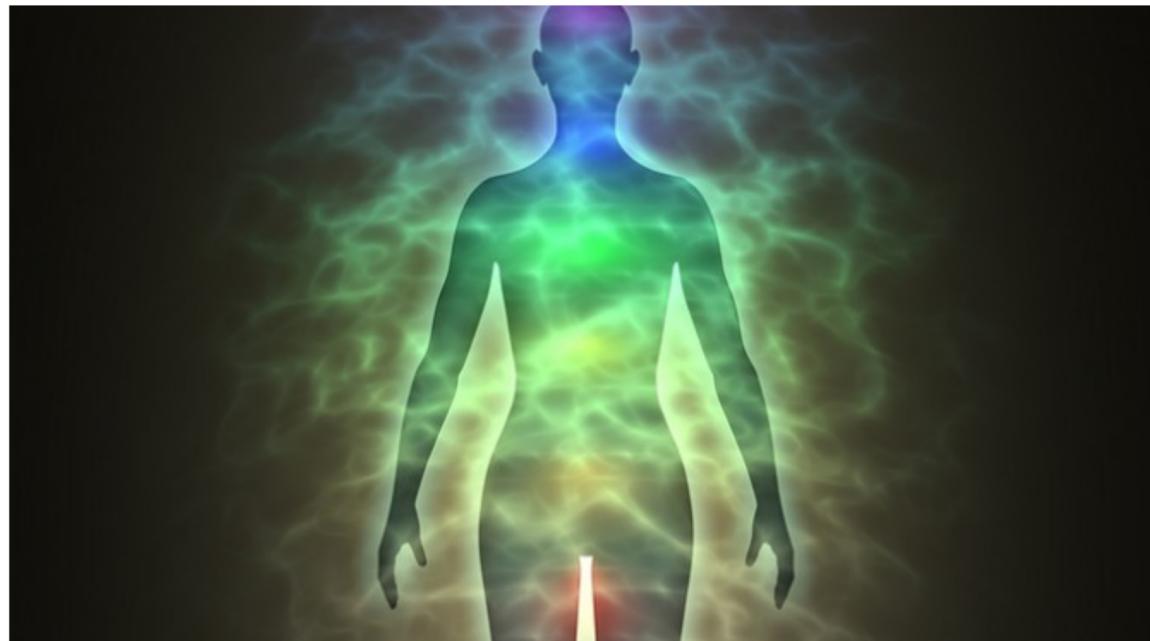


# Population-level profiling of the human microbiome

Leo Lahti | leo.lahti@iki.fi | <http://www.iki.fi/Leo.Lahti>

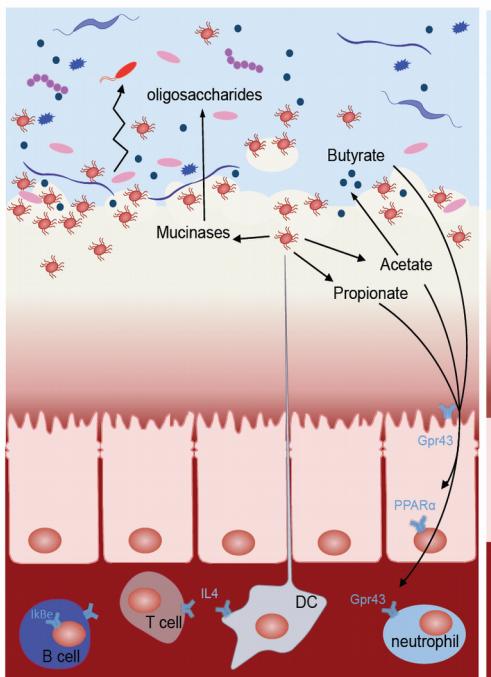
University of Turku, Finland & VIB/KU Leuven, Belgium



Human emit over 10 million biological particles per hour – personal cloud from cradle to grave. Meadows et al. PeerJ 2015 – Metcalf et al. Science 2015

# Gut microbiome: 300-400 m<sup>2</sup> surface area

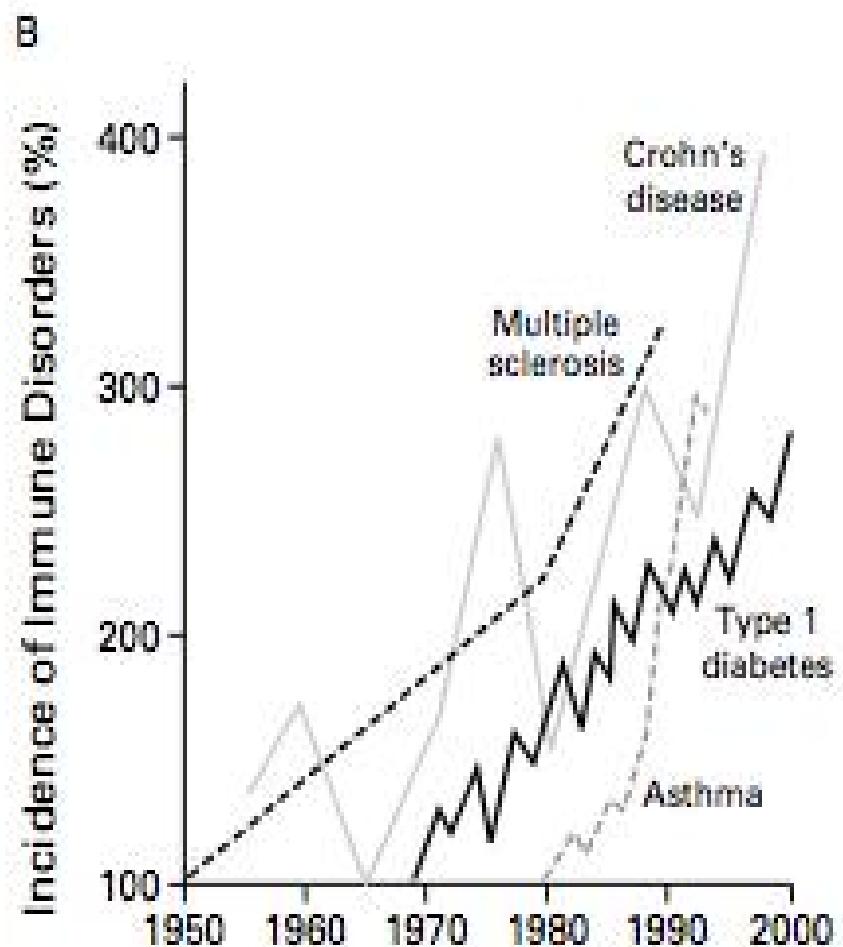
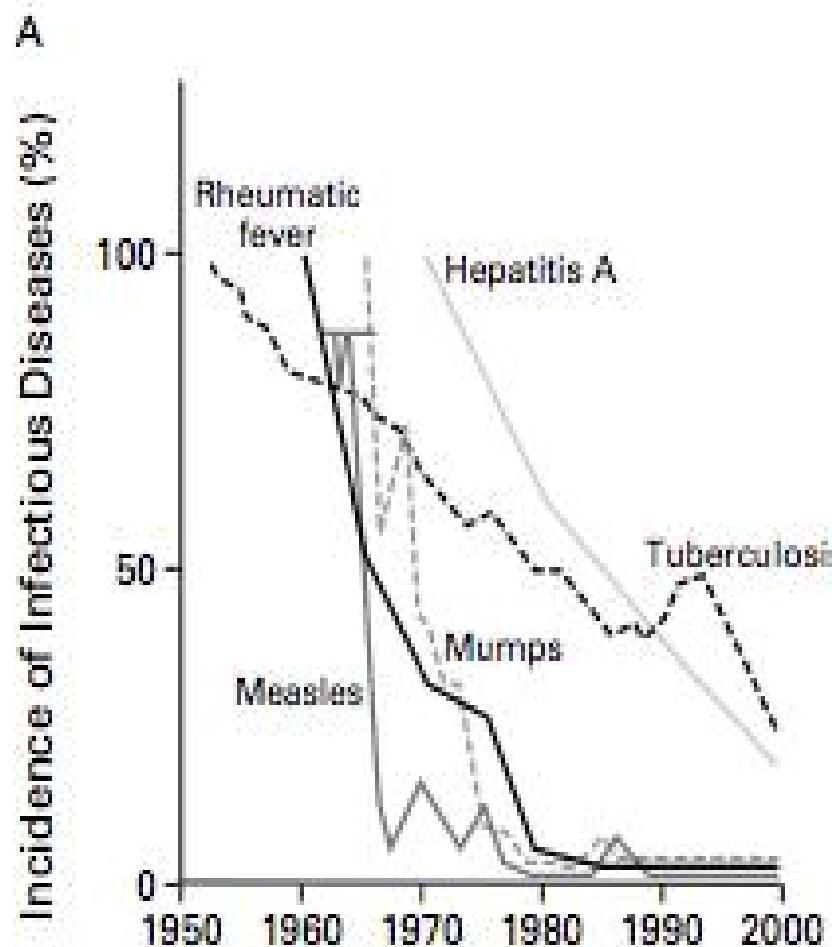
- ~ bacterial cells outnumber our own
- ~ 100 billion bacteria / gram in the gut
- ~ 10,000 gut bacterial species
- ~ 10M uniq genes (500x human genome)
- ~ Plastic, varies in time



