Public Health Ontario | Santé publique Ontario

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https://youtu.be/dj2nue6wDoI

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A step towards understanding neovaginal health for trans women

Jessica Prodger (she/her)

Western University

Jacques Ravel

University of Maryland

“We have described for you a mountain. We have shown you the path to the top. We call upon you to do the climbing.”

The Honourable Mizanay (Mizhana) Gheezhik

Learning Objectives

1. Describe the tissue microstructure of the neovagina created by penile inversion vaginoplasty.
2. Understand how the neovaginal microbiome differs from the natal vagina and penile skin.
3. Gain insight into which neovaginal bacteria are likely beneficial, and which are associated with inflammation.
4. Understand why best-practices, diagnostics, and treatments designed for the natal vagina cannot be applied to the neovagina.

Intersectionality between Sex and Gender

“Not all boys have penises”

Grant Prodger, 3 yrs

- sex matches gender → cisgender
- sex differs from gender → transgender
- Gender isn’t entirely masculine or feminine → non-binary

Gender Affirming Medical Care

- Produce physical traits that better match gender
- Gender dysphoria, anxiety, depression, sexual function, quality of life
- Surgeries
  - Brest reduction / augmentation, **vaginoplasty,** orchiectomy**,** hysterectomy
- Hormone therapy
  - Transmasculine: testosterone
  - Transfeminine: estrogen (and testosterone blockers if no orchiectomy)

The genital microbiome is key to sexual and reproductive health

Vagina (cis women)

- **Bacterial Vaginosis (BV)**
  - Low *Lactobacillus*, diverse anaerobes
  - Symptoms → 10-15 million doctor visits/year in US
- Gynecologic
  - Pelvic inflammatory disease; STIs (HSV-2, HIV, Chlamydia), vaginal odor, itching, discharge
- Obstetric
  - Fertility, Preterm delivery and low birth weight, Premature rupture of membranes (PROM), Postpartum endometritis, Amniotic fluid infection, Chorioamnionitis
- "molecular" BV → high-risk even when asymptomatic

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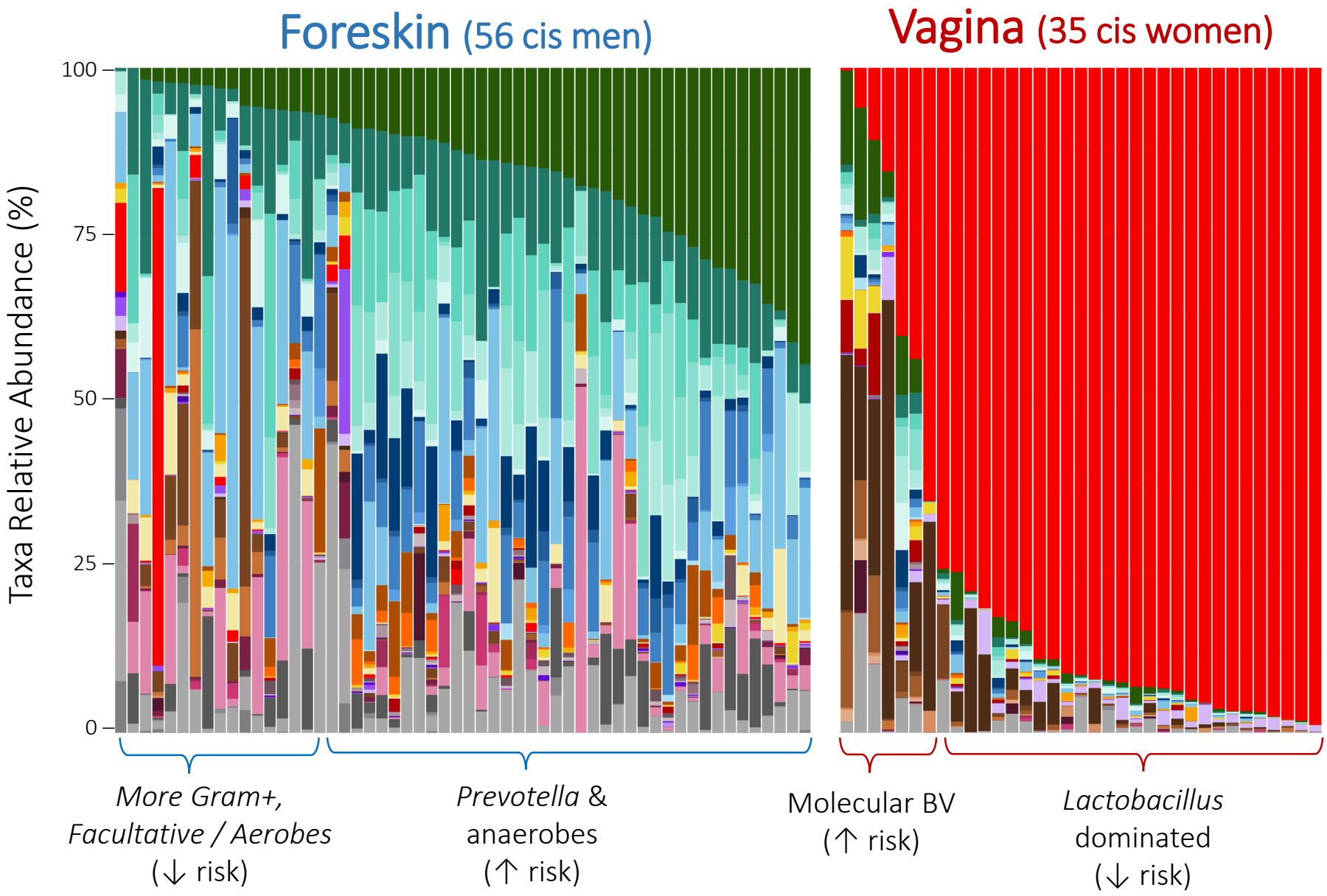
- "molecular" BV → even when asymptomatic

Penis (cis men)

