

The role of the vaginal microbiome and host factors in transgender health and HIV risk

Nichole Klatt, PhD

SCOPE Community E-meeting: Developments in the HIV and STIs Biomedical Prevention Pipeline

May 14th, 2025

Division of Surgical Outcomes and Precision Medicine Research

Department of Surgery

University of Minnesota School of Medicine

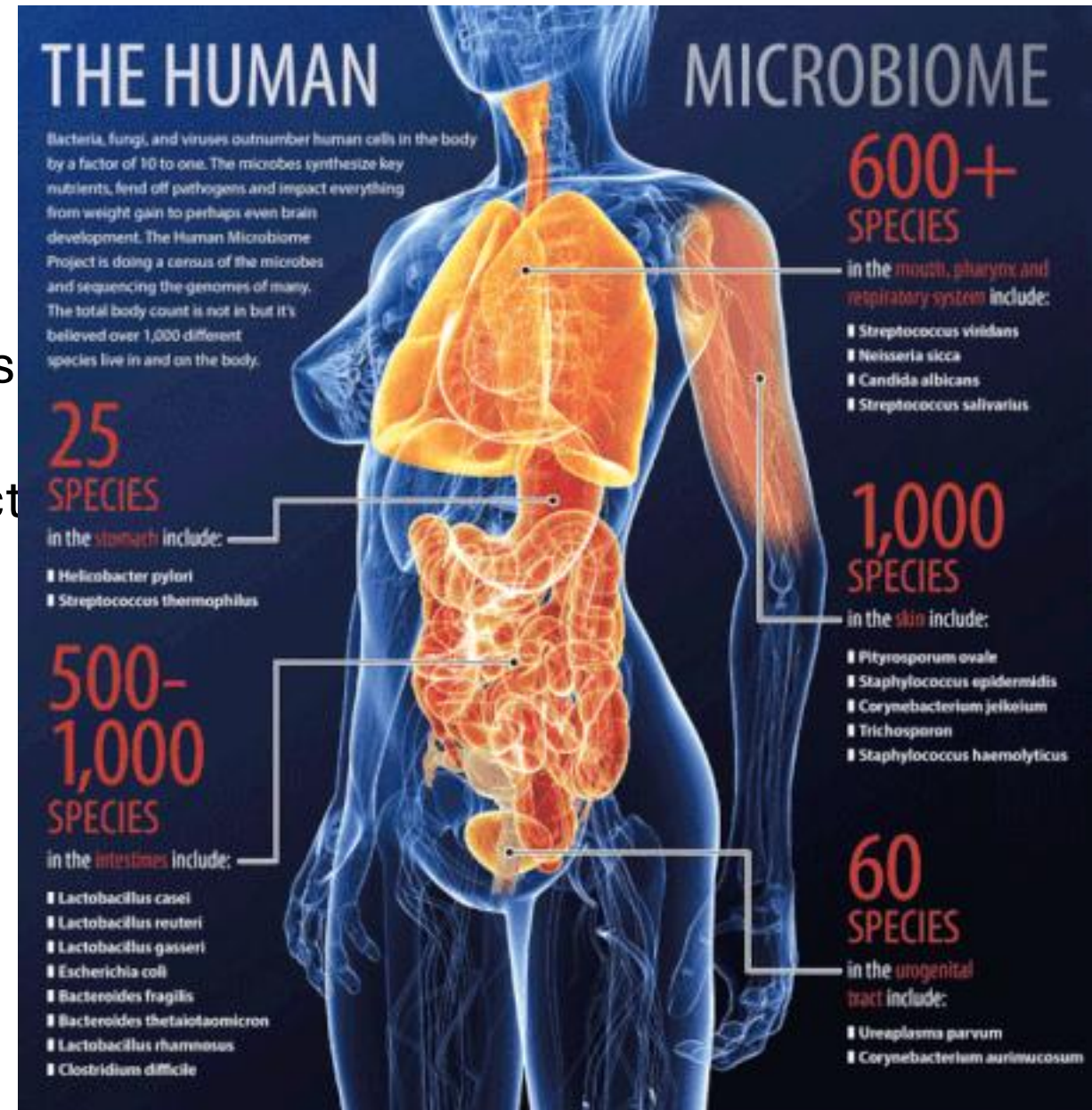


UNIVERSITY OF MINNESOTA

Driven to Discover®

Microbiome

- **Microbiome:** Microorganisms in an environment (10-100 trillion/person)
 - Includes bacteria, viruses, fungi, protists, archaea
 - Includes genes, metabolites and products
- **Dysbiosis:** An imbalanced microbial community
 - Abundance and/or functional changes



Women's
Health

Cancer/
Transplant

Infectious
Diseases (HIV,
Zika, etc)

Sepsis/Surgical
Outcomes

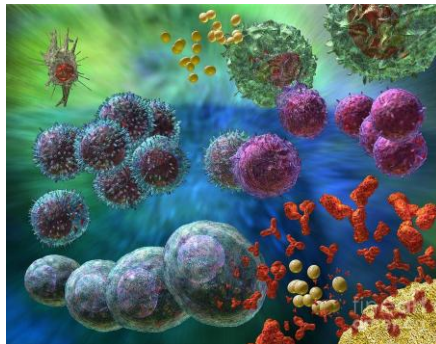
Covid-19

Antibiotics

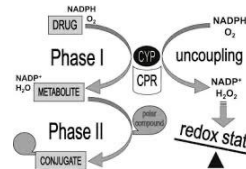
**Systemic Inflammation and
Mucosal Dysfunction**



**Immunity and
Inflammatory Responses**



Drug Metabolism

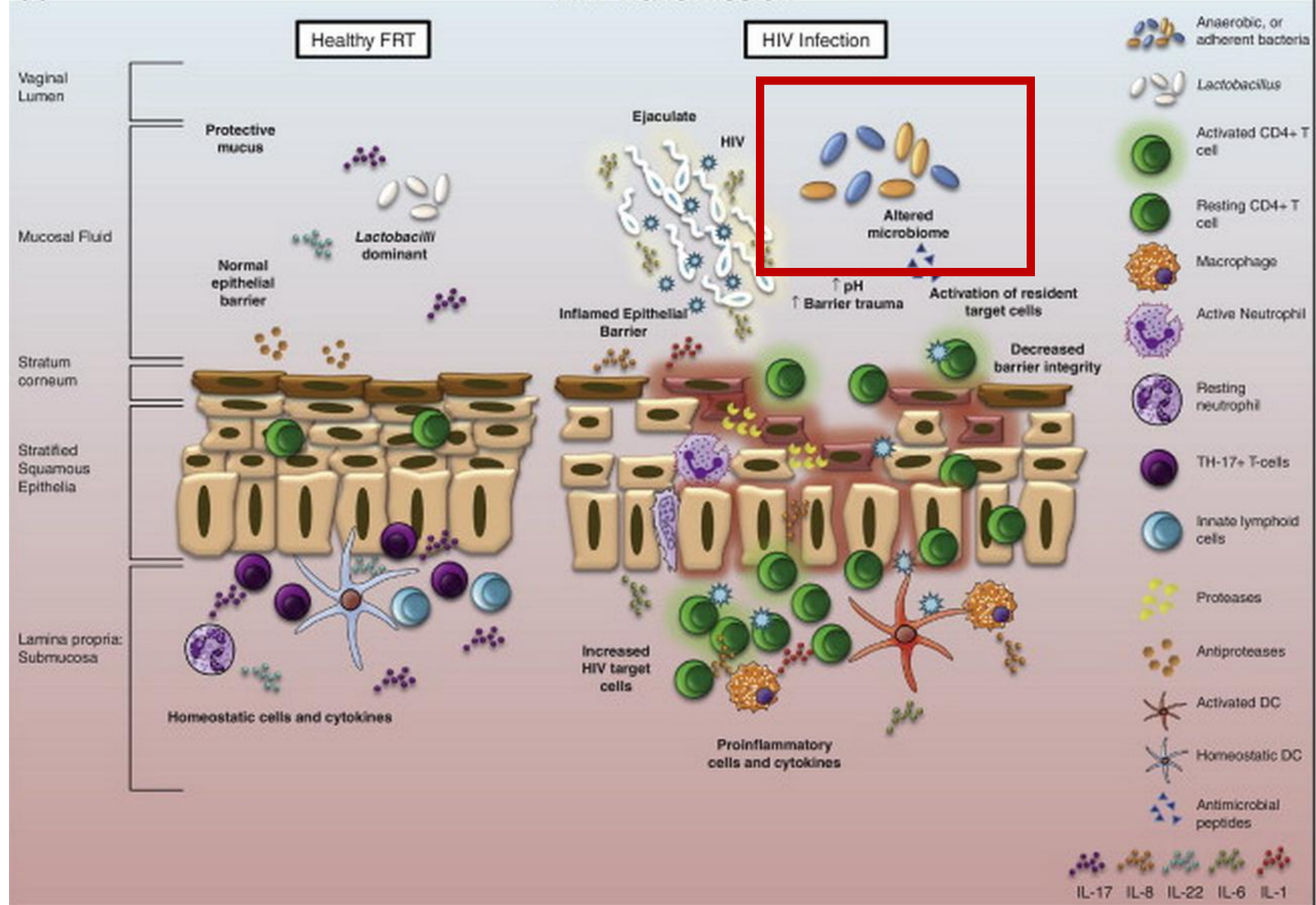


Microbial Dysbiosis



(a)

HIV Transmission



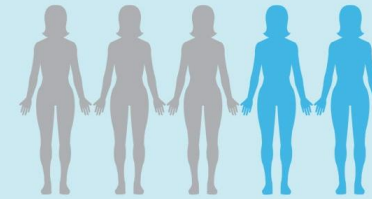
(Burgener, McGowan, Klatt; Curr Opin Immunol 2015)

What is Bacterial Vaginosis?