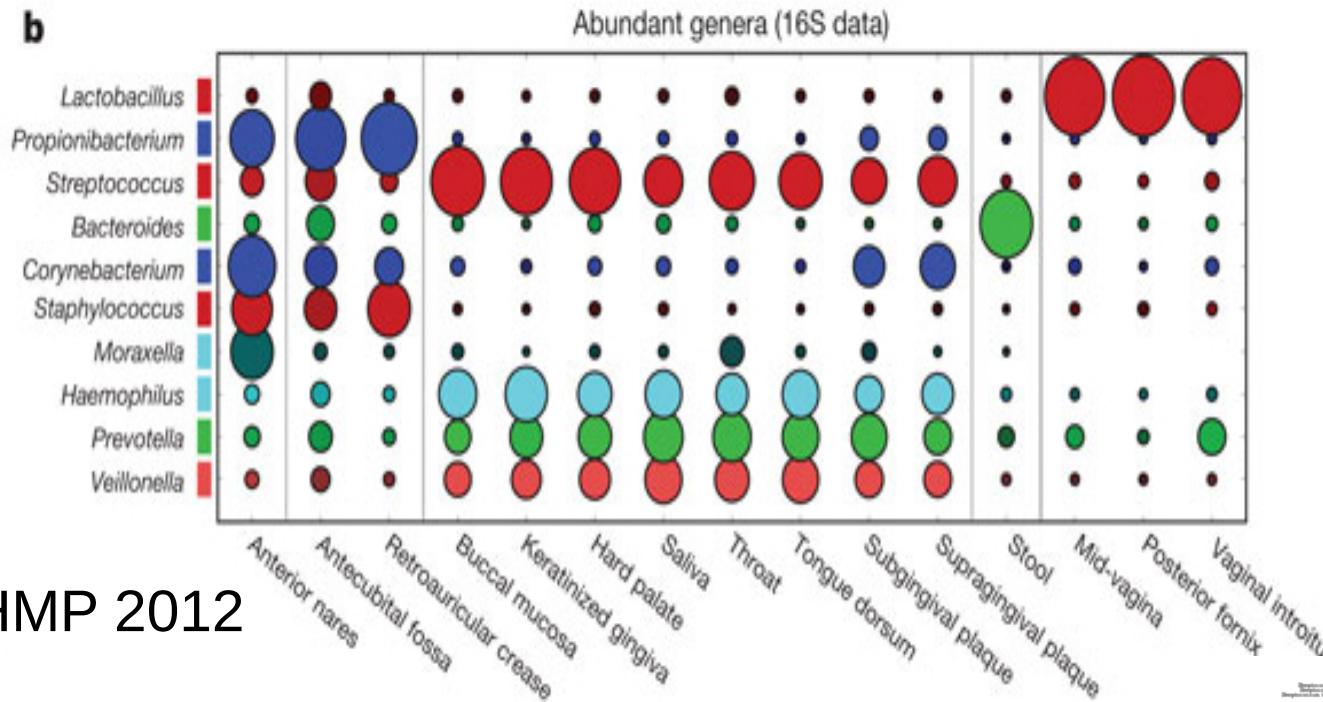
Brussel central square flower carpet



# Diseases linked to gut microbiota are becoming more prevalent !



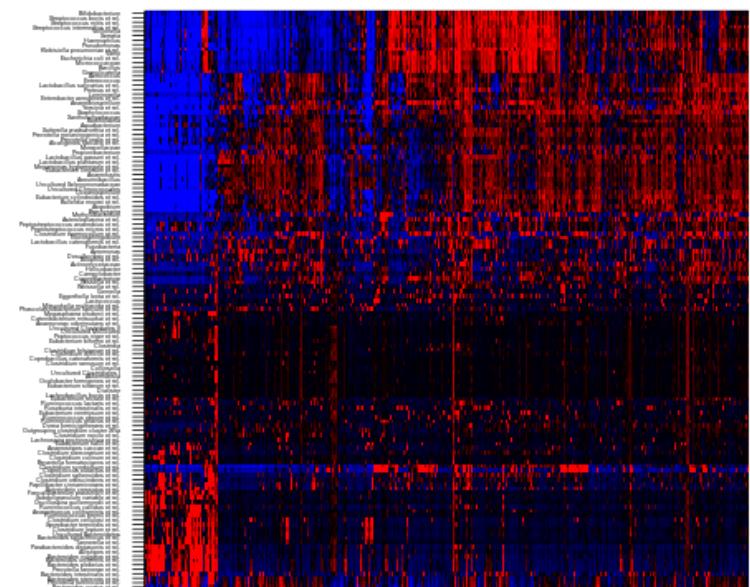
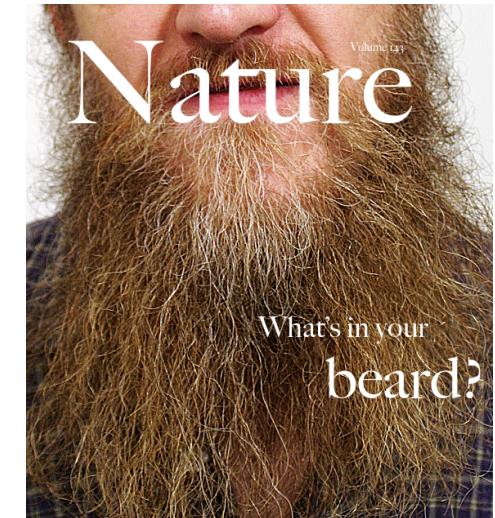
Microbial composition differs among body sites  
and is highly individual



HMP 2012

# Gut microbiota profiling of 5000 Western individuals: HITChip Atlas

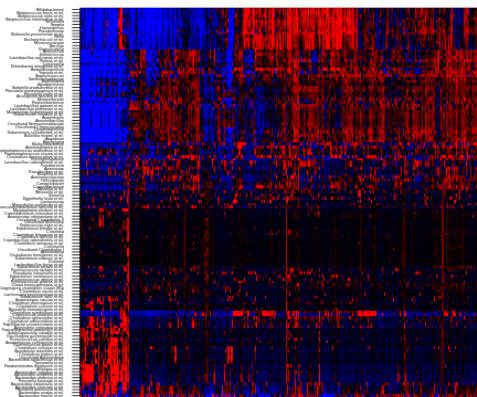
Wageningen University, The Netherlands



# Large & standardized population cohorts now accumulating

## HITChip Atlas (microarrays):

- > 10,000 samples
- > 5,000 subjects
- > 1,000 phylotypes (~0.1%)
- versatile geography
- highly reproducible (>98%)
- long follow-ups (10+ y)
- open data: Lahti et al. 2014



