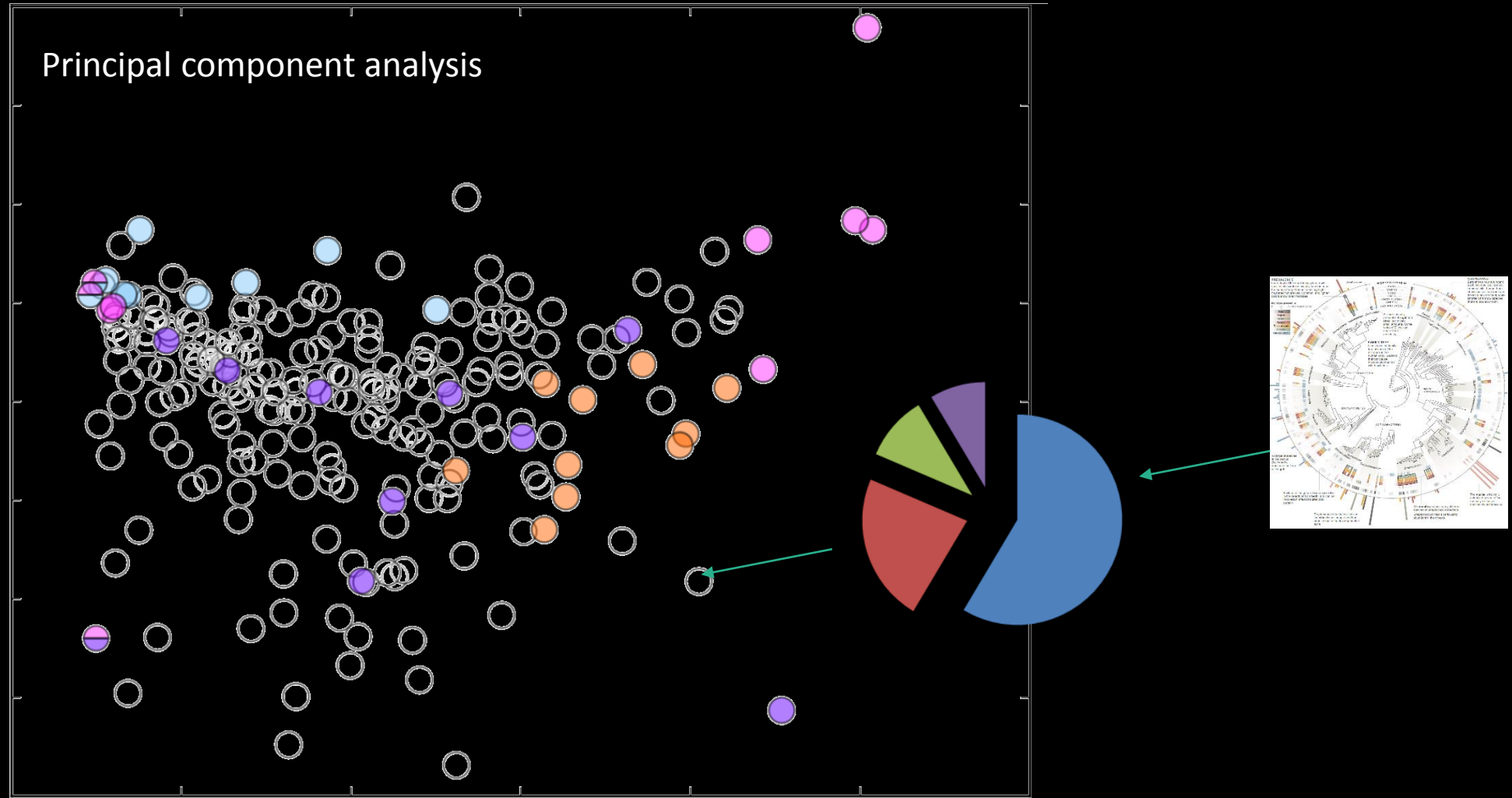
Microbiome/microbiota = collection of microbes on/in any particular environment



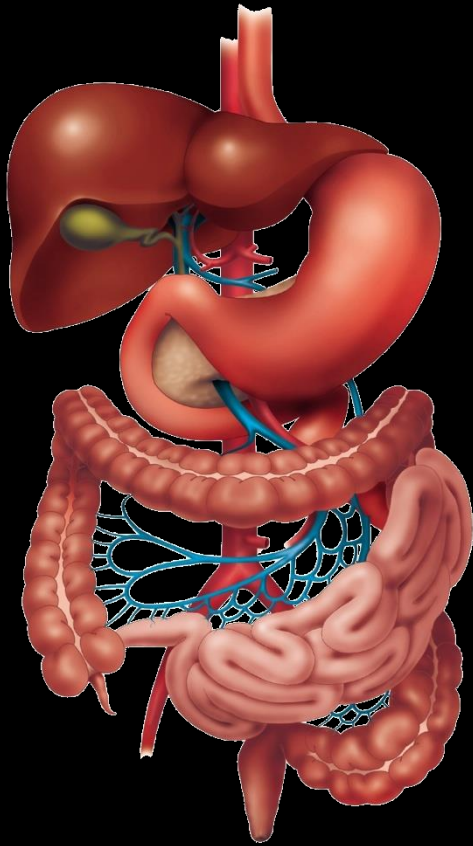
- Bacteroidetes
- Firmicutes
- Actinobacteria
- Proteobacteria