- Highly prevalent inflammatory vaginal disorder
- Symptoms: vaginal odor, discharge, itching, burning
 - Can be asymptomatic
- Increases risk of pregnancy complications, STIs, PID
- Treated with antibiotics (metronidazole)
 - ~90% recurrence after 1 year
- Risk factors and pathogenesis poorly understood

BACTERIAL VAGINOSIS (BV)

is the most common vaginal infection in women ages 15-44



2 IN 5
women have
BV

84%
of those women
don't know they
have it

BV INCREASES YOUR CHANCE OF GETTING STIS SUCH AS

Chlamydia

and

Gonorrhea

These bacteria can sometimes cause **PELVIC INFLAMMATORY DISEASE (PID)**, which can make it difficult or impossible for you to have children.

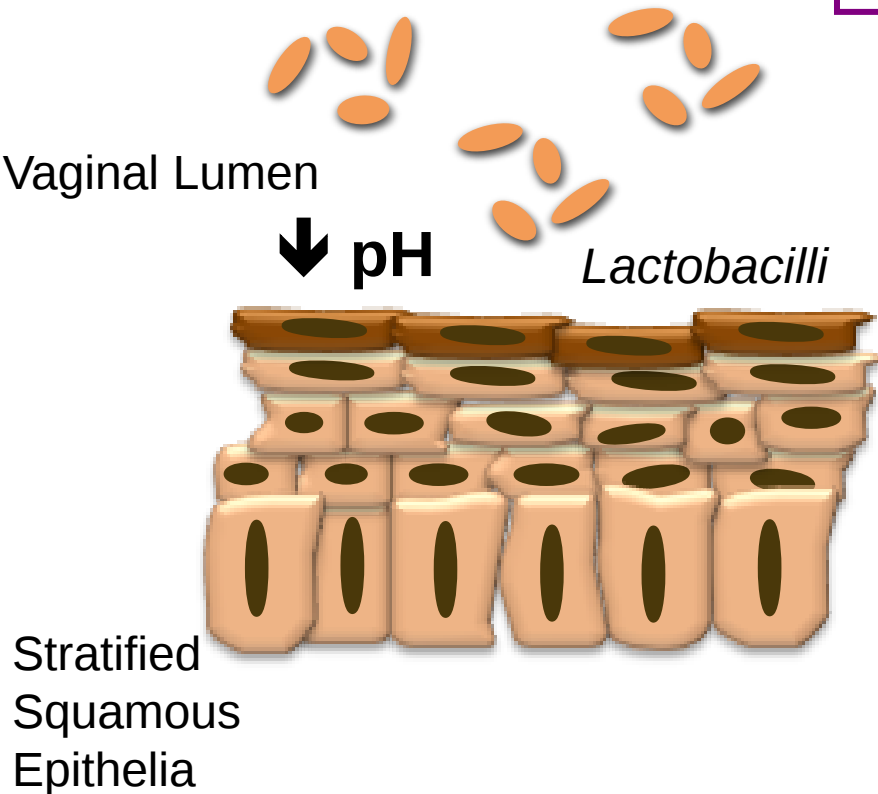
The high concentration of petrochemicals in most Over the Counter personal lubricants may increase risk of BV by up to 2-3x

Vaginal microbial dysbiosis (Bacterial Vaginosis, BV)

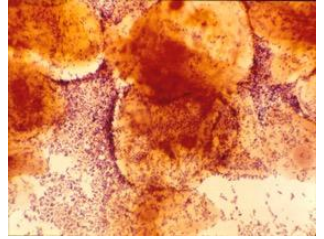
Dominance by *Lactobacillus*



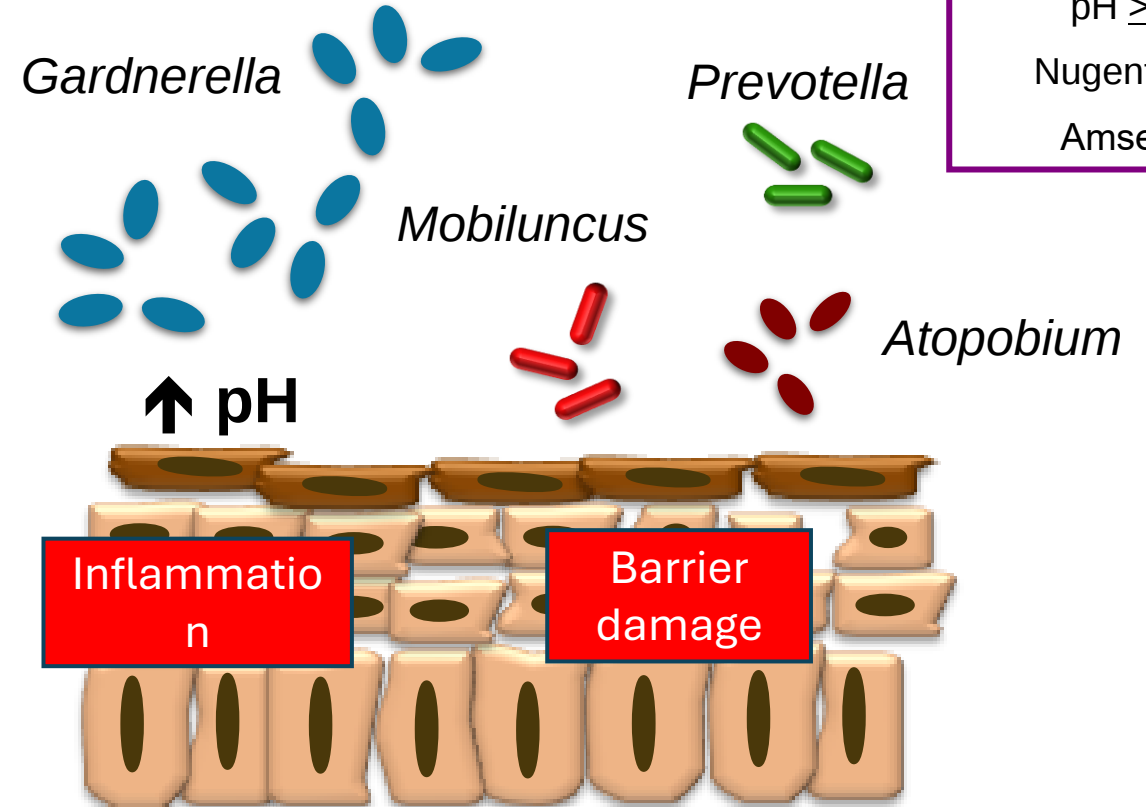
pH < 4.7
Nugent = 0



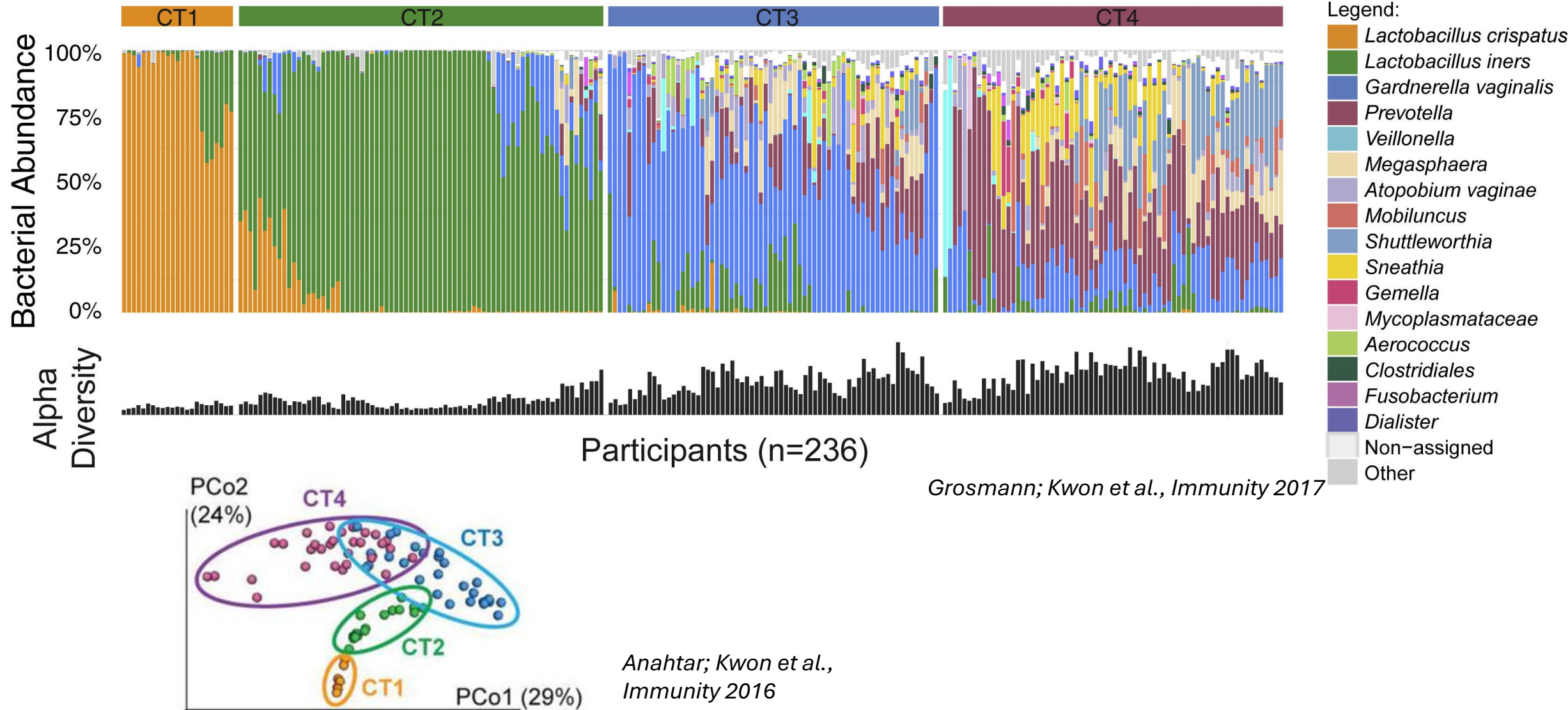
Dominance by polymicrobial anaerobic bacteria