## Flemish Gut Flora (NGS):

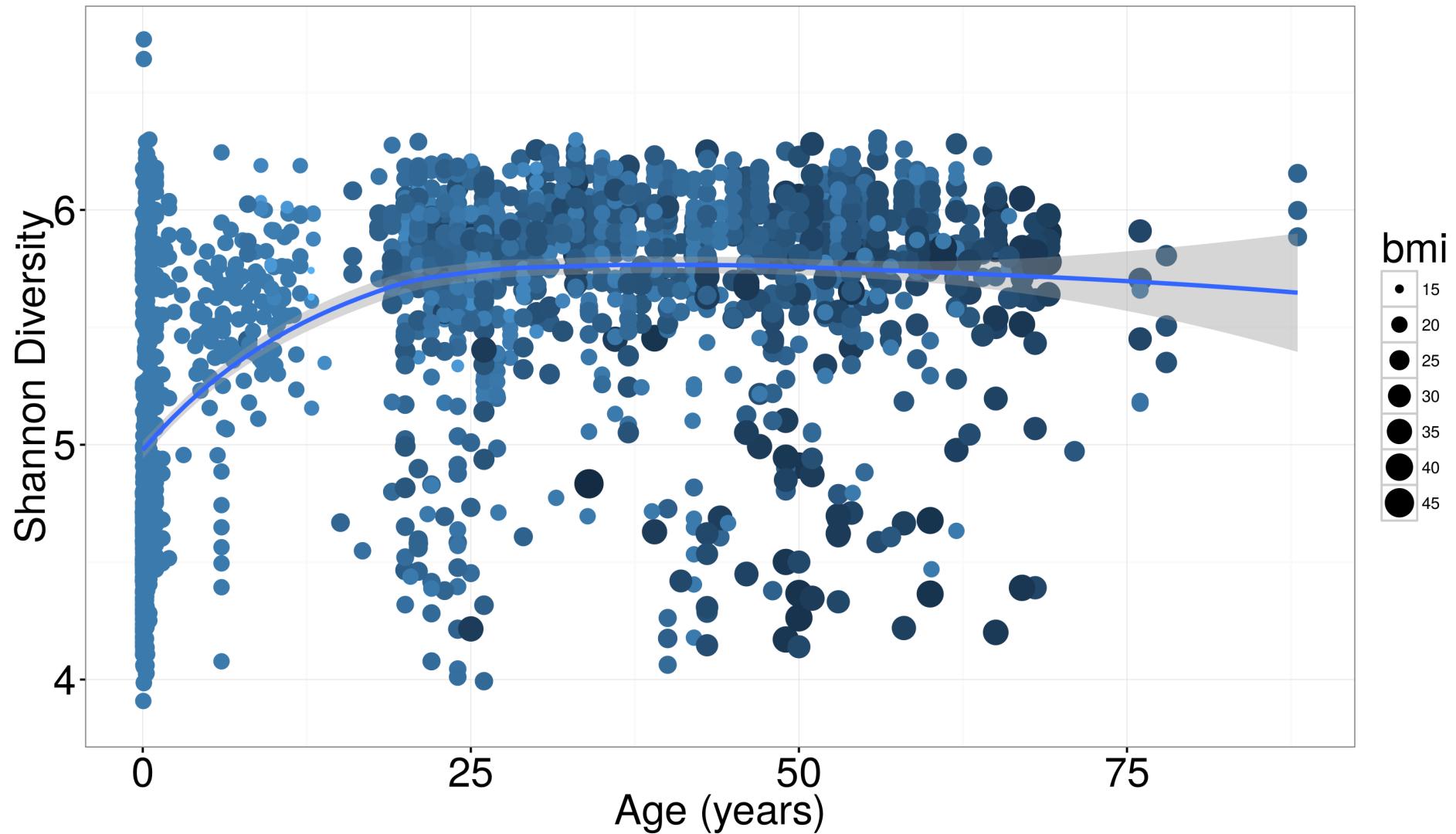
- > 5,000 samples
- > 1,000 subjects
- > 7,000 OTUs
- normal Flemish population
- dense time series
- open data: Falony et al. 2016



Other collections: MetaHIT, Human Microbiome Project, American Gut...

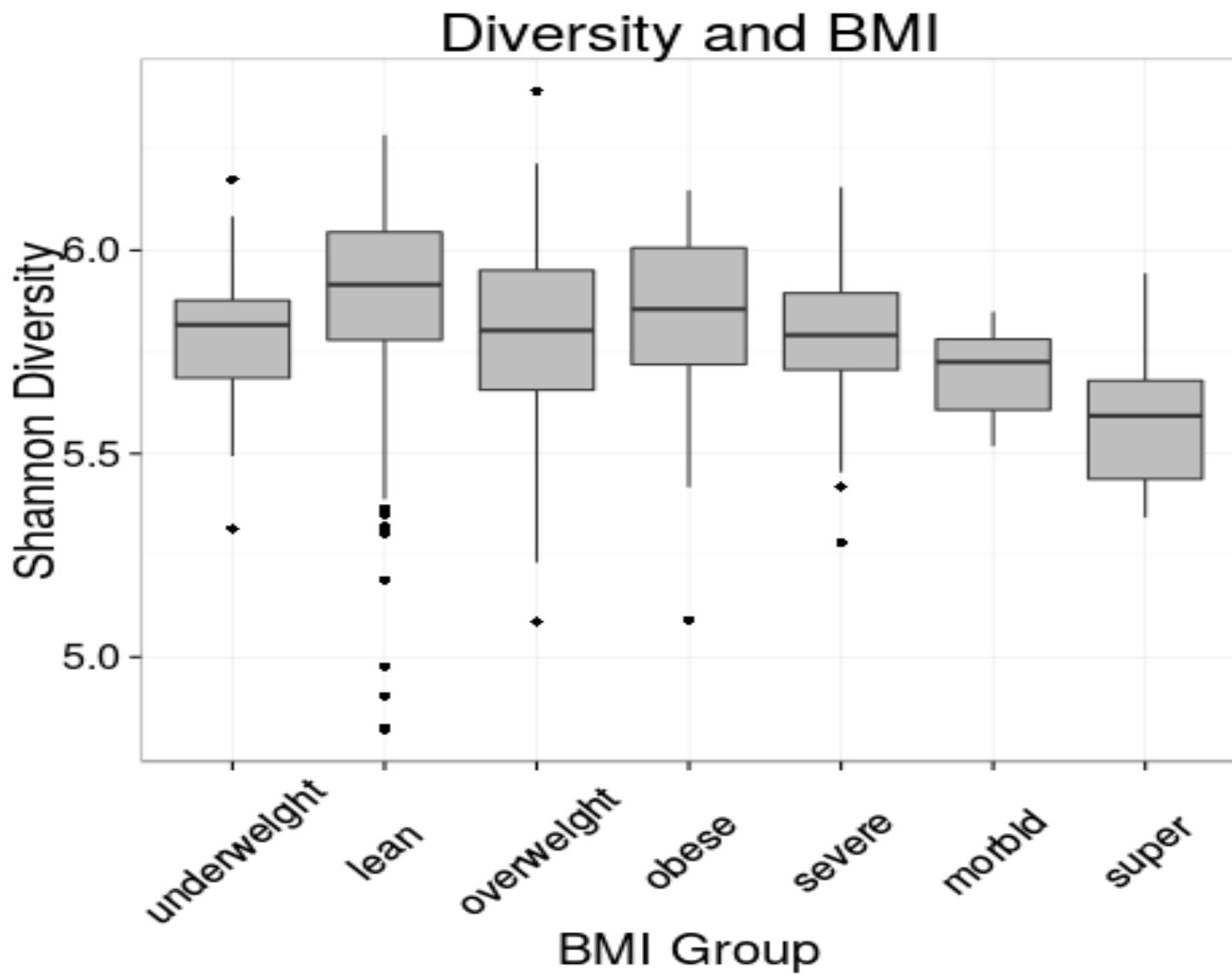
# Microbiome diversity and age: healthy & normal obese subjects