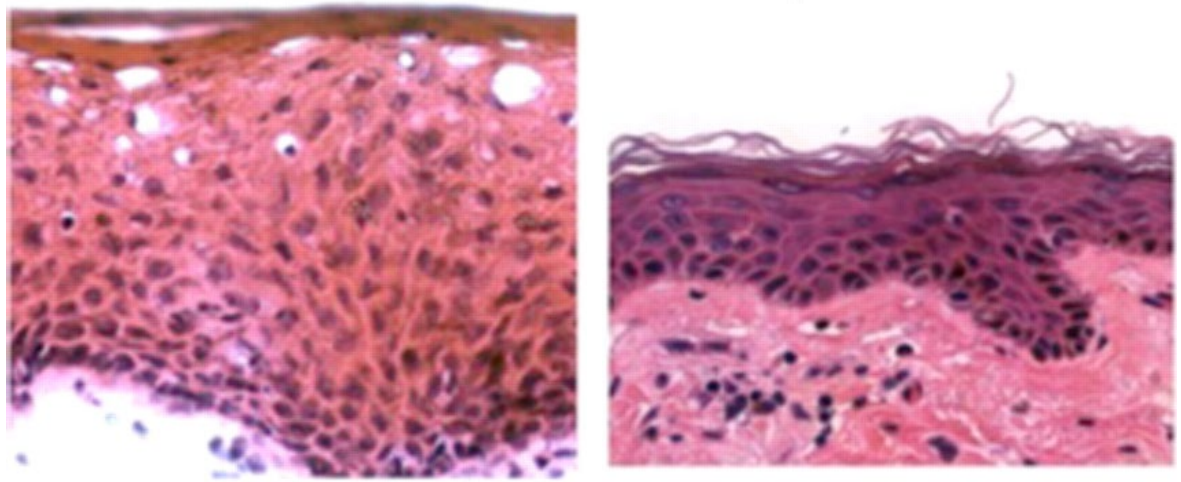
- Penis has a unique microbiome too!
- Highly anaerobic community = chronic inflammation
  - Increased risk of HIV, HR-HPV, prostate cancer
- Circumcision reduces anaerobes:
  - Clearance of HR-HPV
  - Decreased risk of penile cancer, HSV-2 and GUD, UTI, HIV



Ravel J et al, Am J Obstet Gynecol. 2021; Prodger et al, JCI Insight. 2021

Environment shapes microbiome

Reproductive Age Vagina	Penis skin
Thicker	Thinner
Low oxygen levels	Variable oxygen levels
Low water loss + Cervical secretions	High water loss
	Soft-cornified outer layer = corneocytes in a lipid-rich extracellular matrix
Nutrient source = Glycogen rich cells	Nutrient source = Free keratin and fatty acids



Stratified squamous epithelia

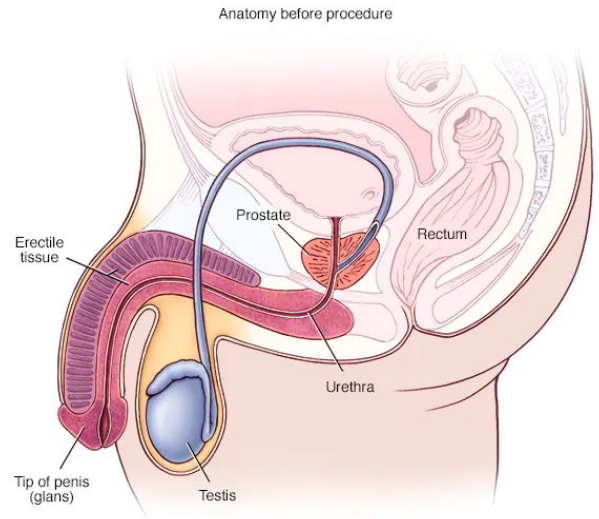
Dinh 2012 *Biol Reprod*

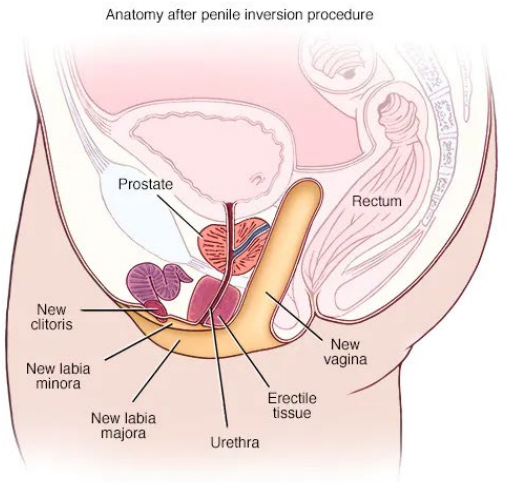
The Neovagina and Vaginoplasty

- Surgical creation of a vulva and vaginal canal
- Most common form = penile inversion
  - Dissect space between bladder and rectum
  - Inversion of penile tube and scrotal tissue into this space

Result:

Vaginal cavity lined with penile / scrotal skin





[Anatomy before and after penile inversion]. (n.d.) https://www.mayoclinic.org/tests-procedures/feminizing-surgery/multimedia/img-20358606

Neovagina: vaginal cavity lined with penile skin

What is the microstructure of the epithelium?

What are the colonizing bacteria?

What bacteria are beneficial? Problematic?

Will diagnostics/treatments designed for ciswomen work?

Transition Related Surgery

- March 2019: Vaginoplasty OHIP code
- Sept 2019: WCH First Solo Vaginoplasty
- >40 vaginoplasty/year

Canada Toronto

Ontario boosts access for trans people seeking gender confirmation surgery

People left waiting 2 years to get surgical referral from CAMH Gender Identity Clinic