The human microbiome

Microbiome/microbiota = collection of microbes on/in any particular environment



Microbiome and health



- Defence against infection
- Role in fat deposition
- Calorific intake (+50%)
- Priming of mucosal immunity
- Peristalsis
- Metabolism of dietary carcinogens
- Synthesis of B & K vitamins
- Epithelial nutrients (e.g. SCFAs)
- Conversion of pro-drugs

Microbiome and health

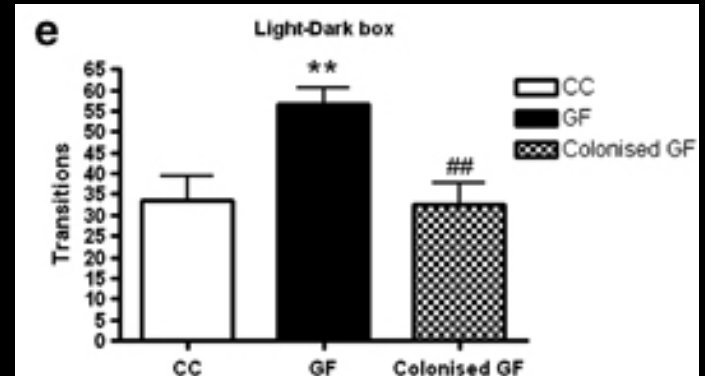
The human genome
does not encode enough
information for correct
development of our
internal organs