N = 2363



Data: HITChip Atlas;  
healthy fecal RBB samples

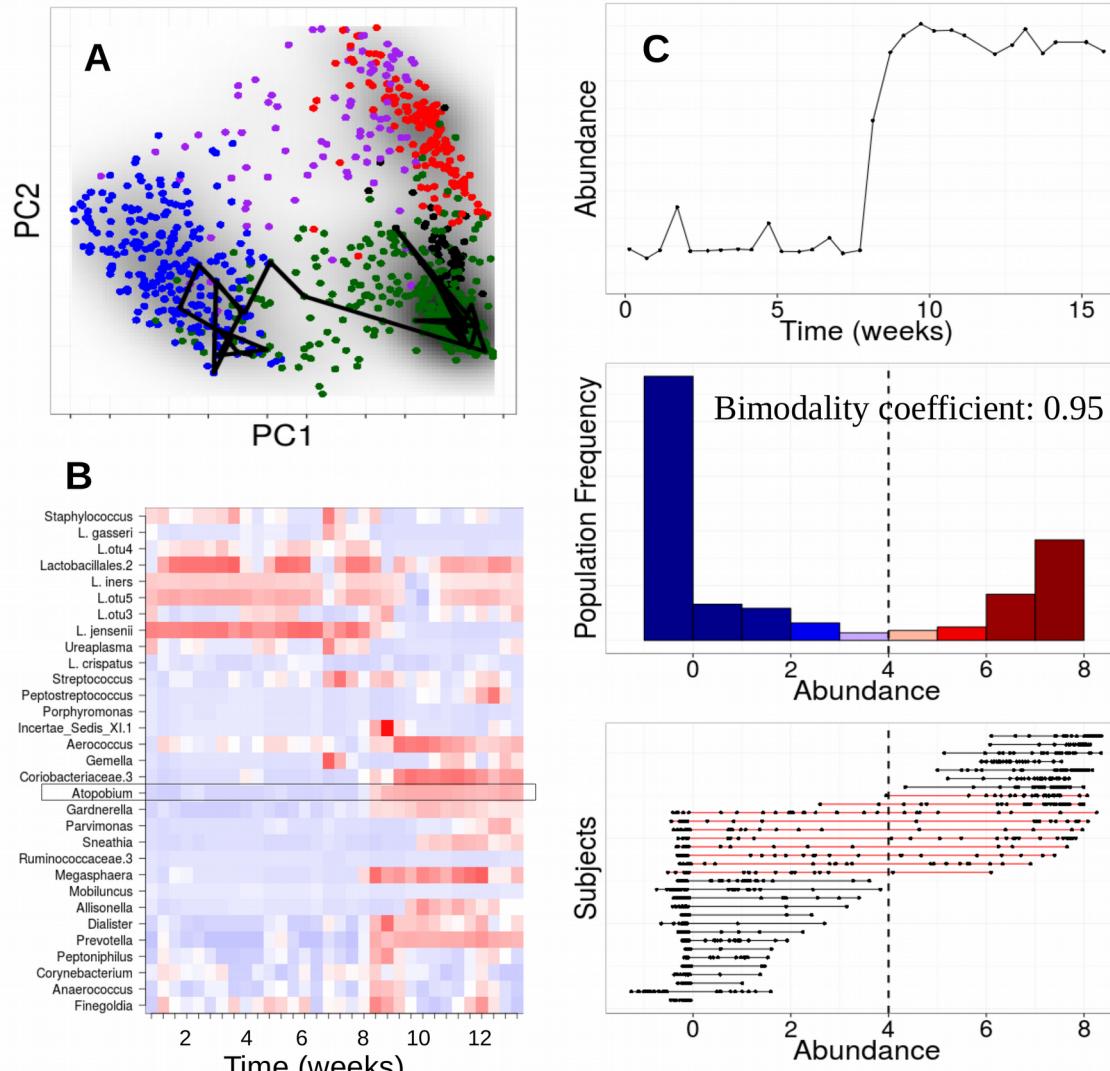
# Microbial diversity decreases with obesity



N = 611

# Community types and dynamics:

Dynamical analysis of the vaginal microbiome supported by pooling limited longitudinal data from multiple individuals



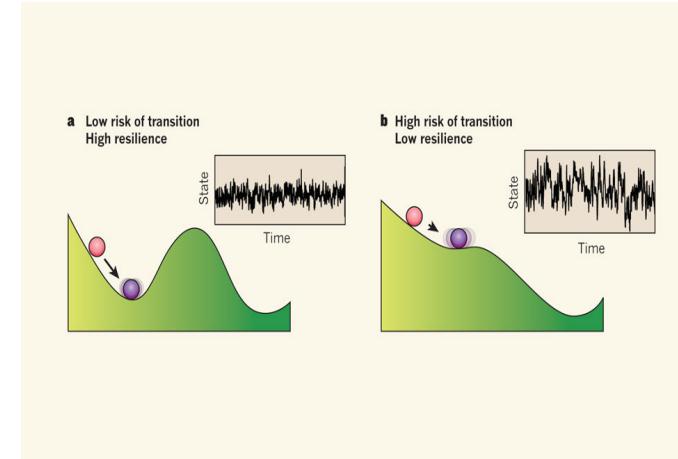
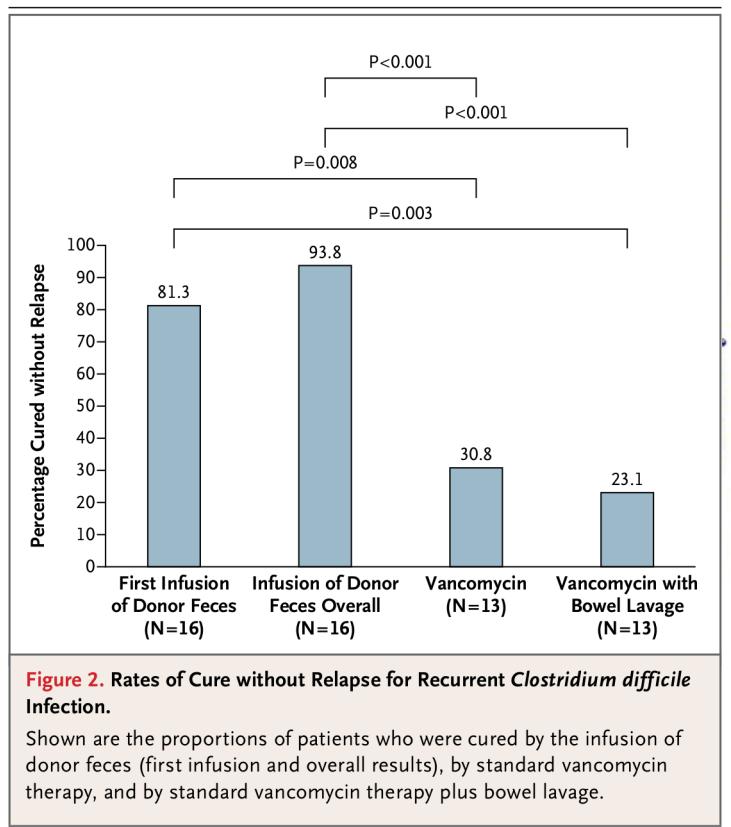
Data: Gajer et al. 2012