pH ≥ 4.7
Nugent 7 -10
Amsel's +

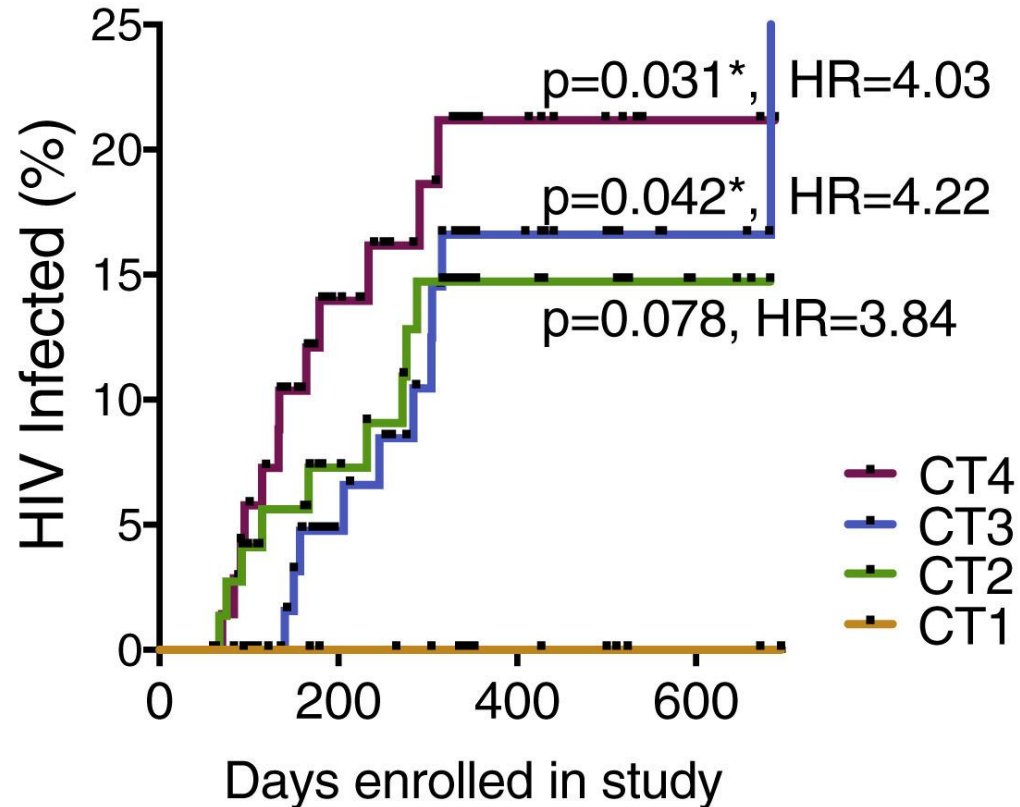


Vaginal microbiome can be broken into distinct community type (CT) structures



Vaginal dysbiosis and BV increase HIV infection risk

A All participants

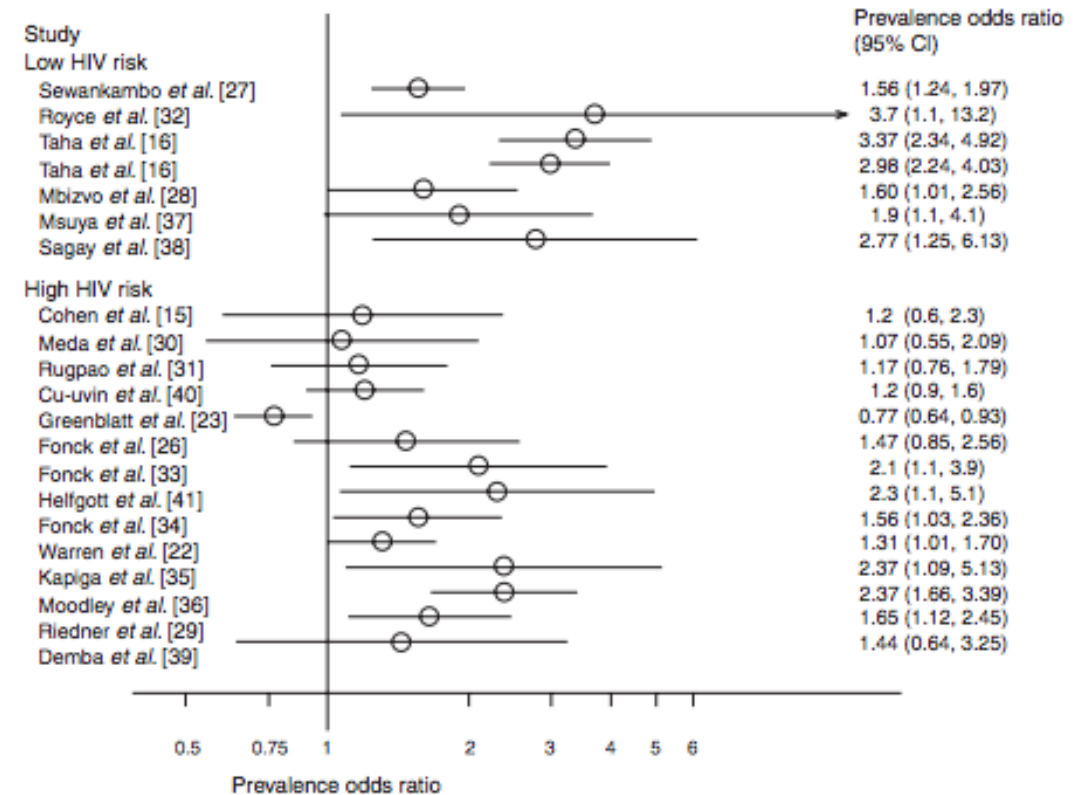


Grosmann; Kwon *et al.*, *Immunity* 2017

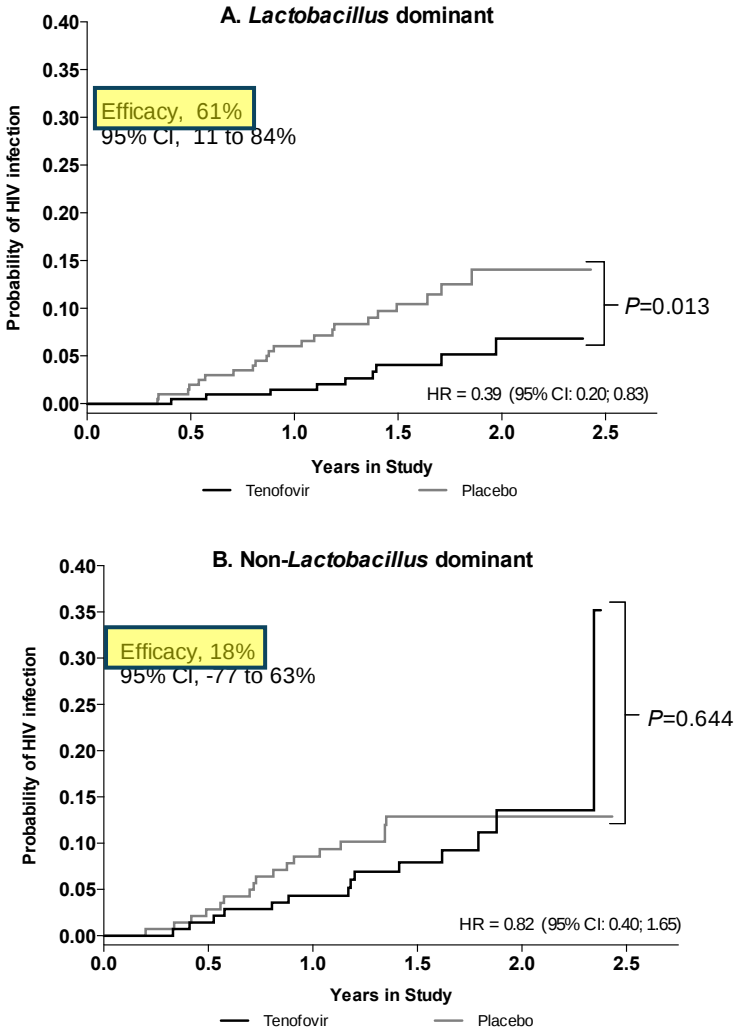
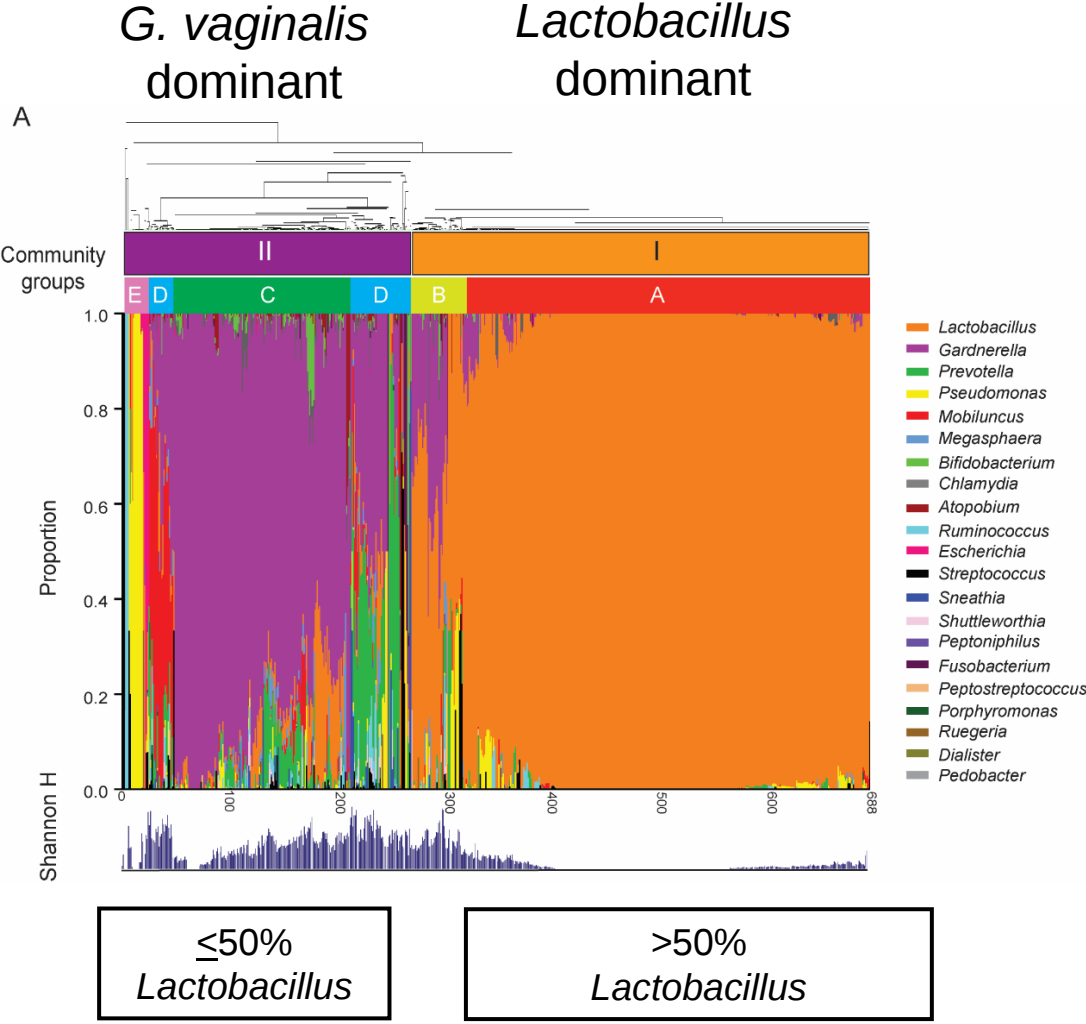
Bacterial vaginosis and HIV acquisition: a meta-analysis of published studies