Or cognition and stress
responses

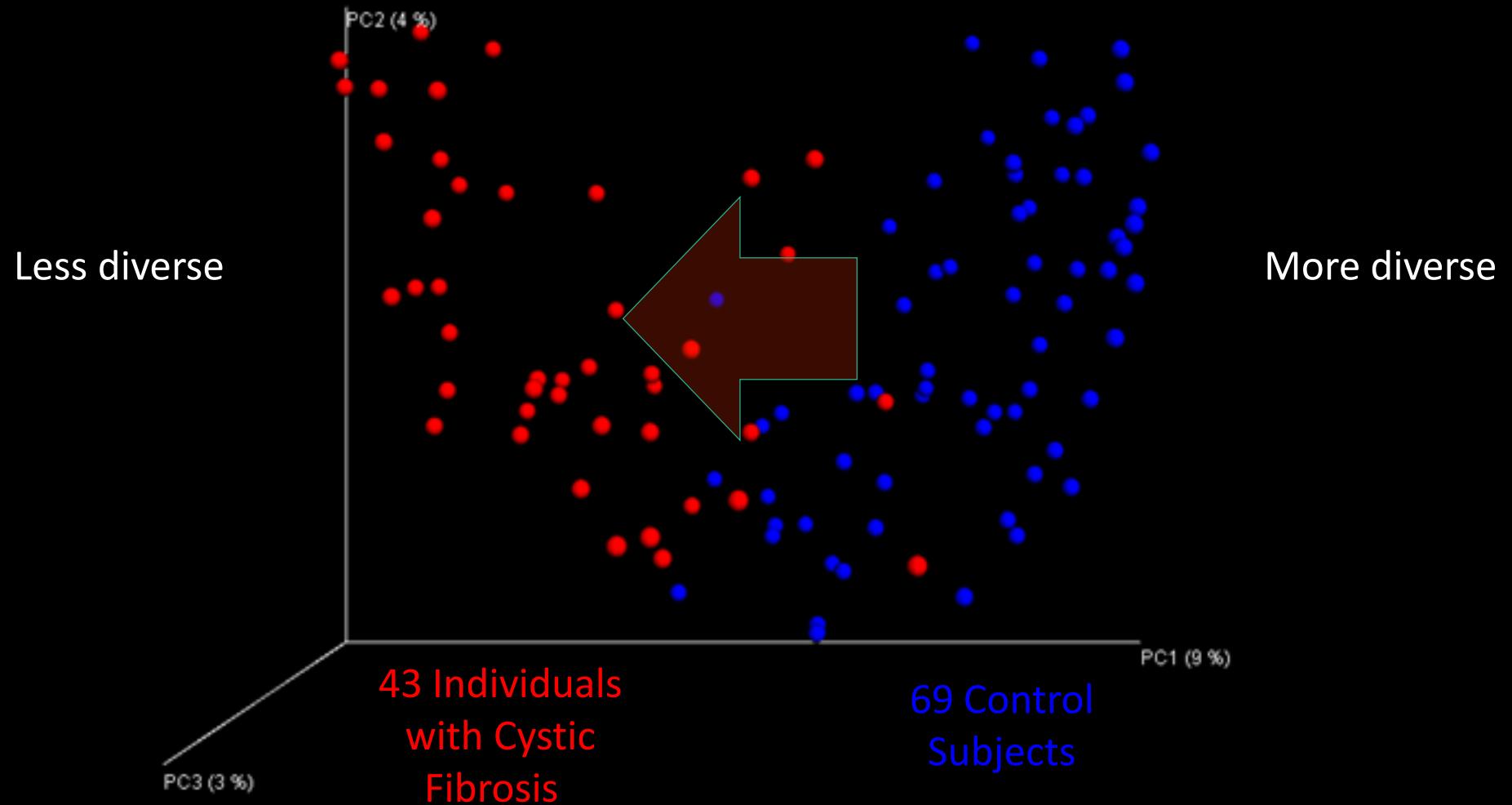


Germfree

Normal



Antibiotics affect the microbiome



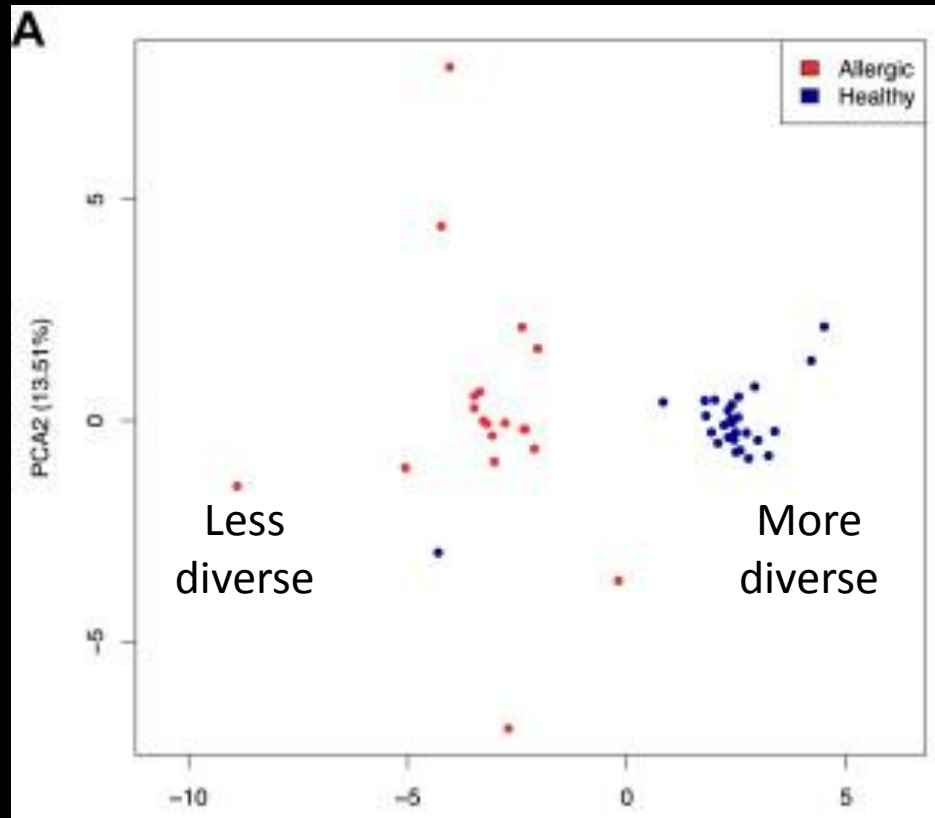
Associations with chronic diseases are common

Table 1 Intestinal microbiota-associated diseases, syndromes, or other aberrations, with summaries of multiple studies that support an association between the microbiota and the indicated aberration.