Figure: Faust et al. Curr. Op. Microbiol. 2015

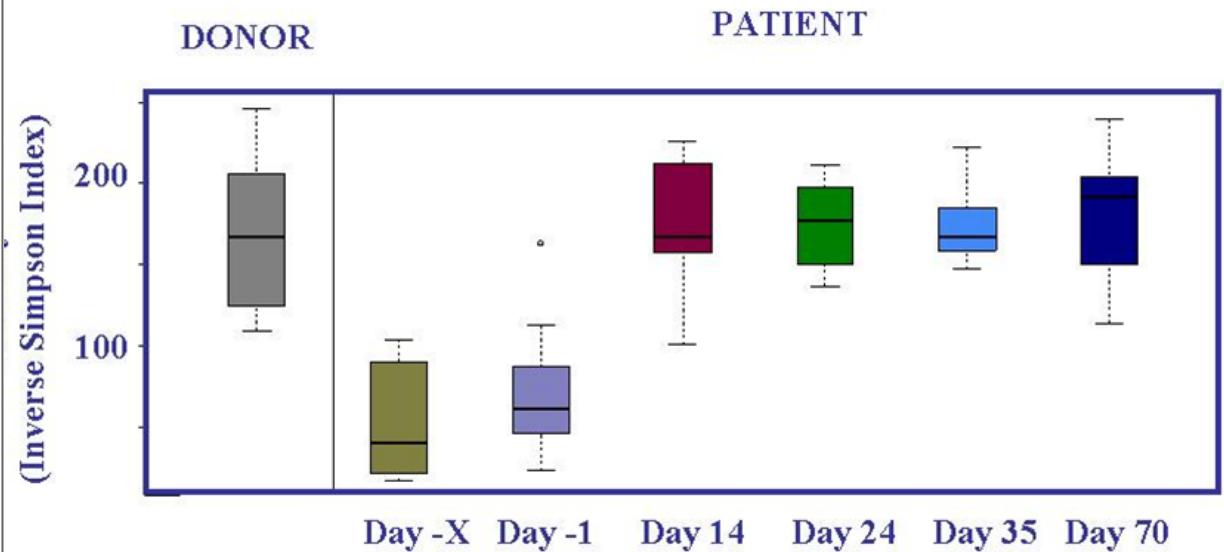
# Fecal transplant induced ecosystem level state shift

Efficient treatment in *C. difficile* infected patients.  
Shift from Bacilli- and Proteobacteria-dominated state to a healthy state dominated by *Bacteroides* and many butyrate producing taxa

Better than antibiotics !



Patient gets donor microbiota -> Donor farms!?