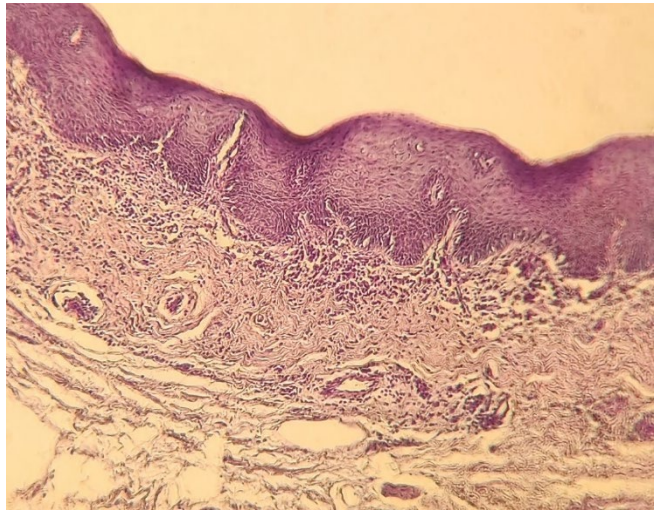
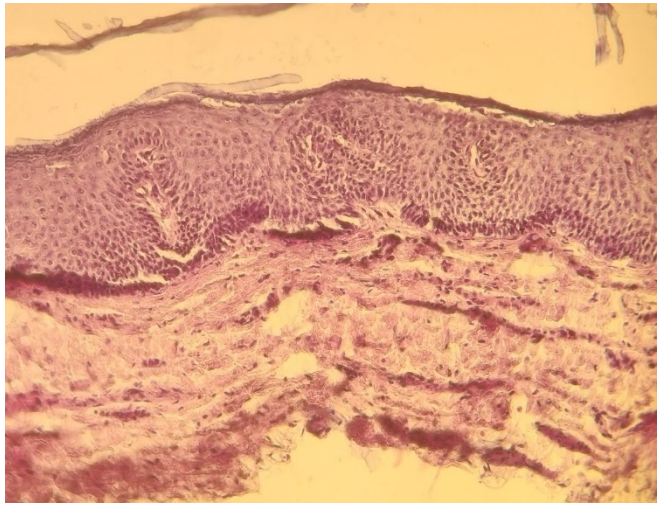
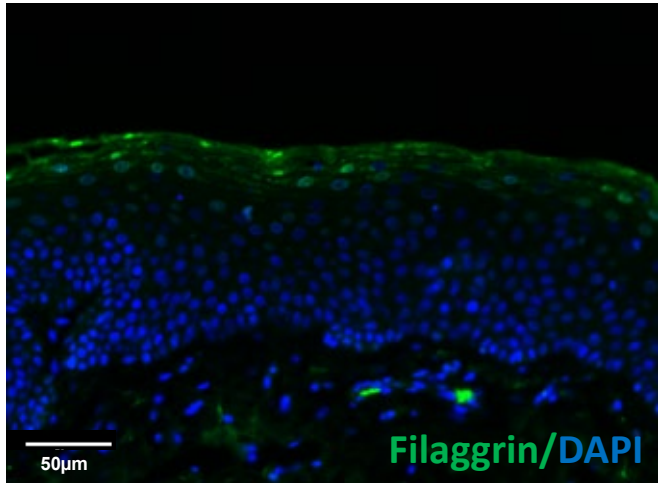
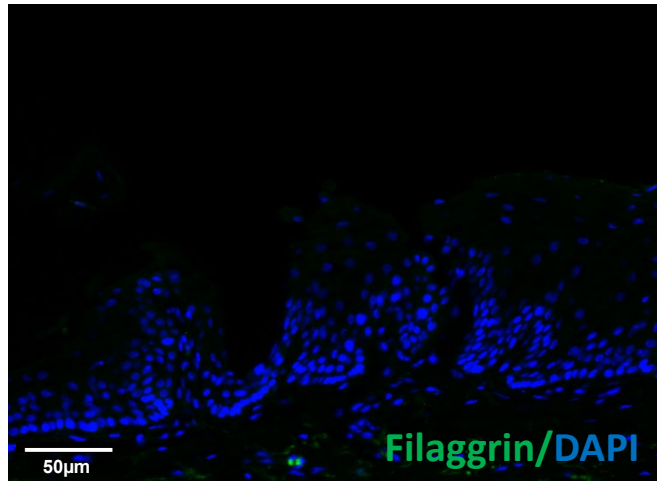
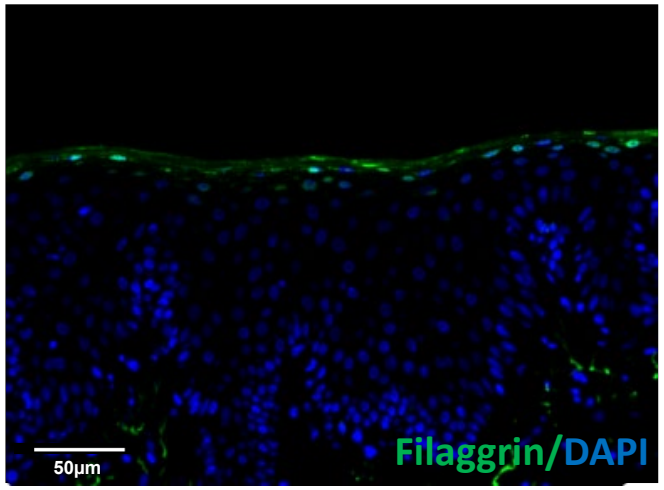
By Laura Fraser, CBC News Posted: Mar 06, 2016 8:02 PM ET | Last Updated: Mar 07, 2016 6:55 AM ET

Emery Potter & Yonah Krakowsky

Reeya Parmar

Emery Potter

Microenviroment

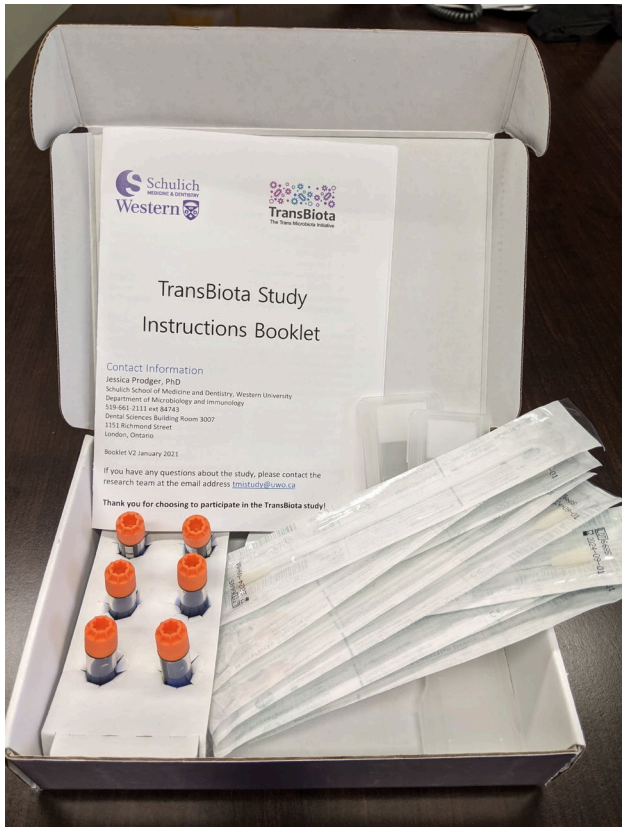
	Penis (cis male)	Vagina (cis female)	Neovagina (trans woman)
Glycogen (Periodic Acid-Schiff)			
Soft Cornification			

TransBiota

The Trans Microbiota Initiative

Jacques Ravel
UM

Greta Bauer
UWO



- Fully contactless design
  - Self-collect swabs for 3 weeks:
    - pH & glass slide
    - DNA/RNA shield
    - Protein-stabilization buffer
  - Online questionnaire
- Study population:
  - **n = 47 tF, with vaginoplasty >1 year prior**
  - n = 90 tM, on T for >1 year

Participants

	Participants (n=47)
Age, in years (mean, range)	41 (23-69)
Years since vaginoplasty (mean, range)	4.3 (1 - 19)
Circumcised pre-vaginoplasty (n, %)	24 (51.1)
Ethnicity (n, %)	
White	42 (89.4)
East Asian	1 (2.1)
South Asian	0
Middle Eastern	0
Mixed Ethnicity	2 (4.3)
Other	2 (4.3)
Behavioural Group (n, %)	
Minimal exposures	6 (12.8)
Dilating only	18 (38.3)
Douching and dilating	12 (25.5)
Diverse exposures	11 (23.4)