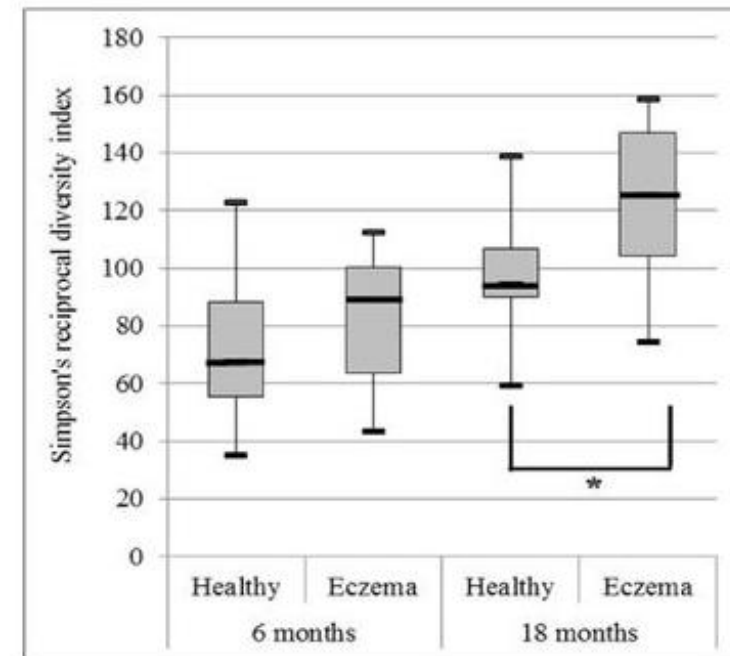
Aberration	Most relevant observations and potential correlation	References
Crohn's disease	Diversity decrease – reduced <i>F. prausnitzii</i>	Kaser et al. 2010 ⁵¹ ; Sokol et al. 2009 ⁵² ; Willing et al. 2010 ⁵³
Ulcerative colitis	Diversity decrease – reduced <i>A. muciniphila</i>	Png et al. 2010 ⁵⁴ ; Kaser et al. 2010 ⁵¹ ; Lepage et al. 2011 ⁵⁵
Irritable bowel syndrome	Global signatures – increased <i>Dorea</i> and <i>Ruminococcus</i>	Salonen et al. 2010 ³⁶ ; Saulnier et al. 2011 ⁵⁶ ; Rajilić-Stojanović et al. 2011 ¹³
<i>Clostridium difficile</i> infection	Strong diversity decrease – presence of <i>C. difficile</i>	Grehan et al. 2010 ⁵⁷ ; Khoruts et al. 2010 ⁵⁸
Colorectal cancer	Variation in <i>Bacteroides</i> spp. – increased fusobacteria	Sobhani et al. 2011 ⁵⁹ ; Wang et al. 2012 ⁶⁰ ; Marchesi et al. 2011 ⁶¹
Allergy/atopy	Altered diversity – specific signatures	Stsepetova et al. 2007 ⁶² ; Bisgaard et al. 2011 ⁶³ ; Storrø et al. 2011 ⁶⁴
Celiac disease	Altered composition, notably in small intestine	Nistal et al. 2012 ⁶⁵ ; Di Cagno et al. 2011 ⁶⁶ ; Kalliomäki et al. 2012 ⁶⁷
Type 1 diabetes	Signature differences	Vaarela 2011 ⁶⁸ ; Giongo et al. 2011 ⁶⁹ ; Brown et al. 2011 ⁷⁰
Type 2 diabetes	Signature differences	Larsen et al. 2010 ⁷¹ ; Wu et al. 2010 ⁷² ; Kootte et al. 2012 ⁷³
Obesity	Specific bacterial ratios (<i>Bacteroidetes/Firmicutes</i>)	Ley et al. 2006 ⁷⁴ ; Turnbaugh et al. 2009 ¹⁰ ; Musso et al. 2011 ⁷⁵