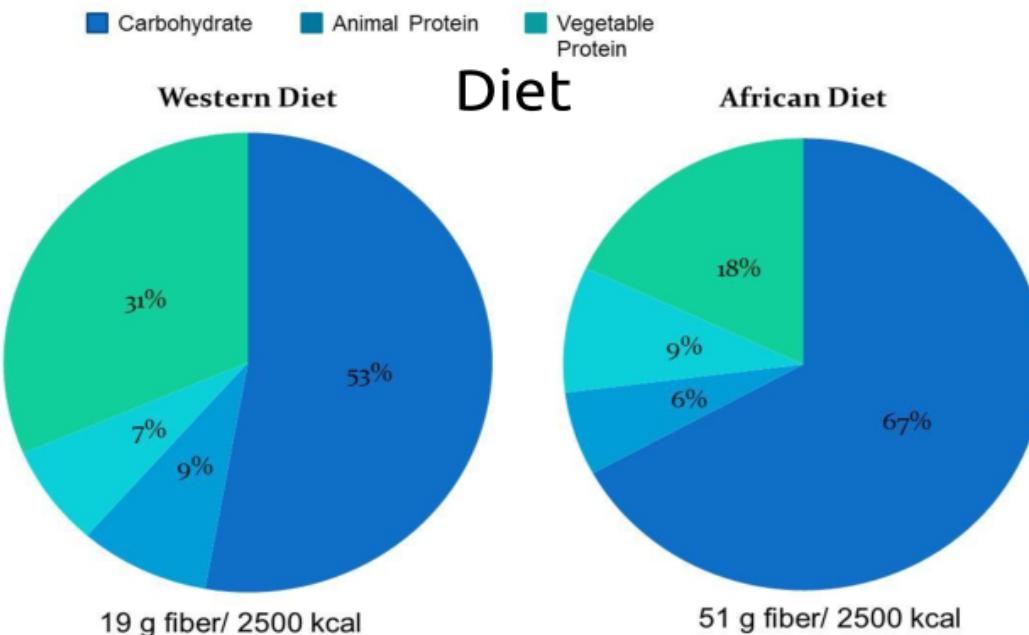


Els van Nood et al., NEJM 368(5) 2013  
Fuentes et al. ISME J, 8:1621-33, 2014

# Diet is a major driver of the gut microbiome



West

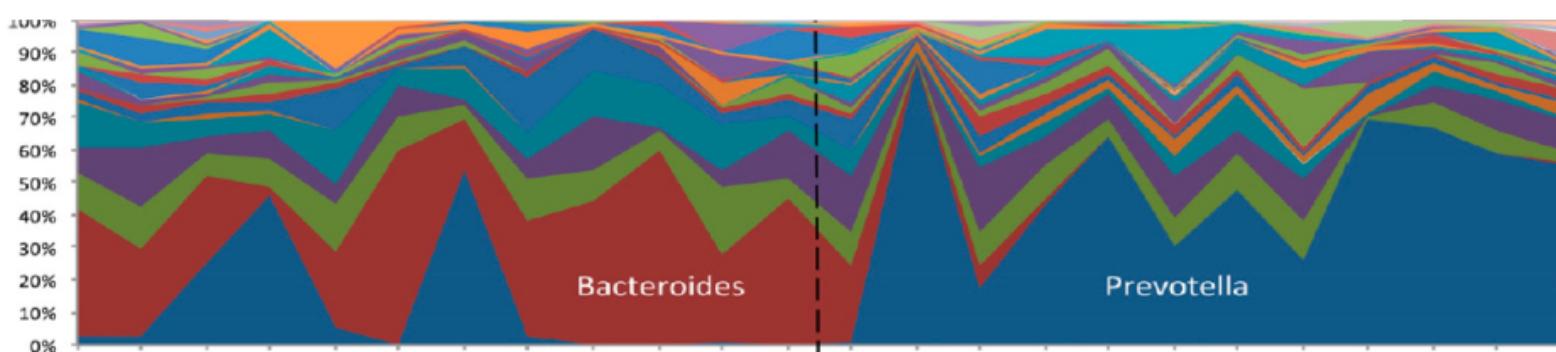


Africa

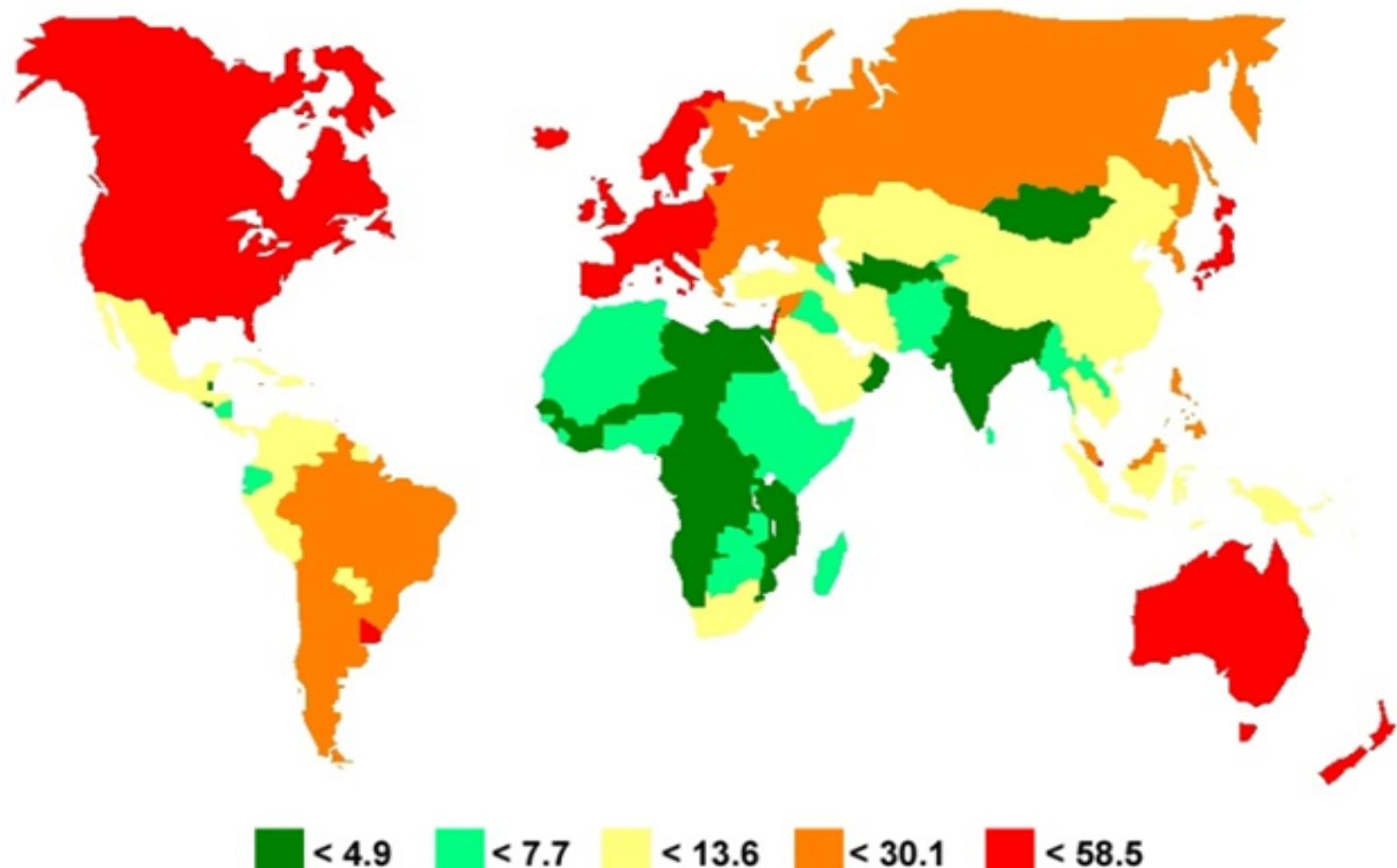
Microbiota  
composition

Colon cancer rates:  
-Africans:<10:100,000  
-African Americans:>65:100,000

Ou et al. Am J Clin Nutr.  
Jul 2013; 98(1): 111–120



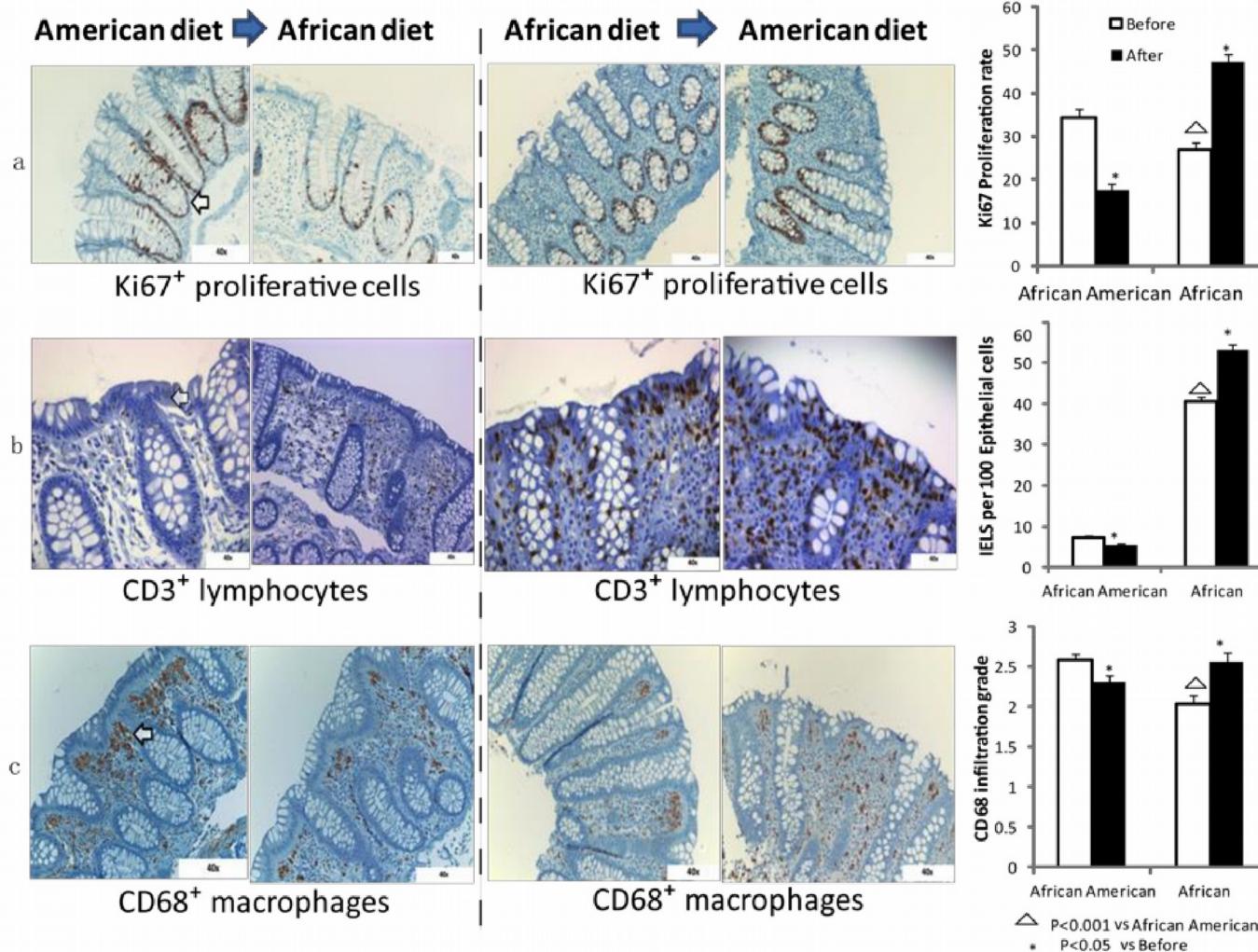
# Colon cancer prevalence



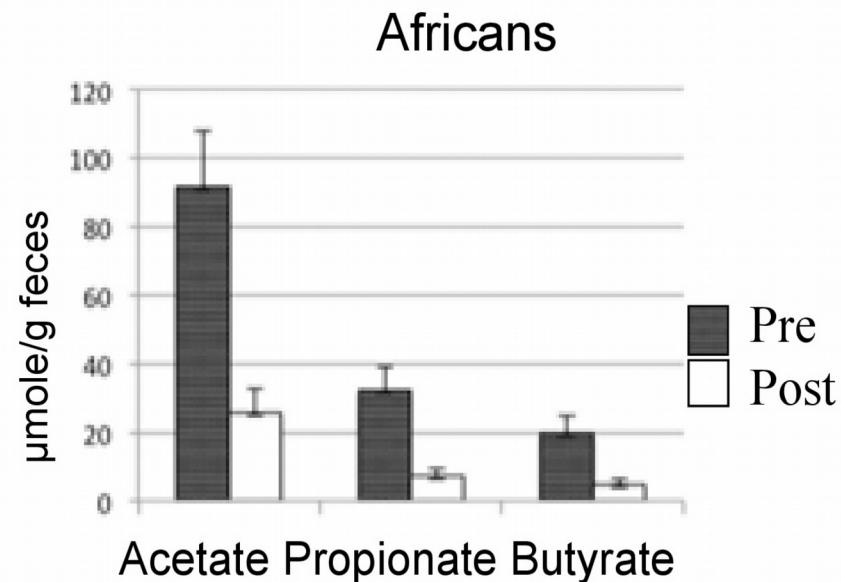
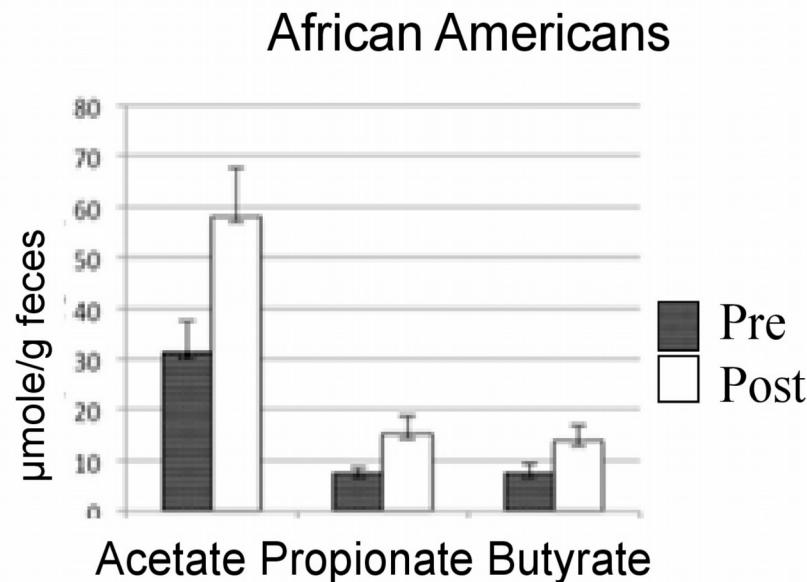
Colon cancer rates per country

# Diet swap (2 weeks) and colon cancer risk

Reciprocal impact on epithelial biomarkers for colon cancer risk seen already after two weeks !



# Impact diet exchange on SCFA

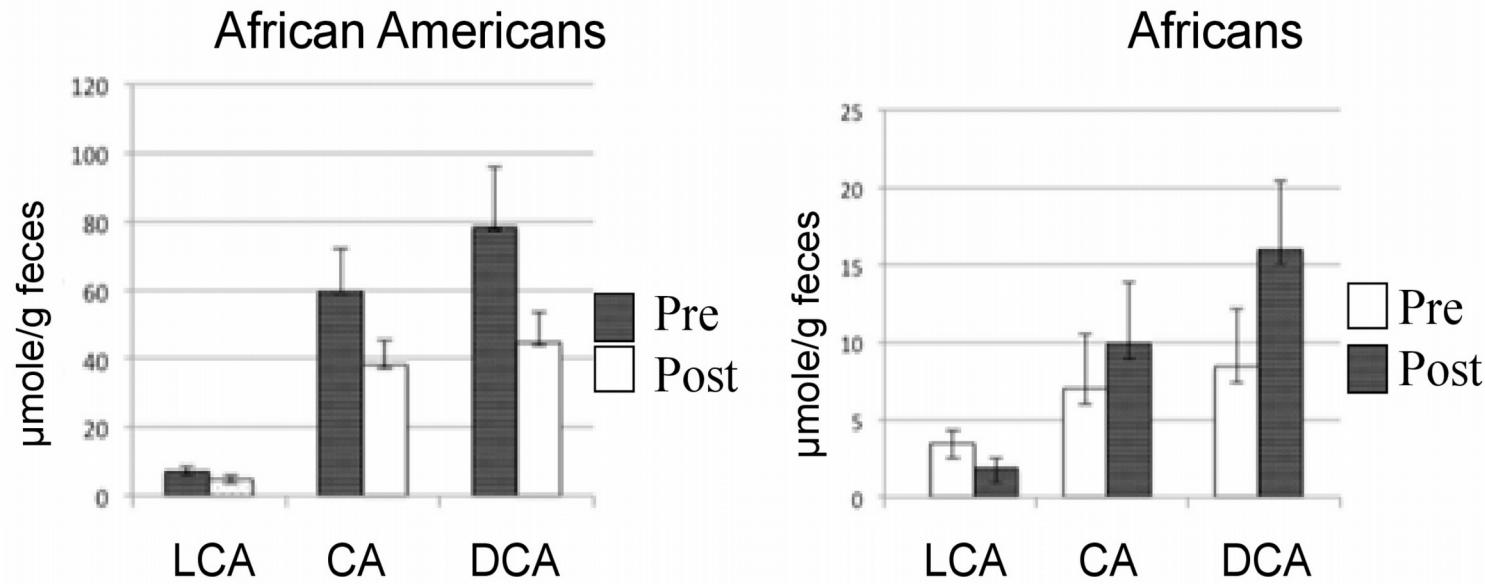


Reciprocally increased SCFA production with African diet: reported anti-inflammatory and anti-carcinogenic properties !

See also  
Louis et al. Nat. Rev.  
Microbiol Sept 2014

O'Keefe et al. Nat. Comm. 6:6342, 2015