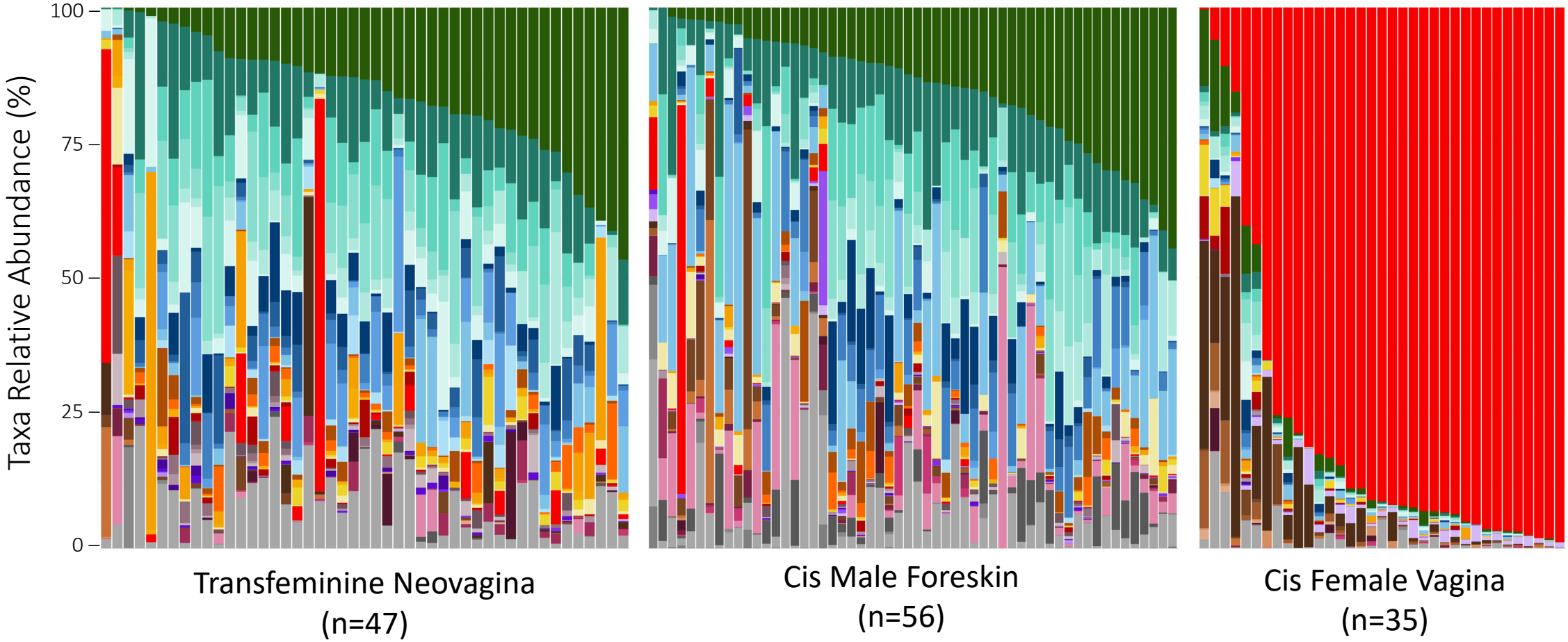
Samples

	Samples (n=133)
Symptom (n, %)	
No symptoms	98 (73.7)
Bleeding	19 (14.3)
Discharge	10 (7.5)
Itch/Burn	7 (5.2)
Odour	6 (4.5)
Pain	6 (4.5)
Neovaginal pH (mean, range)	5.7 (3 - 8)

Hallarn *J Sex Med* 2023

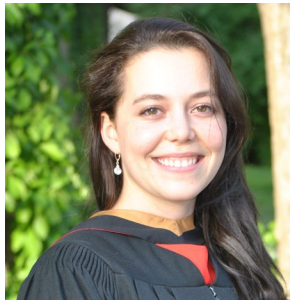
Bern Monari
U Maryland

Bacteriome



Genus	Prevalence tF (%)	Median Relative Abundance (%)				
		tF	cM	P-value	cF	P-value
Prevotella	99.25	13.45	12.64	0.590	0.51	< 0.0001
Peptoniphilus	98.50	10.68	10.21	0.739	0.17	< 0.0001
Anaerococcus	97.74	3.04	0.53	< 0.0001	0.20	< 0.0001
Dialister	97.74	3.30	1.42	0.030	0.24	< 0.0001
Ezakiella	93.98	6.44	3.30	0.046	0.03	< 0.0001
Campylobacter	92.48	1.13	2.96	0.015	0.01	< 0.0001
Porphyromonas	92.48	6.49	5.39	0.260	0.01	< 0.0001
Lawsonella	91.73	0.34	0.03	< 0.0001	0.01	< 0.0001
Varibaculum	90.98	1.19	0.33	< 0.0001	0.00	< 0.0001
Actinomyces	89.47	0.23	0.30	0.083	0.01	< 0.0001
Finegoldia	87.97	0.90	5.09	< 0.0001	0.24	0.006
Prevotella_6	82.71	1.45	1.41	0.822	0.05	< 0.0001
Streptococcus	81.95	0.38	0.03	< 0.0001	0.02	< 0.0001
Atopobium	79.70	0.27	0.03	< 0.0001	0.03	0.036
Mobiluncus	78.95	0.43	0.35	0.809	0.00	< 0.0001
Murdochiella	78.95	0.40	0.02	0.003	0.00	< 0.0001
Fusobacterium	76.69	1.01	0.00	< 0.0001	0.01	< 0.0001
Parvimonas	70.68	0.44	0.00	< 0.0001	0.00	< 0.0001
Fastidiosipila	66.17	0.19	0.00	< 0.0001	0.02	0.241
Lactobacillus	60.90	0.07	0.06	0.430	91.31	< 0.0001