Julius Atashili^{a,b}, Charles Poole^a, Peter M. Ndumbe^b,
Adaora A. Adimora^a and Jennifer S. Smith^a

AIDS 2008, **22**:1493–1501



Vaginal microbial groups in CAPRISA 004 alter efficacy



Transgender health and the microbiome



Descriptive summary

Variable	N = 10 ¹
Race	
Black/African American	1 (10%)
Other	1 (10%)
White	8 (80%)
Age	41 (18)
Number of sexual partners in the last month	4.0 (5.0)
Number of partners the participant had receptive anal sex within the last month	0.40 (0.70)
Number of times participant had receptive anal sex with no condom in the last month	0.30 (0.67)
Number of partners the participant had receptive vaginal sex within the last month	4.0 (5.1)
Number of times participant had receptive vaginal sex with no condom in the last month	2.30 (2.58)

¹ n (%); Mean (SD)

Made into categorial mean variables

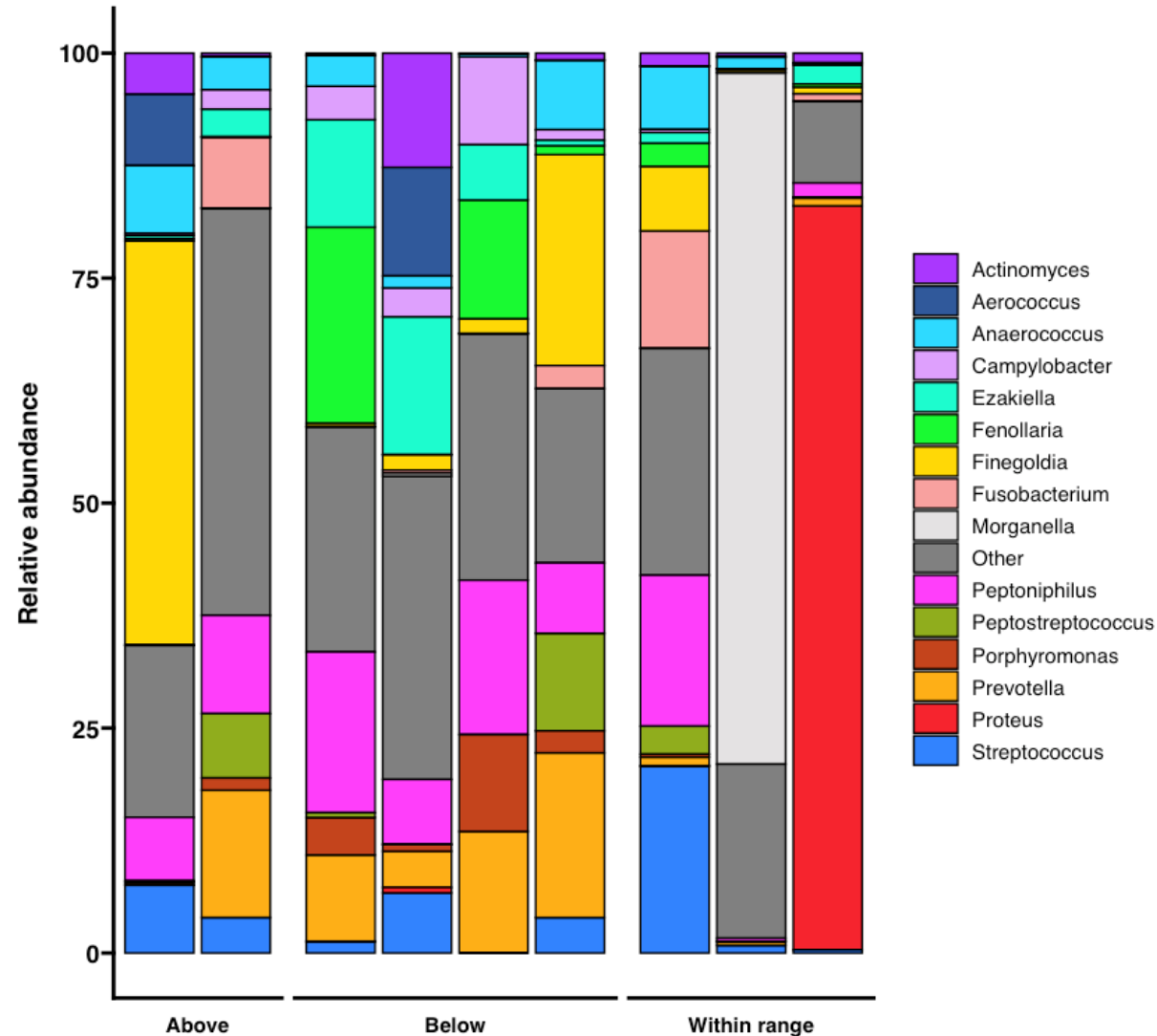
Descriptive summary

Variable	N = 10 ¹	Variable	N = 10 ¹
Type of estradiol use		Currently using prep	
Injections	6 (60%)	No	2 (20%)
Patches	1 (10%)	Yes	8 (80%)
Pills	3 (30%)	Current smoker	
Estrogen level	198 (227)	No	3 (30%)
Progesterone level	0.92 (2.21)	Yes	7 (70%)
¹ n (%); Mean (SD)		¹ n (%); Mean (SD)	

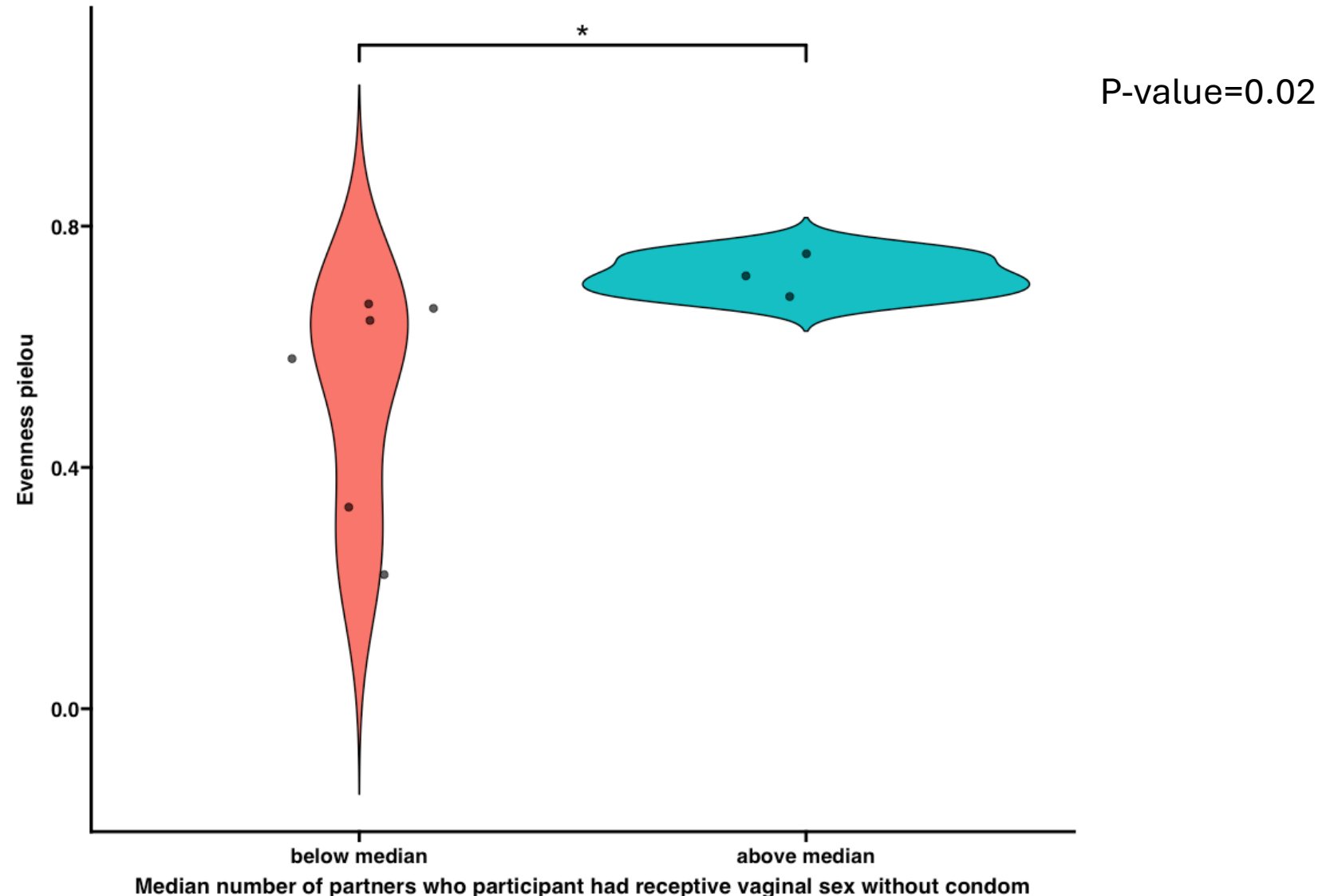
Made a mean
categorical
estrogen and
progesterone
variables and
a below,
above, and
within range
variable for
estrogen