Associations with chronic diseases are common

Allergy



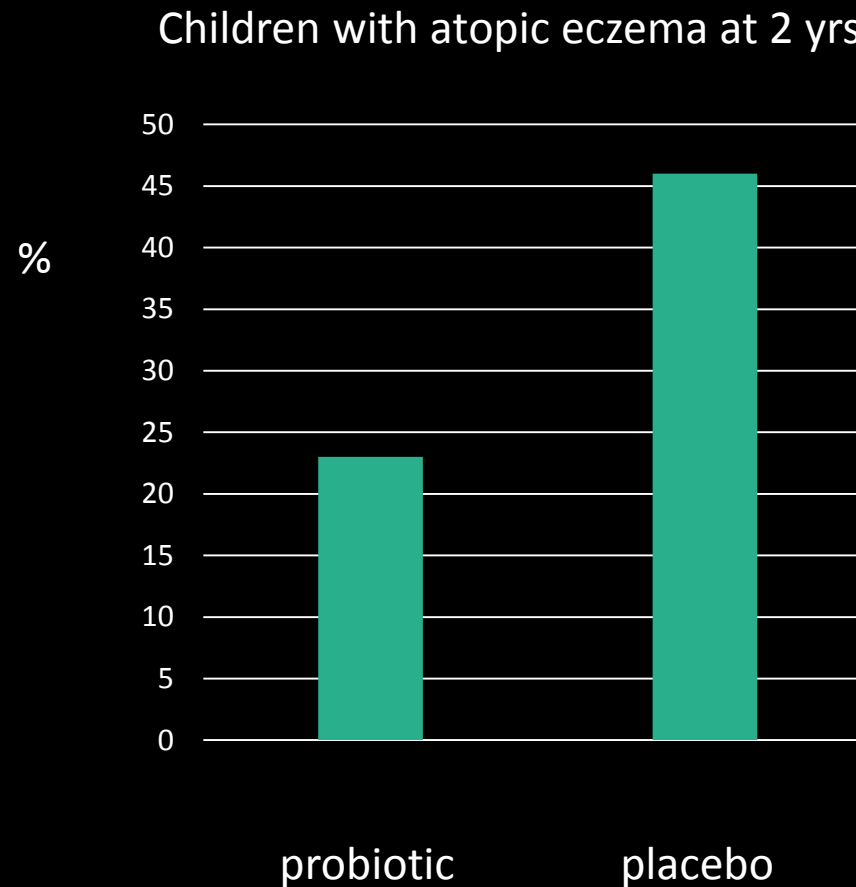
Eczema



↑
Diversity

Microbes (probiotics) and atopic disease

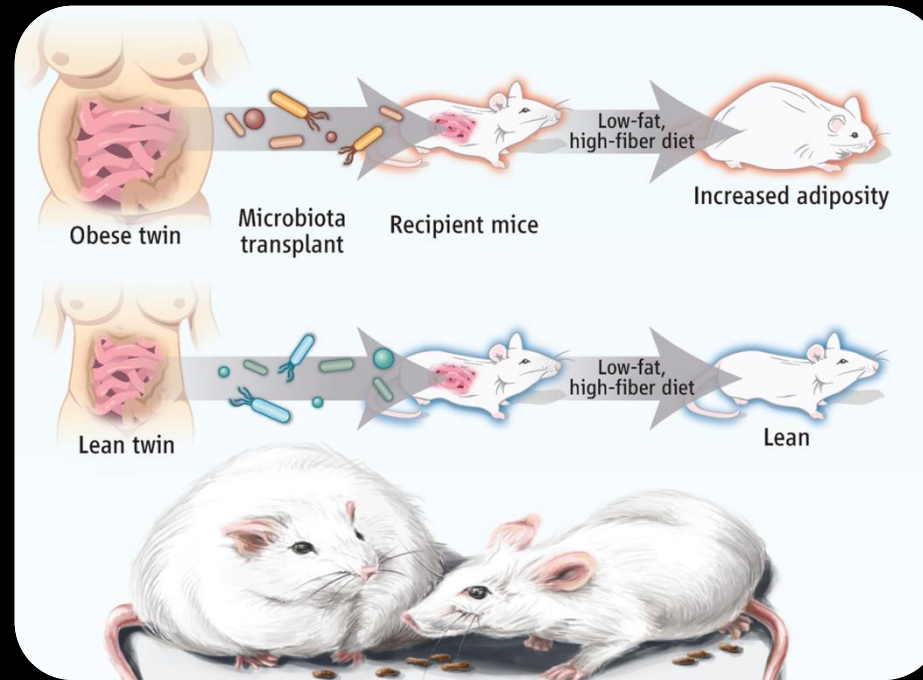
- Pregnant women carrying high risk children were given a probiotic for the last month of pregnancy
- Babies were given the same probiotic for first 6 months of life



The microbiome and obesity



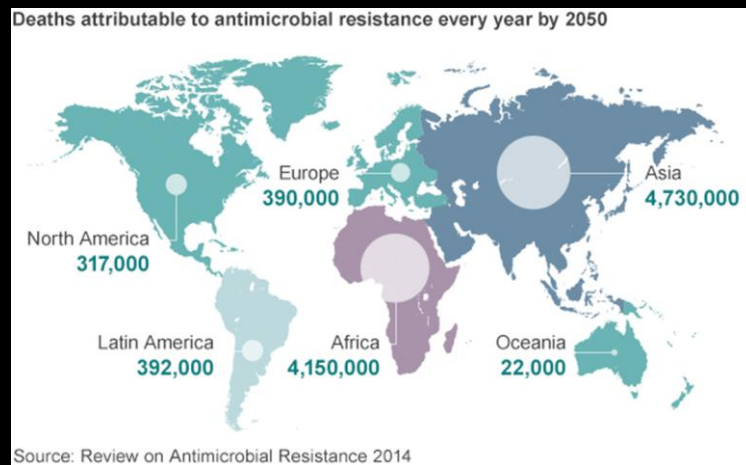
- Bacteroidetes
- Firmicutes
- Actinobacteria
- Proteobacteria



Infectious disease and antibiotics



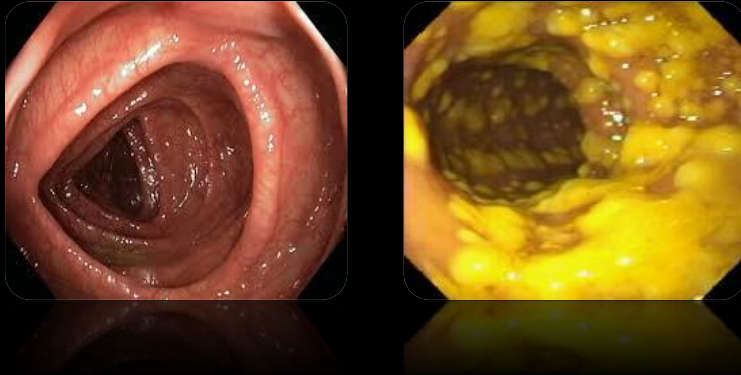
The 'fresh air' cure for children with TB (1932)



Child with blood poisoning treated with penicillin (1942)

CDAD – a disease OF the microbiome?