cM = cis Male
cF = cis Female
tF = transfeminine



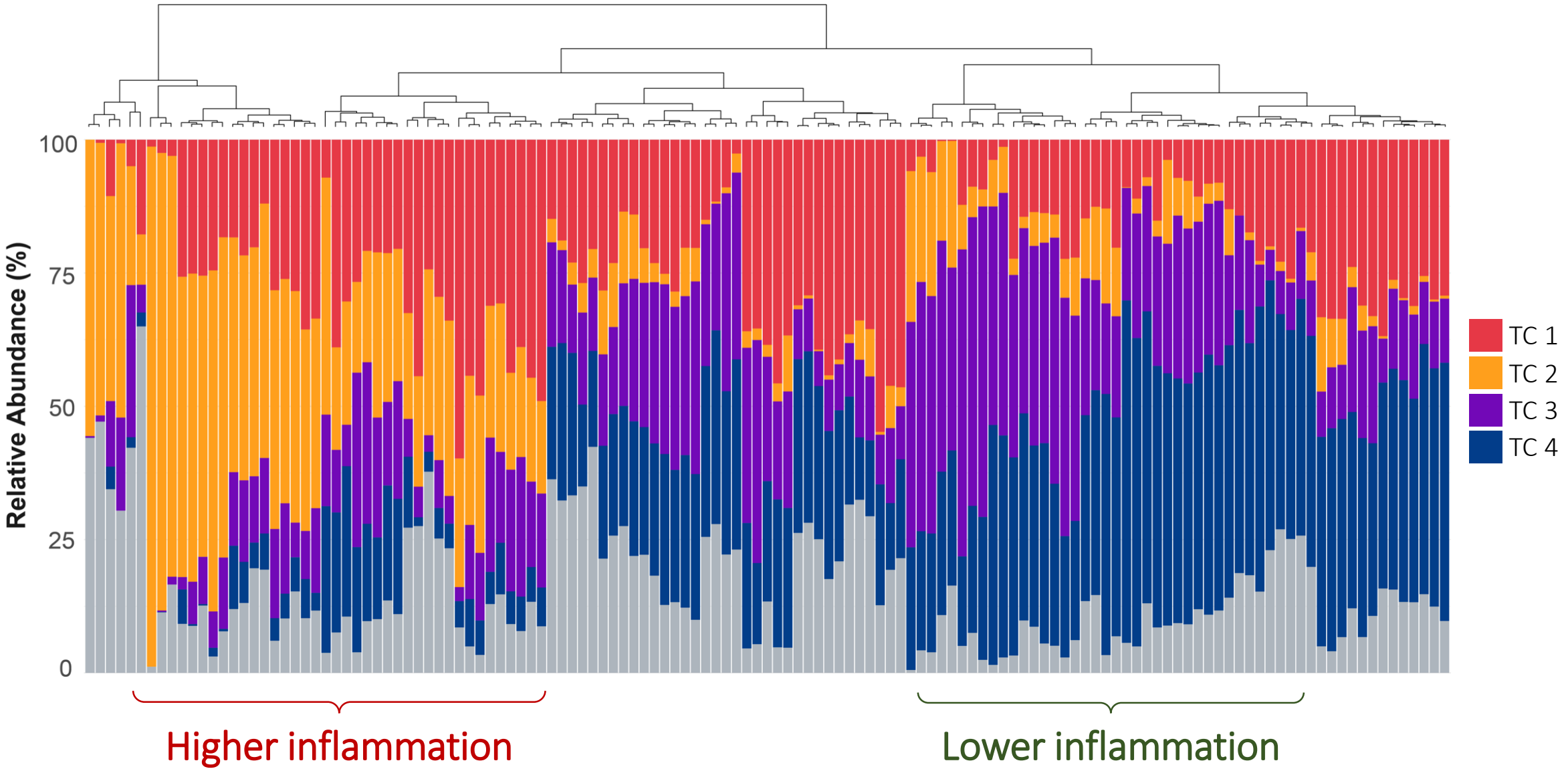
Hannah Wilcox

Bacterial Correlations

1.0
0.5
0.0
-0.5
-1.0

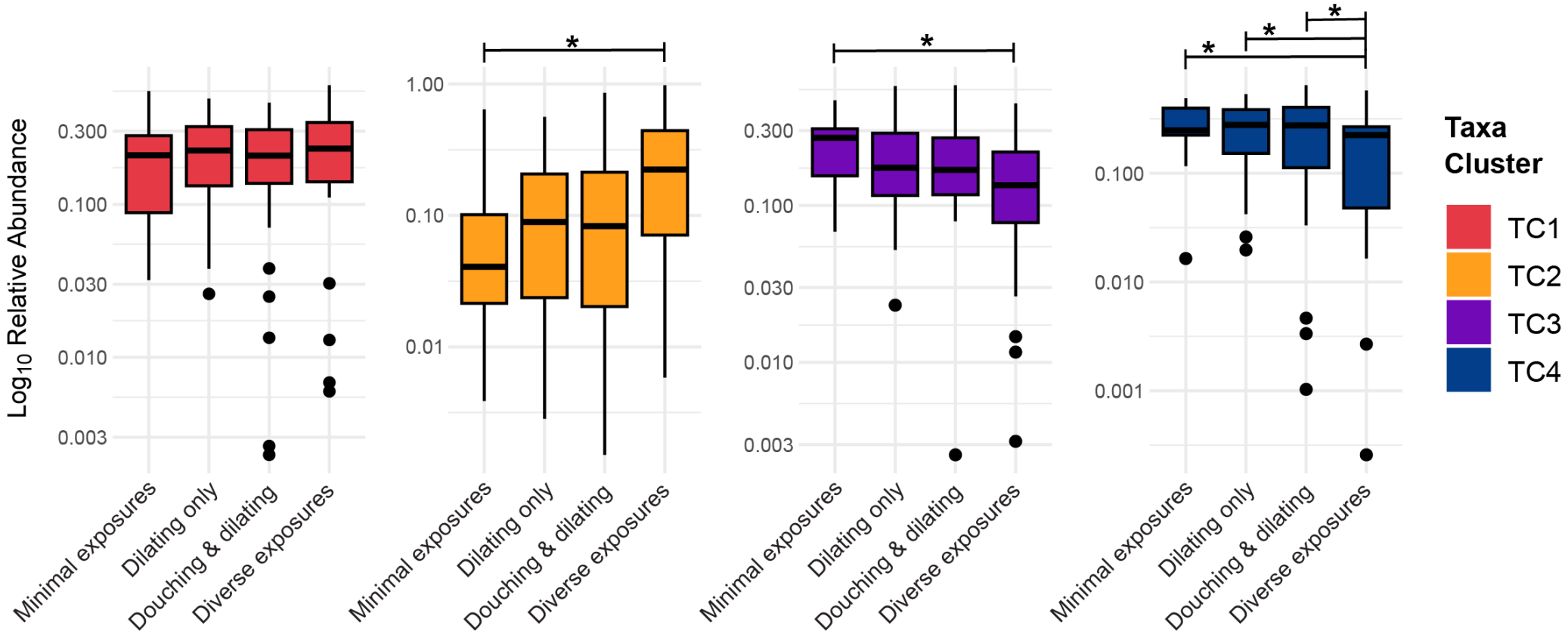
47 participants contributing 133 samples