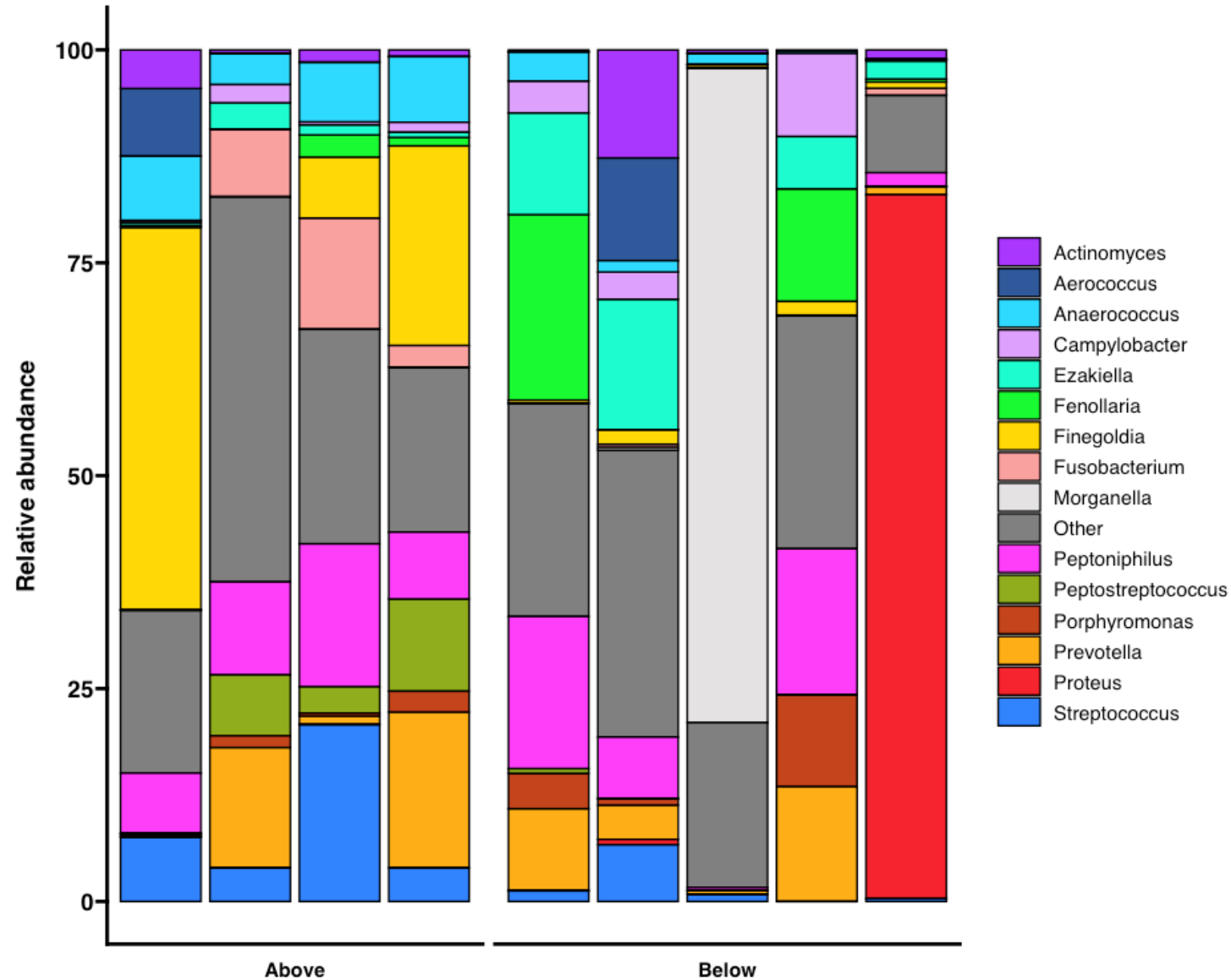
Microbial taxa profiles of samples grouped by estrogen level range



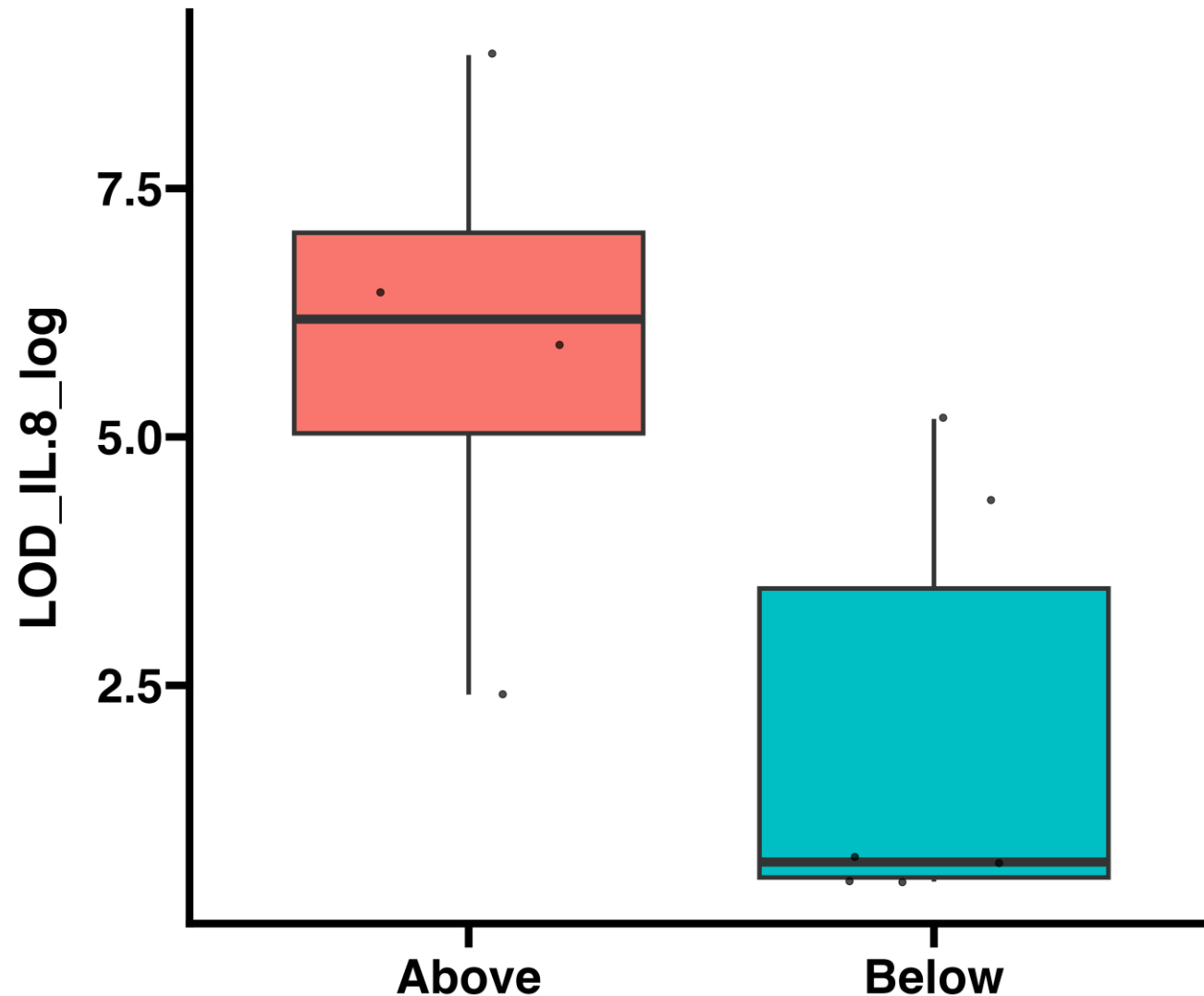
Significant difference found between the median number of participants that had receptive vaginal sex without a condom



Microbial taxa profiles of samples grouped by mean number of men participants had receptive vaginal sex with