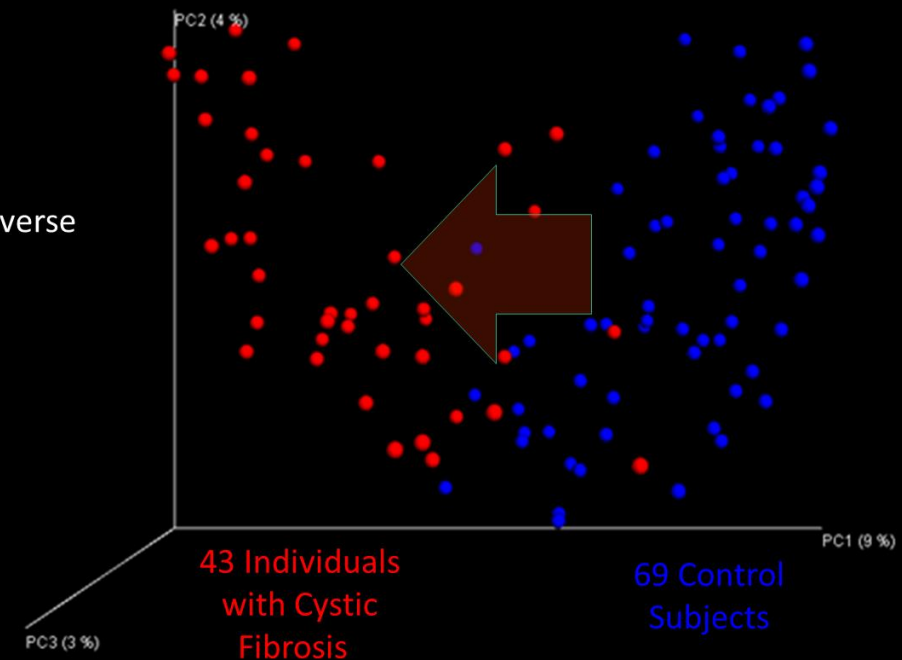
Gram positive, anaerobic, sporeforming superbug



Less diverse

More diverse

- Patient gets antibiotics (usually in hospital)
- Subsequently gets *C. difficile* associated diarrhoea (CDAD)
- Gets more antibiotics
- Gets CDAD again
- etc



FMT Faecal microbiome transplants



MEDICAL RESEARCH

The Promise of Poop

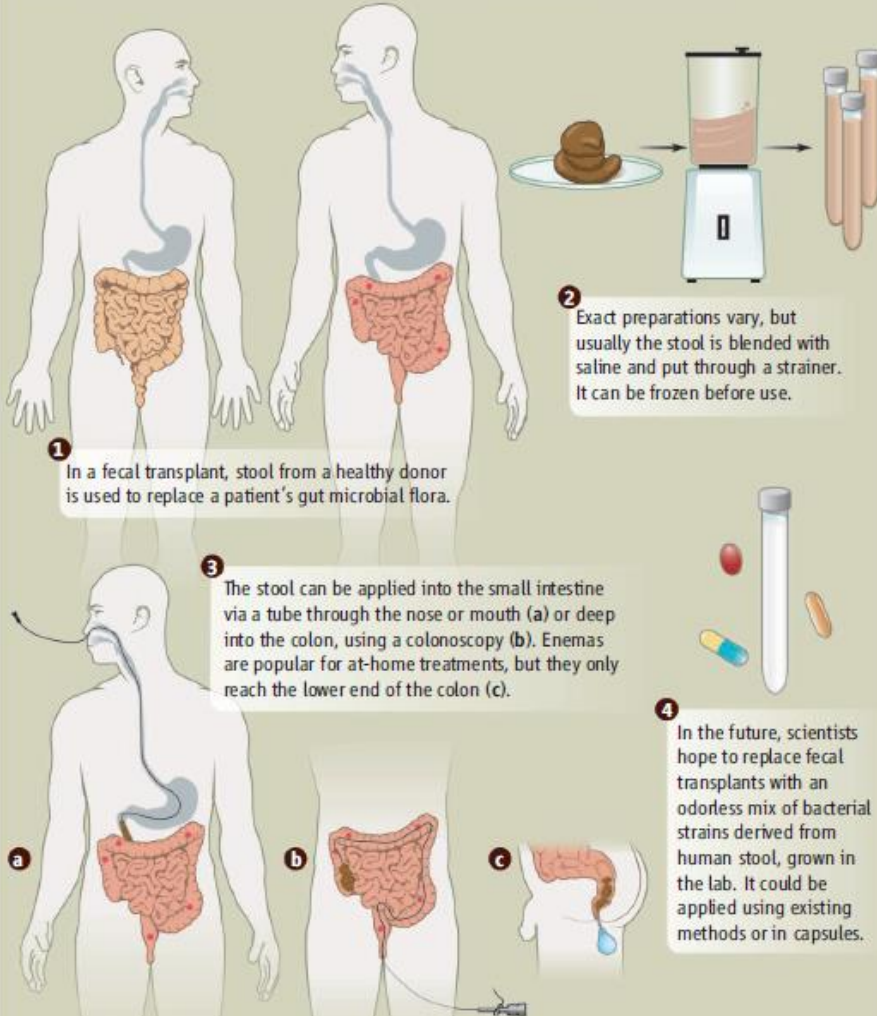
Fecal transplants offer hope for treating many diseases. But they need to be studied more scientifically, says one of the treatment's pioneers

more scientifically says one of the treatment's pioneers

The Promise of Poop

MEDICAL RESEARCH

HOW FECAL TRANSPLANTATION WORKS



That study compared fecal transplants with vancomycin, the standard treatment for *C. difficile*, or vancomycin combined with bowel flushing. The researchers aimed to enroll 120 patients, but the study's data and safety monitoring board halted the study after just 43 patients, because continuing would be unethical: Ninety-four percent of the transplant patients were cured, versus 31% and 23%, respectively, in the control groups. The resulting *NEJM* paper "did bring

the procedure closer to mainstream medicine. The resulting *NEJM* paper "did bring 31% and 23% respectively in the control