Abundance of Taxa Clusters (TC) in Neovaginal Samples

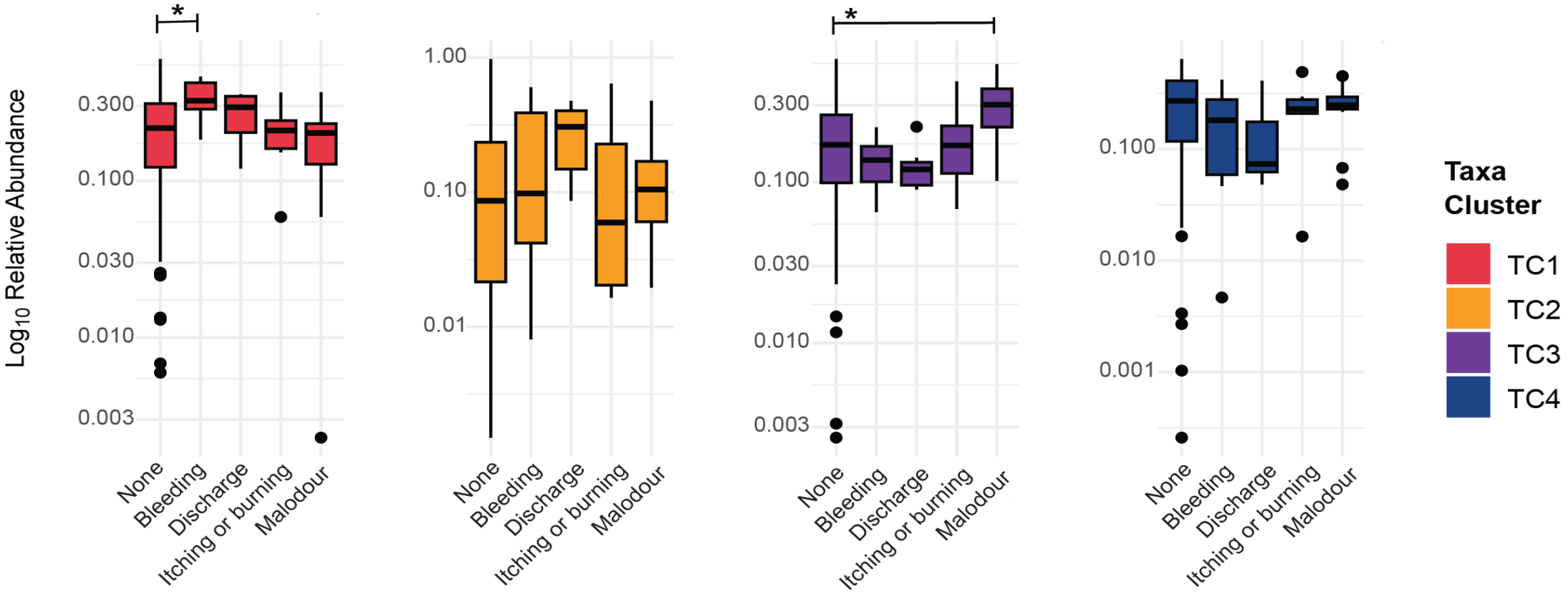


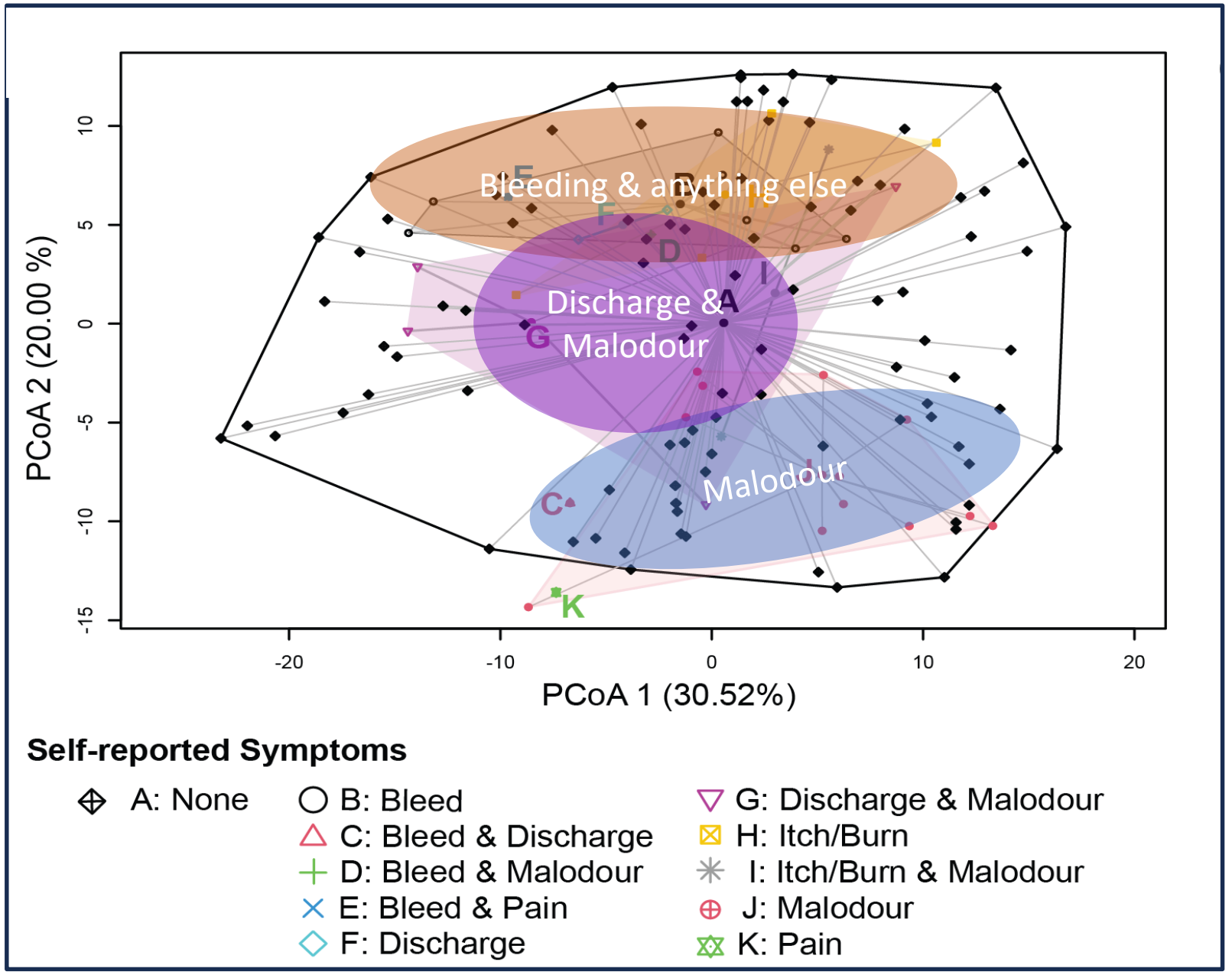
47 participants, 133 swabs

Behaviours and Bacteria… chicken or egg?