# Impact diet exchange on bile acids



LCA: Lithocholic Acid, CA: Cholic Acid, DCA: Deoxycholic Acid

Primary and secondary bile acids  
reciprocally increased with American diet:  
reported pro-inflammatory and  
carcinogenic properties !

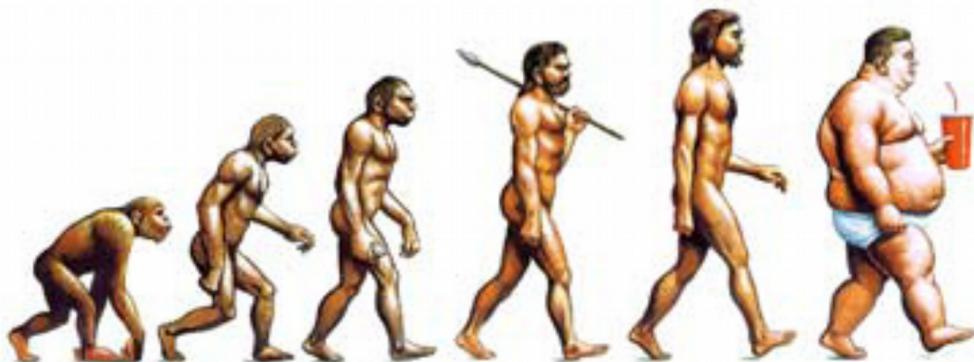
See also  
Louis et al. Nat. Rev.  
Microbiol Sept 2014

home > science

Medical research

## Bowel cancer risk may be reduced by rural African diet, study finds

Tests on subjects who swapped a fatty, meat-heavy diet for foods rich in beans and vegetables found a drop in biological markers for cancer in just two weeks



## Diet swap – Two weeks ?

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### Fat, fibre and cancer risk in African Americans and rural Africans

Stephen J. D. O'Keefe, Jia V. Li, Leo Lahti, Junhai Ou, Franck Carbonero, Khaled Mohammed, Joram M. Posma, James Kinross, Elaine Wahl, Elizabeth Ruder, Kishore Vipperla, Vasudevan Naidoo, Lungile Mtshali, Sebastian Tims, Philippe G. B. Puylaert, James DeLany, Alyssa Krasinskas, Ann C. Benefiel, Hatem O. Kaseb, Keith Newton <sup>✉</sup> et al.