Individuals with higher MIP-1b concentrations have higher number of receptive vaginal sex partners

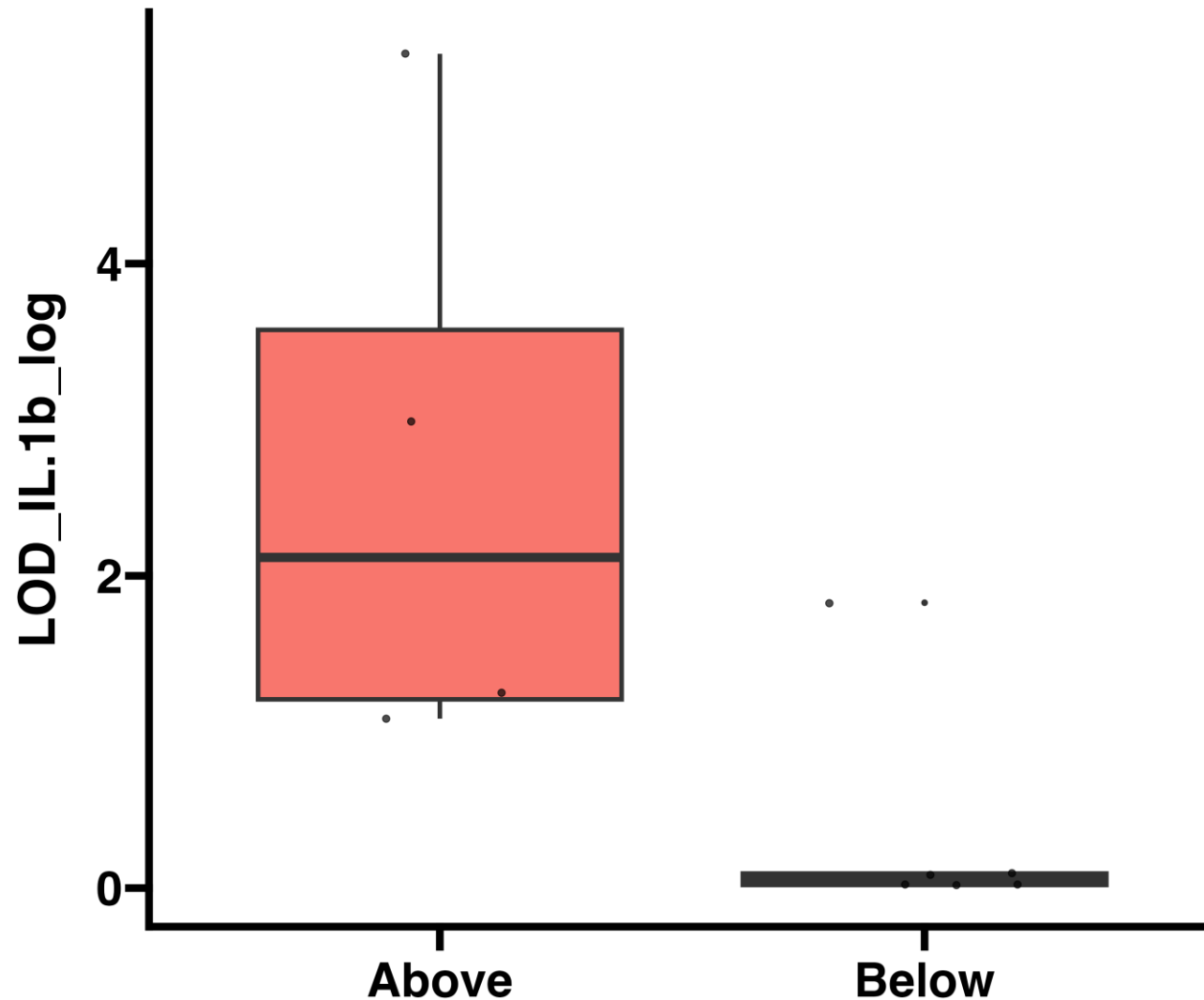


- P value = 0.0421
- Wilcoxon test
- When FDR was done p value was no longer significant

Above: 4 individuals

Below: 5 individuals

Individuals with higher IL-1b concentrations have higher number of receptive vaginal sex partners



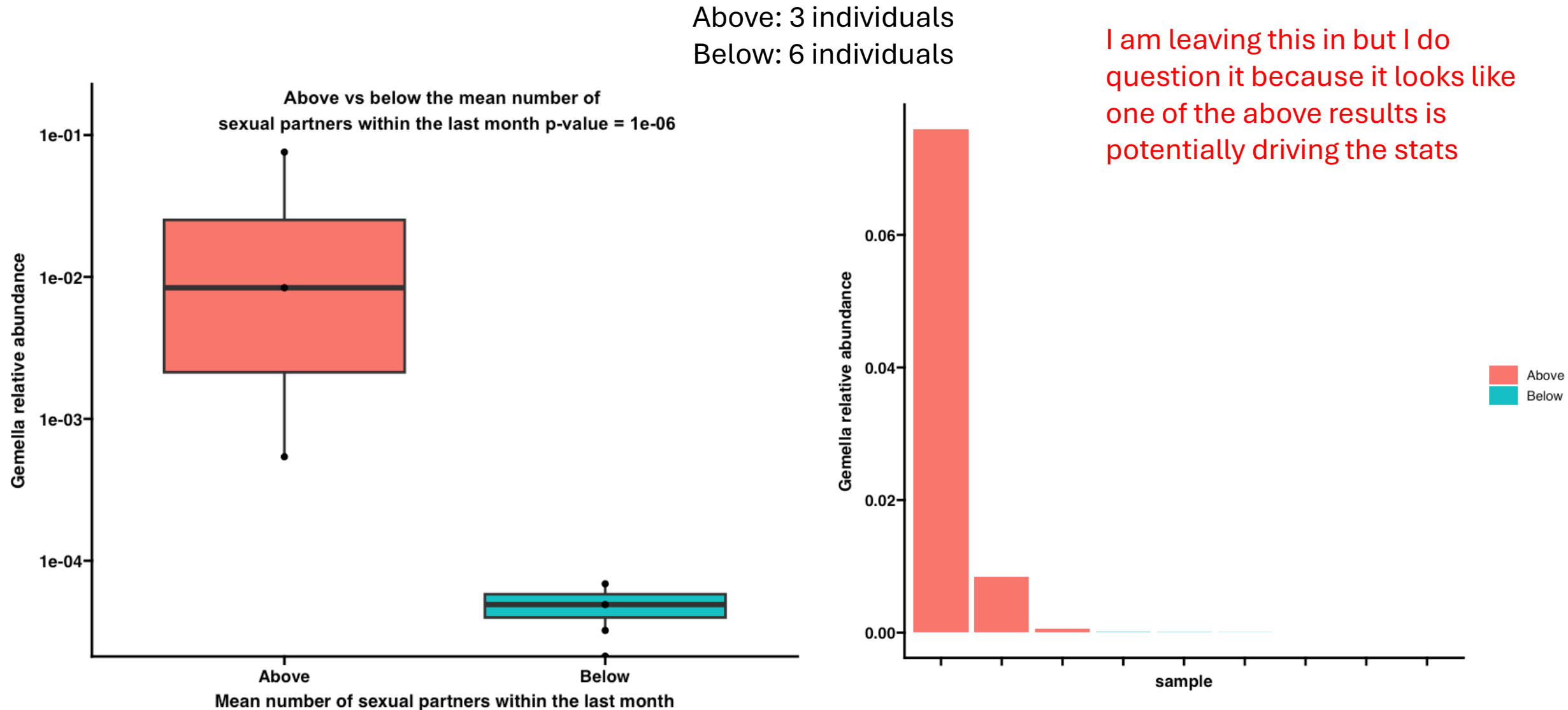
- P value = 0.0403
- Wilcoxon test
- When FDR was done p value was no longer significant