Symptoms and Bacteria

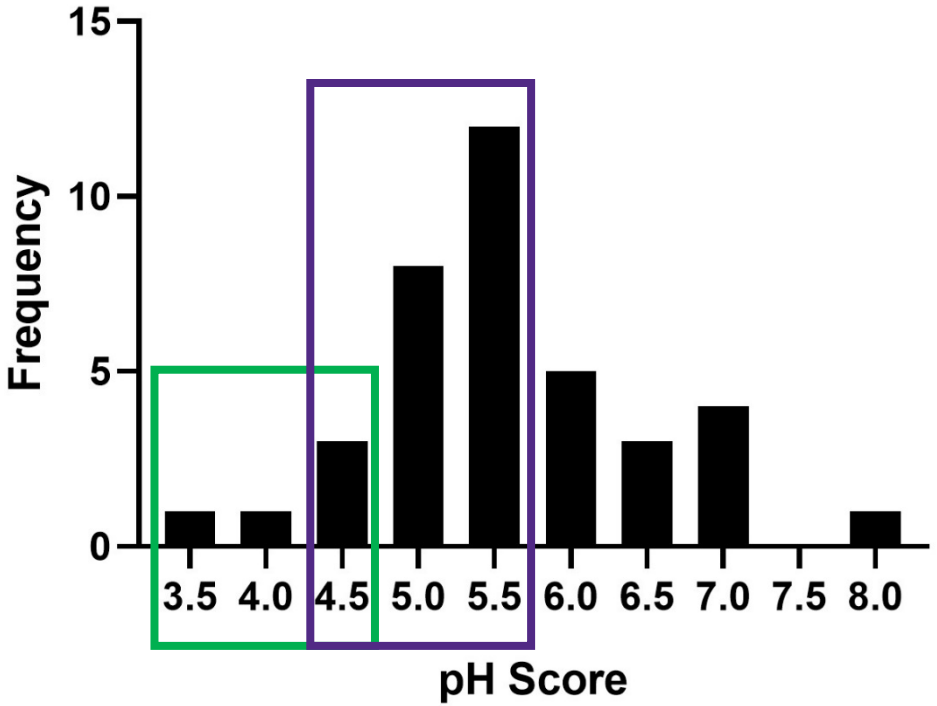



Bleeding & anything else
Discharge & Malodour
Malodour
A
B
C
D
E
F
G
H
I
J
K
PCoA 2 (20.00 %)
PCoA 1 (30.52%)
10
5
0
-5
-10
-15
-20
-10
0
10
20
Self-reported Symptoms
A: None
B: Bleed
C: Bleed & Discharge
D: Bleed & Malodour
E: Bleed & Pain
F: Discharge
G: Discharge & Malodour
H: Itch/Burn
I: Itch/Burn & Malodour
J: Malodour
K: Pain

Diagnostic Tools for Bacterial Vaginosis

Amsel

1. Abnormal vaginal discharge
2. Vaginal pH >4.5
   - pH of skin is 4.5 – 5.5



Diagnostic Tools for Bacterial Vaginosis

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1. Abnormal vaginal discharge
2. Vaginal pH >4.5
   - pH of skin is 4.5 – 5.5, and this is maintained in neovagina
3. “Fishy” odor when vaginal fluid is exposed to 10% KOH
   - Only detects biogenic amines

Neovaginal Malodour

Diagnostic Tools for Bacterial Vaginosis

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   - Only detects biogenic amines (1/6 of transfeminine participants)
4. **Nugent / clue cells on wet mount**

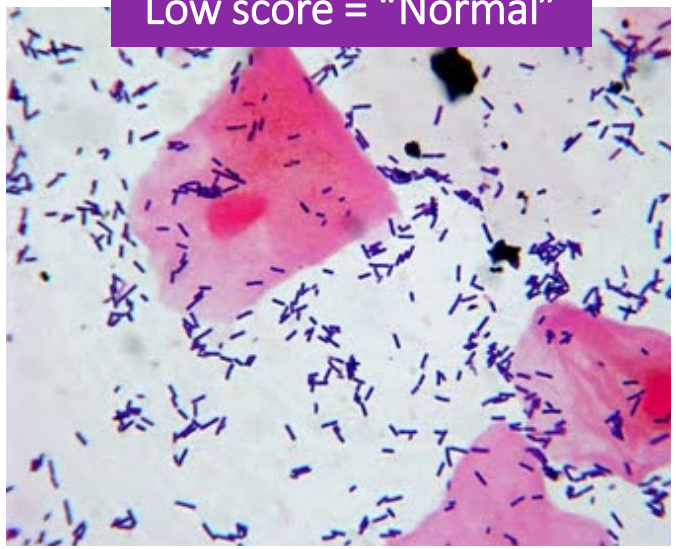
Reeya Parmar

Nugent score

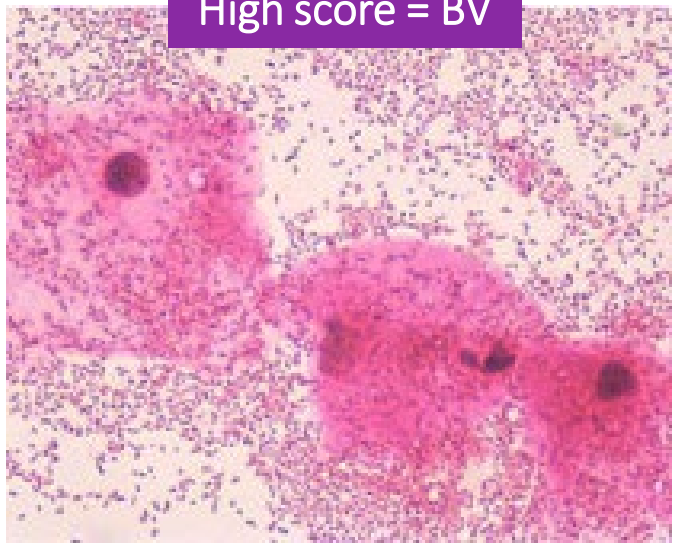
Vaginal smears + Gram staining → score 0 – 10

- 0 – 3 = Normal
- 4 – 6 = Inconclusive
- 7 – 10 = BV

Low score = "Normal"