"cure rates range from 81 to 94 percent in patients recovery observed within 24 hours to 12 days durable and well tolerated"

Borody et al., 2016

FMT Faecal microbiome transplants



FMT has also been trialled in:

- Inflammatory bowel disease
- Irritable bowel syndrome
- Obesity
- Chronic constipation
- Parkinson's
- Chronic fatigue syndrome

Weight Gain After Fecal Microbiota Transplantation

Neha Alang¹ and Colleen R. Kelly²

¹Department of Internal Medicine, Newport Hospital, and ²Division of Gastroenterology, Center for Women's Gastrointestinal Medicine at the Women's Medicine Collaborative, The Miriam Hospital, Warren Alpert School of Brown University, Providence, Rhode Island

Fecal microbiota transplantation (FMT) is a promising treatment for recurrent *Clostridium difficile* infection. We report a case of a woman successfully treated with FMT who developed new-onset obesity after receiving stool from a healthy but overweight donor. This case may stimulate further studies on the mechanisms of the nutritional-neural-microbiota axis and reports of outcomes in patients who have used non-ideal donors for FMT.

Keywords. *Clostridium difficile* infection; fecal microbiota transplantation; gut microbiota; obesity.

Clostridium difficile infection (CDI) is characterized by a high recurrence rate after treatment. Fecal microbial transplantation (FMT) is a promising approach to recurrent CDI that is being increasingly used clinically, although data remain limited on the full spectrum of possible adverse effects. We report a case of significant weight gain in a woman after FMT from an overweight stool donor.

metronidazole with only partial improvement. Her diarrhea and abdominal pain escalated after completing the metronidazole treatment, and her stool tested positive for *Clostridium difficile* toxin polymerase chain reaction (PCR). She was treated with a 14-day course of oral vancomycin. Testing done around the same time showed *Helicobacter pylori* infection (positive fecal antigen). Nausea and abdominal pain persisted after treatment of the CDI, so the *H. pylori* was treated with a course of triple therapy (amoxicillin, clarithromycin, and proton pump inhibitor). Her abdominal pain and diarrhea escalated again a few weeks later, and her stool tested positive for *C. difficile* toxin PCR. She was treated with a 12-week tapering course of oral vancomycin with improvement, but diarrheal symptoms recurred again within 2 weeks of completing the course, and she was prescribed a course of rifaximin with *Saccharomyces boulardii*. Around this time, she underwent esophagogastroduodenoscopy, which showed persistence of *H. pylori* infection. She had no significant past medical history and had always been of normal weight. Review of systems was positive for diarrhea, and there was frustration over her ongoing diarrheal symptoms. Her weight before FMT was stable at 136 pounds (body mass index of [BMI] 26). Physical examination was unremarkable.

After extensive discussion, the patient elected to undergo fecal transplant. As per the patient's request, her 16-year-old daughter was chosen as the stool donor. At the time of FMT, her daughter's weight was ~140 pounds (BMI of 26.4), but it increased later to 170 pounds. Her daughter had no other health

BRIEF REPORT

BBC

Sign in

News

Sport

Weather

Shop

Earth

Travel

NEWS

Home

Video

World

UK

Business

Tech

Science

Magazine

Entertainment &

Health

Woman's stool transplant leads to 'tremendous weight gain'