Above: 4 individuals

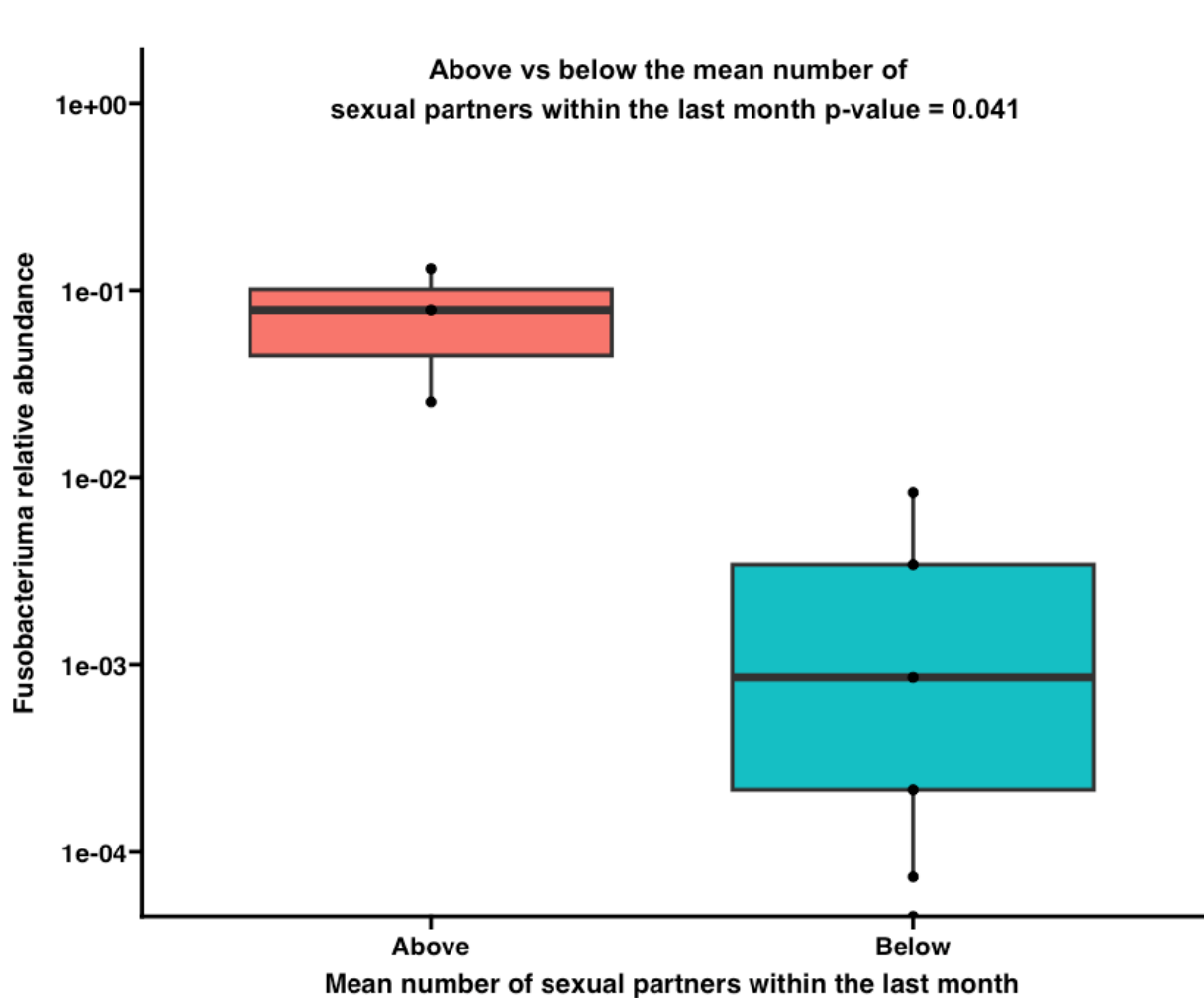
Below: 5 individuals

Differential abundant bacteria and Sexual behaviors

Individuals with more than 4 sexual partners within the last month had a significantly higher relative abundance of Gemella

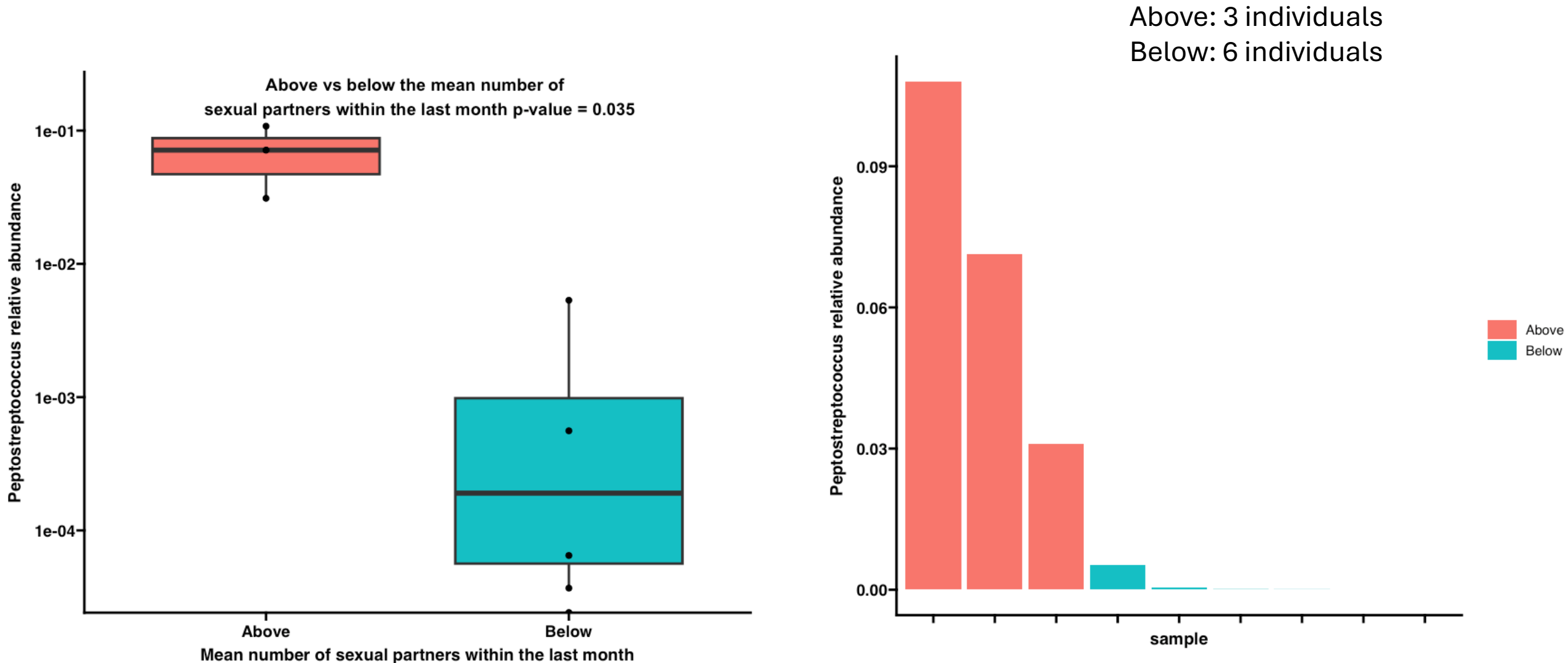


Individuals with more than 4 sexual partners within the last month had a significantly higher relative abundance of Fusobacterium