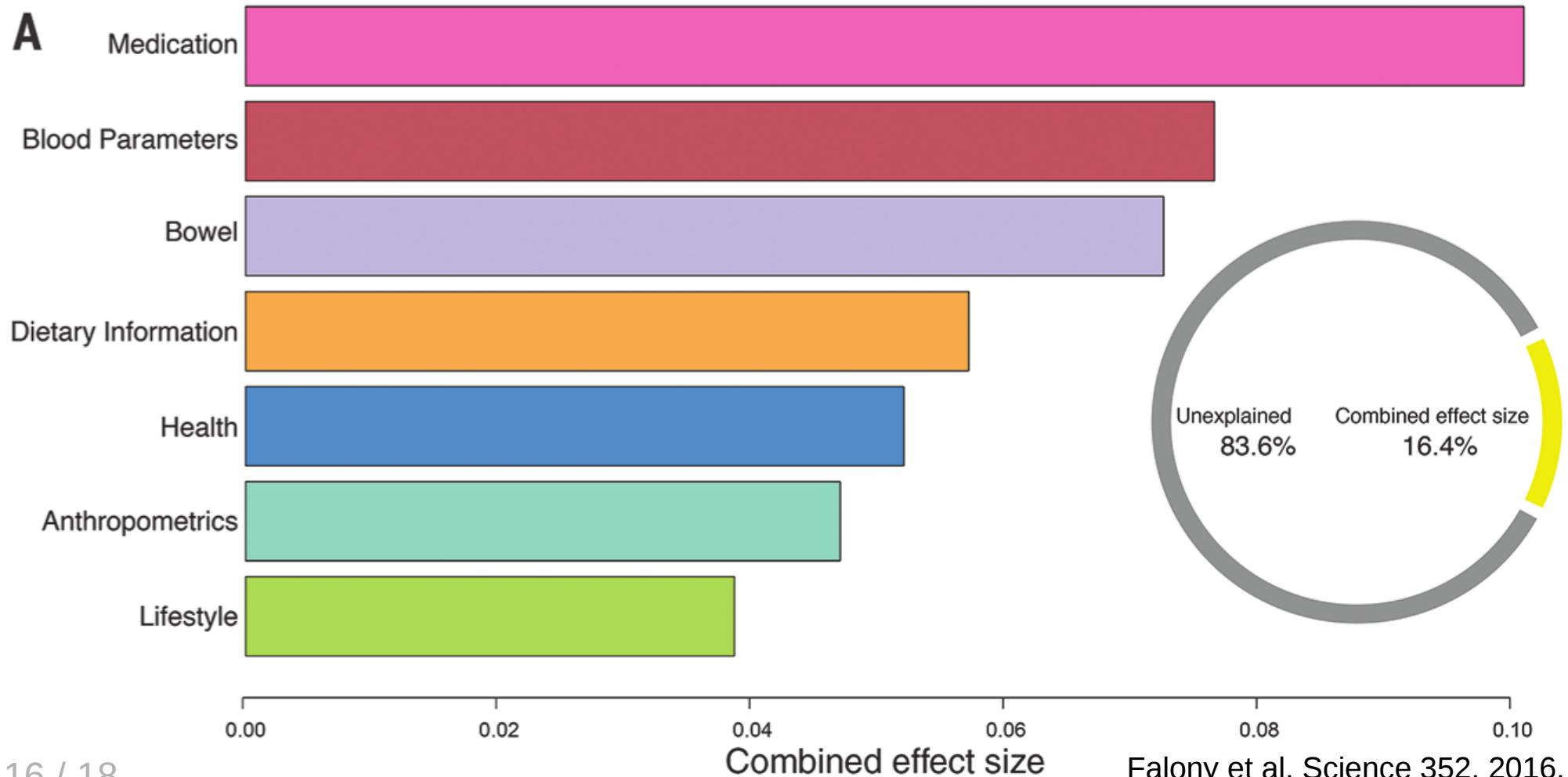
[Affiliations](#) | [Contributions](#) | [Corresponding author](#)

*Nature Communications* 6, Article number: 6342 | doi:10.1038/ncomms7342  
Received 23 May 2014 | Accepted 20 January 2015 | Published 28 April 2015

# Total explained variation only 16.4%

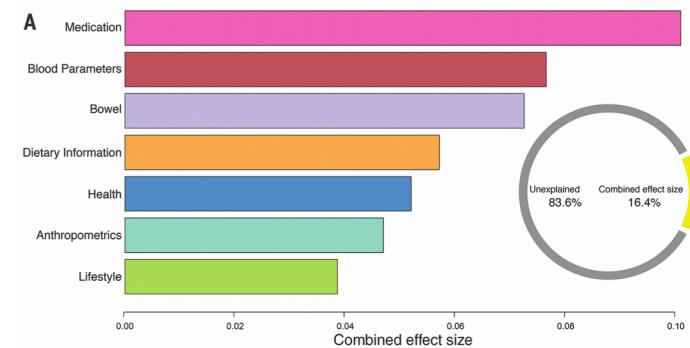
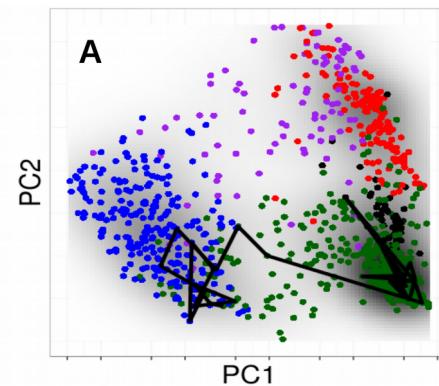
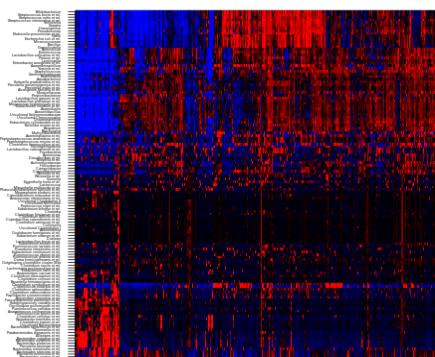
## (Flemish Gut Flora Project)

Proposed disease marker genera associated to host covariates and medication - inclusion in study design is essential !



# Summary

- Individuality and temporal dynamics better understood in the context of larger populations
- Majority (>80%) of total variation still to be explained
- Standardization, study design and confounder analysis remain essential yet easily overlooked
- Open data & algorithms can advance research



# Thank You !

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Stephen O'Keefe

Univ. Turku, Dpt.  
Mathematics & Statistics

Univ. Helsinki, Dpt.  
Veterinary Biosciences

Wageningen University, Lab.  
Of Microbiology, Netherlands

VIB/KU Leuven, Center for  
Biol. Of Disease, Belgium

<http://microbiome.github.io>



Intestinal microbiome landscaping: Insight into community assemblage and implications for microbial modulation strategies. Shetty, SA et al. FEMS Microbiology Reviews 2017, fuw045

Population-level analysis of gut microbiome variation. Falony et al. Science 352(6285):560-4, 2016

Metagenomics meets time series analysis: unraveling microbial community dynamics. Faust, Lahti et al. *Current Opinion in Microbiology* 15:56-66 2015

Improved taxonomic assignment of human intestinal 16S rRNA sequences by a dedicated reference database Ritari et al. BMC Genomics 16:1056, 2015.

Fat, Fiber and Cancer Risk in African, Americans and Rural Africans. O'Keefe et al. *Nat. Comm.* 6:6342, 2015

Impact of diet and individual variation on intestinal microbiota composition and fermentation products in obese men. Salonen et al. *ISME Journal* 8:2218-30, 2014

Tipping elements in the human intestinal ecosystem. Lahti et al. *Nat. Comm.* 5:4344, 2014