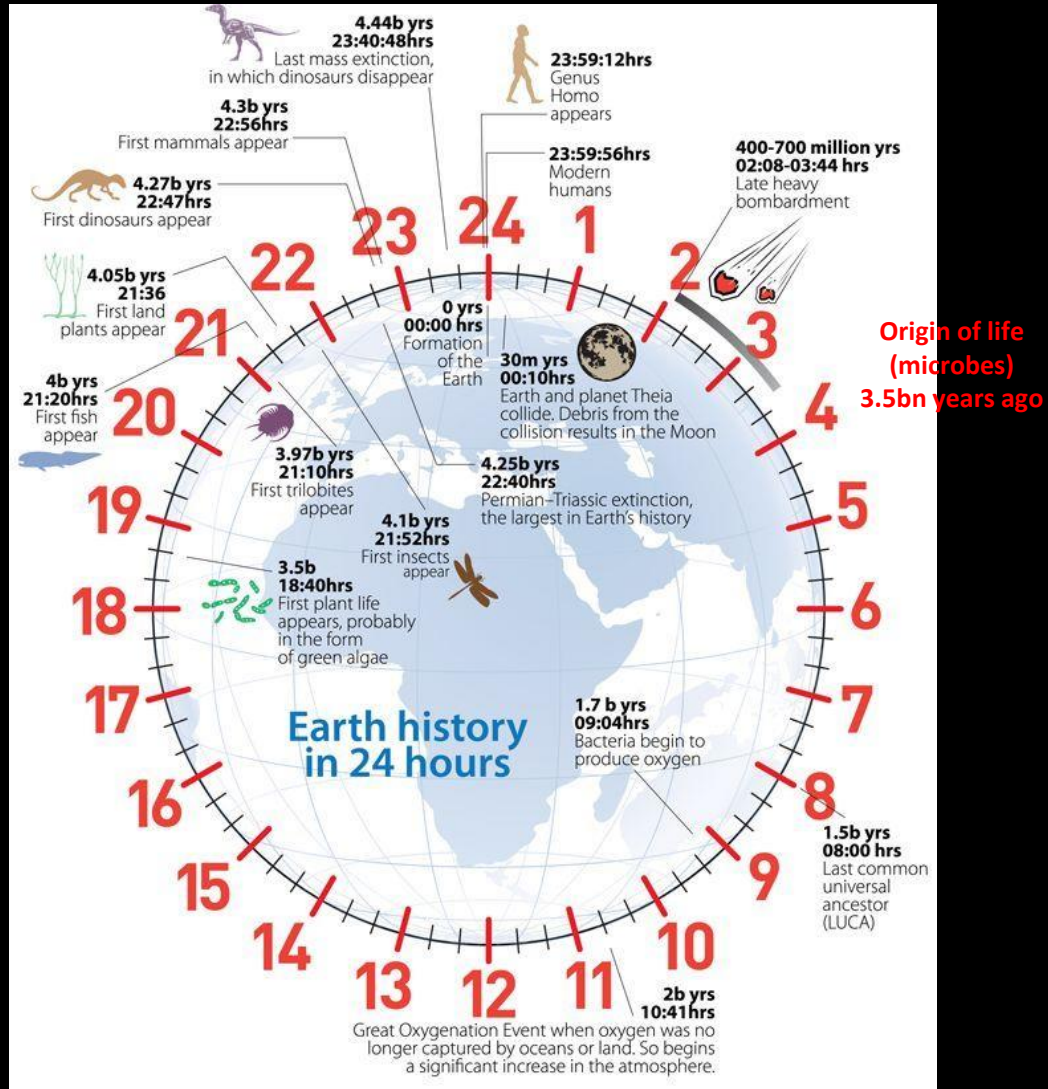
By James Gallagher
Health editor, BBC News website

7 February 2015 | Health

f t w e Share



So, what does the microbiome have to do with hygiene?



We evolved in, and are born in, a microbial world

A baby's immune system (nervous system, GI tract, skin) 'expects' to encounter large numbers of bacteria from birth

Mother's milk is designed to facilitate the formation of the microbiome

We want a diverse and healthy microbiome, while avoiding infection

Diverse diet



Diverse microbes



Fly agaric



Holly



Ivy



Raw chicken



Raw milk



Rare burgers



We want a diverse and healthy microbiome, while avoiding infection

Diverse environment



Unsafe environment



We want a diverse and healthy microbiome, while avoiding infection

Born by SVD rather than C-section

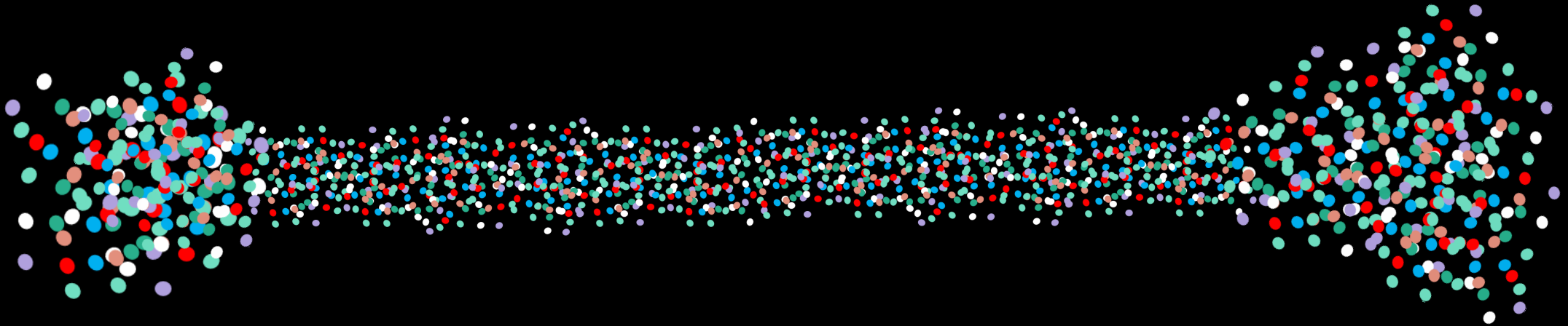
Breast-fed rather than formula-fed

Eat a diverse diet

Eat fermented foods

Take pre and probiotics

Maintain a diverse diet in old age



Practise good hygiene, both in environment and in food

Use antibiotics, but only where necessary

Vital to maintain good food hygiene



Conclusions

We live in a microbial world – we have evolved to tolerate and to ‘expect’ to encounter microbes on a daily basis (in environment and in food)

Our microbes play a vital role in our health – we need to acquire and maintain a diverse microbiome

However, we need to avoid exposure to pathogens (practise good hygiene)

Unhygienically prepared food can be a source of pathogens

The road to a healthy microbiome is not sterile, but it is not ‘dirty’ either



We need to maintain a diverse diet and a diverse microbiome, but without compromising basic good hygiene