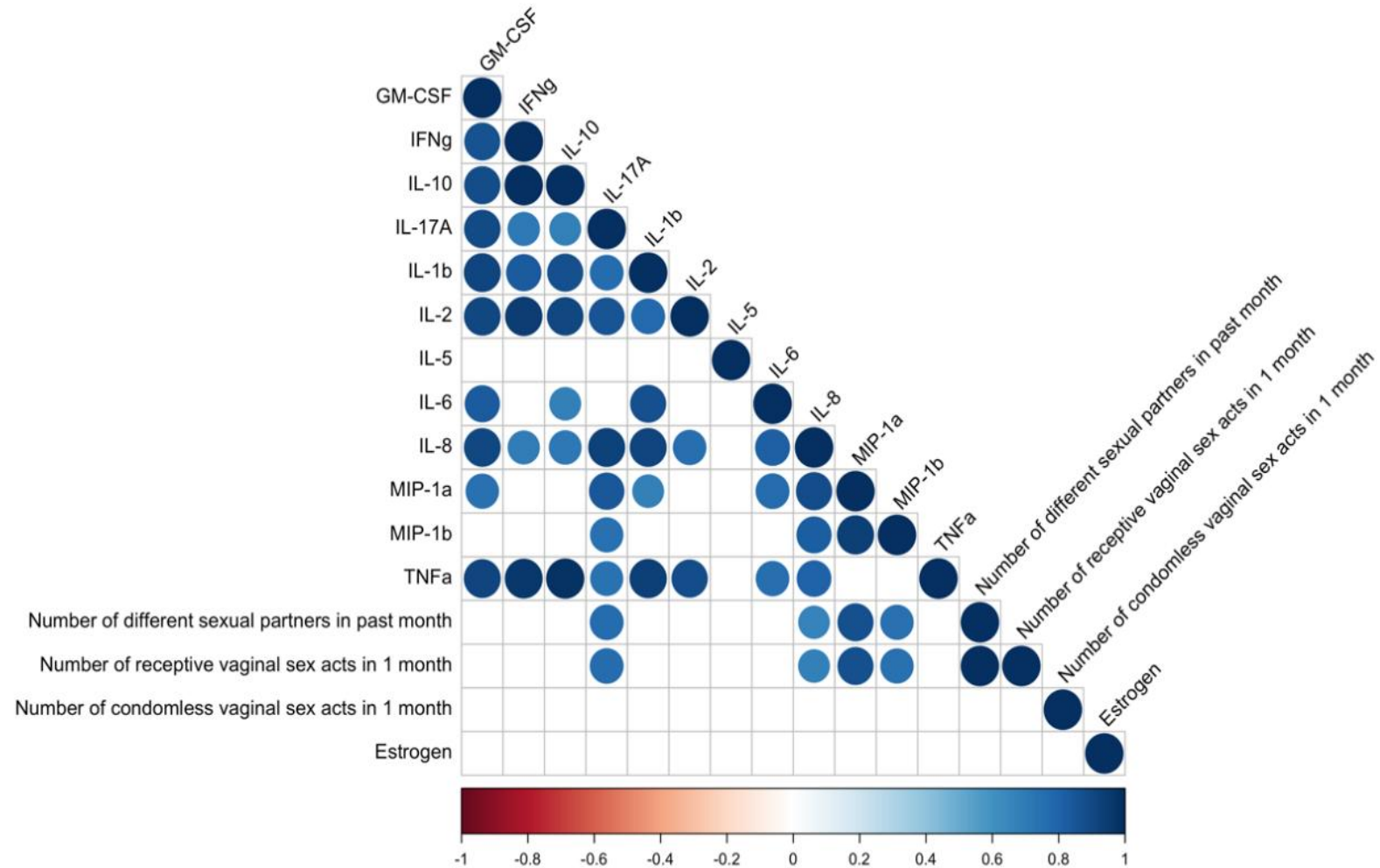


Above: 3 individuals
Below: 6 individuals

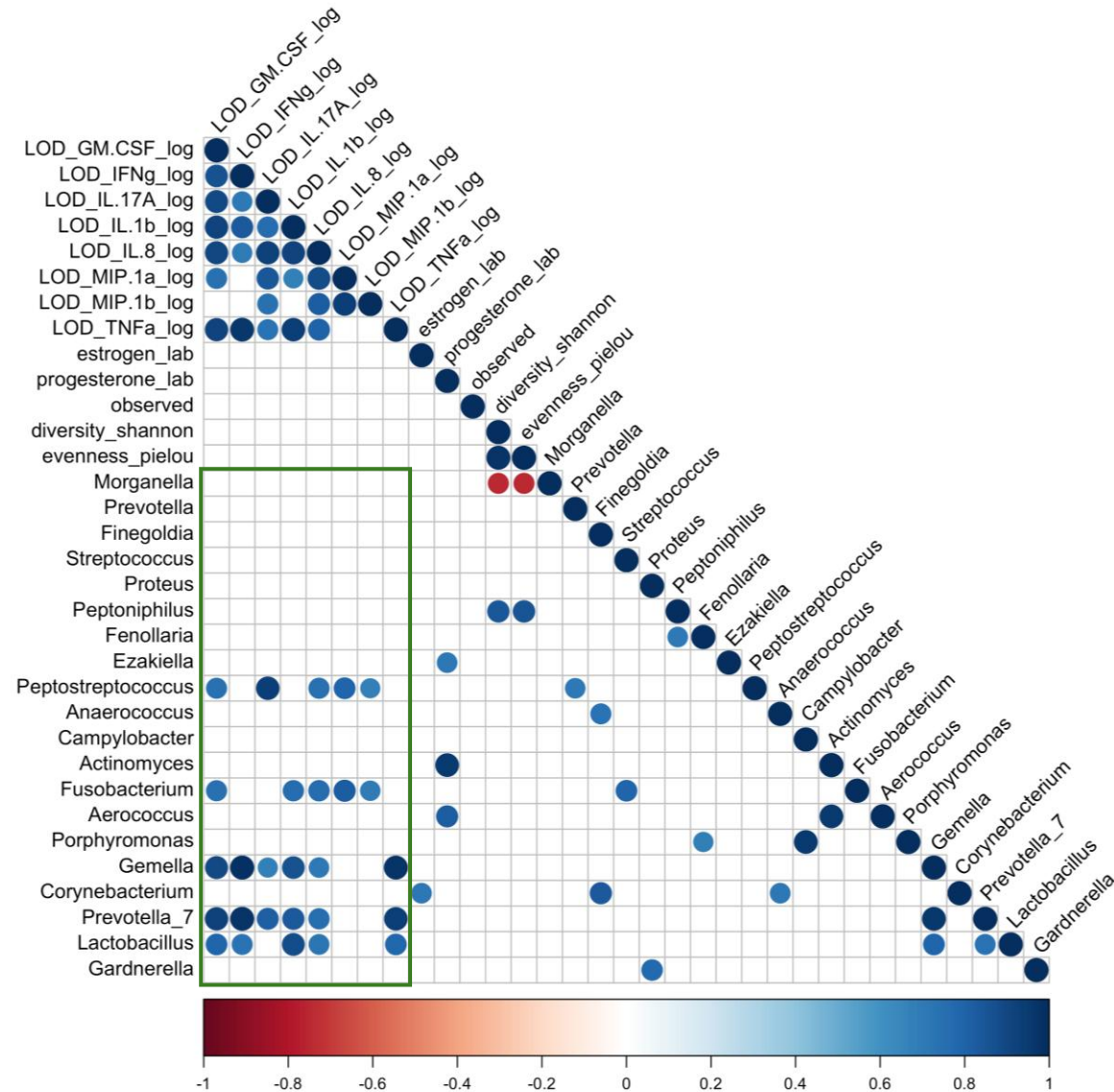
Individuals with more than 4 sexual partners within the last month had a significantly higher relative abundance of *Peptostreptococcus*



Cytokines IL-17, IL-8 and MIP-1b are associated with sexual partners

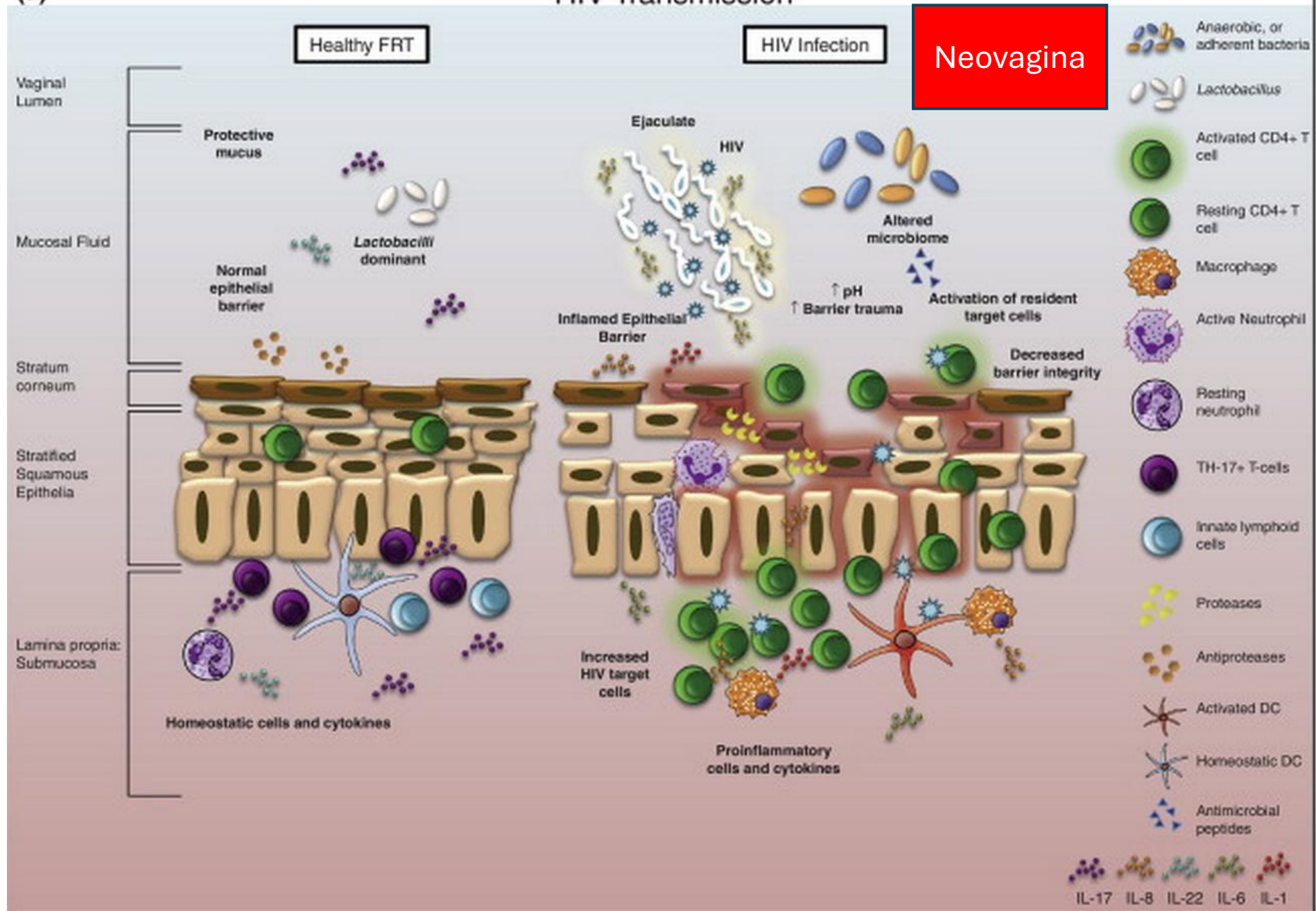


Top differential microbial genera are positively associated with various inflammatory markers



(a)

HIV Transmission



(Burgener, McGowan, Klatt; Curr Opin Immunol 2015)

Conclusions

- In BV in cisvaginas and in all neovaginas measured, polymicrobial anaerobic communities dominate the microbial communities
- Dysbiotic vaginal and neovaginal microbes are associated with inflammation and could lead to increased HIV risk
- Increased sexual partners in TG are associated with increased dysbiosis of microbes and with increased cytokine expression, potentially a biological mechanism of increased HIV risk
- More studies to fully understand the biological mechanisms underlying increased HIV risk in transgender populations is critical

- Klatt Lab
- University of Minnesota Dept. of Surgery
- Division of Surgical Outcomes and Precision Medicine Research
 - Chris Basting
 - Courtney Broedlow
 - Ty Schroeder
 - Erik Swanson
 - Asthma Chakrawarti
 - Robert Langat
 - Sophie Lebakken
 - Charlotte Hemilla
 - Erica Tieman
 - *Luca Schifanella*
 - *Ross Cromarty*
 - *Andrew Gustin*
 - *Ryan Cheu*
 - *Charlene Miller*
 - *Jennifer Manuzak*

- University of Miami
 - Lydia Fein
 - Maria Alcaide
 - Patricia Del Carmen
 - Alejandro Mantero
 - Ana Salazer Zetina
 - Nicholas Fonseca
 - Deborah Jones
 - Emily Cherenack
- UMN Genomics Core (UMGC)
 - Kenny Beckman
 - Elyse Froehling
- UMN Center for Mass Spectrometry and Proteomics
 - Candace Guerrero
 - Tim Griffin
 - Bruce Witthuhn
- University of Maryland
 - Jacques Ravel
 - Johana Holm
 - Michael France

- UMN Collaborators
 - Tim Schacker
 - Jodi Anderson
 - Kevin Escandon
 - Sayeed Ikramuddin
 - Melanie Graham
 - Michael Gale
 - Ryan Hunter
 - Dan Knights
 - Carolyn Bramante
 - Chris Tignanelli
- UCLA
 - Otto Yang
 - Jennifer Fulcher
 - Grace Aldrovandri



Special thanks to all study participants!

- NIH/NIAID 1K22AI098440
- NIH/NIAID 1R01AI117828
- NIH/NIDDK R01DK112254