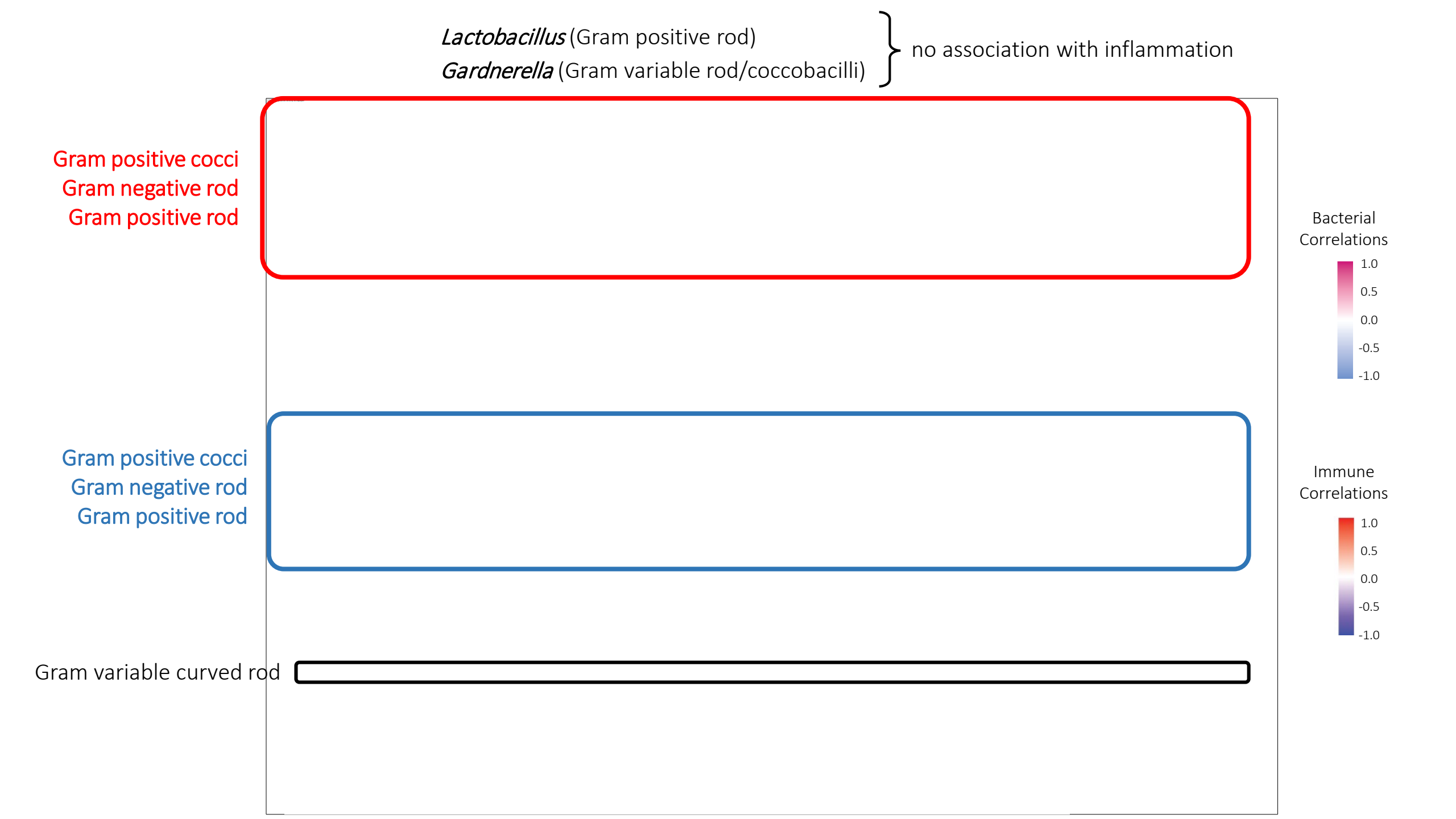
High score = BV



Wang et al. *J Clin Microbiol. 2021*

Score	*Lactobacillus* morphotype per field	*Gardnerella* morphotype per field	Curved bacteria (*Mobiluncus*) per field
0	>30	0	0
1	5–30	<1	1–5
2	1–4	1–4	>5
3	<1	5–30	
4	0	>30	

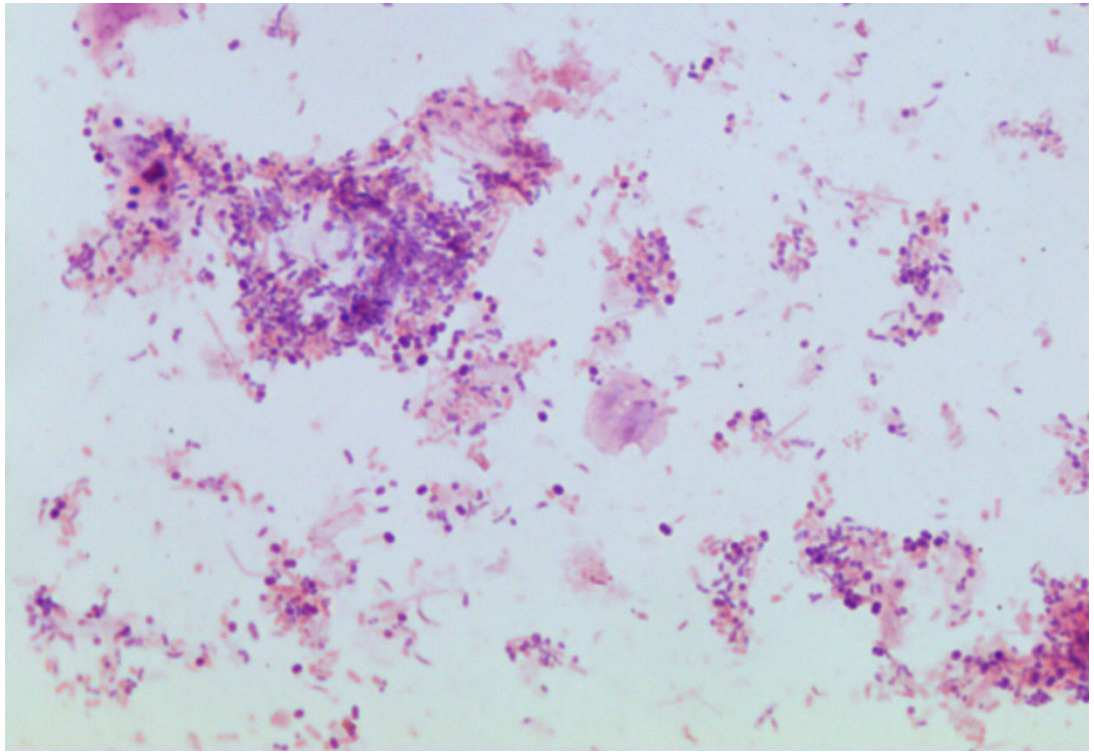
Larsson et al. *Sex Transm Infect. 2004*


Lactobacillus (Gram positive rod)
Gardnerella (Gram variable rod/coccobacilli)
no association with inflammation
Gram positive cocci
Gram negative rod
Gram positive rod
Gram positive cocci
Gram negative rod
Gram positive rod
Gram variable curved rod
Bacterial Correlations
1.0
0.5
0.0
-0.5
-1.0
Immune Correlations
1.0
0.5
0.0
-0.5
-1.0

The (f)utility of Nugent scoring

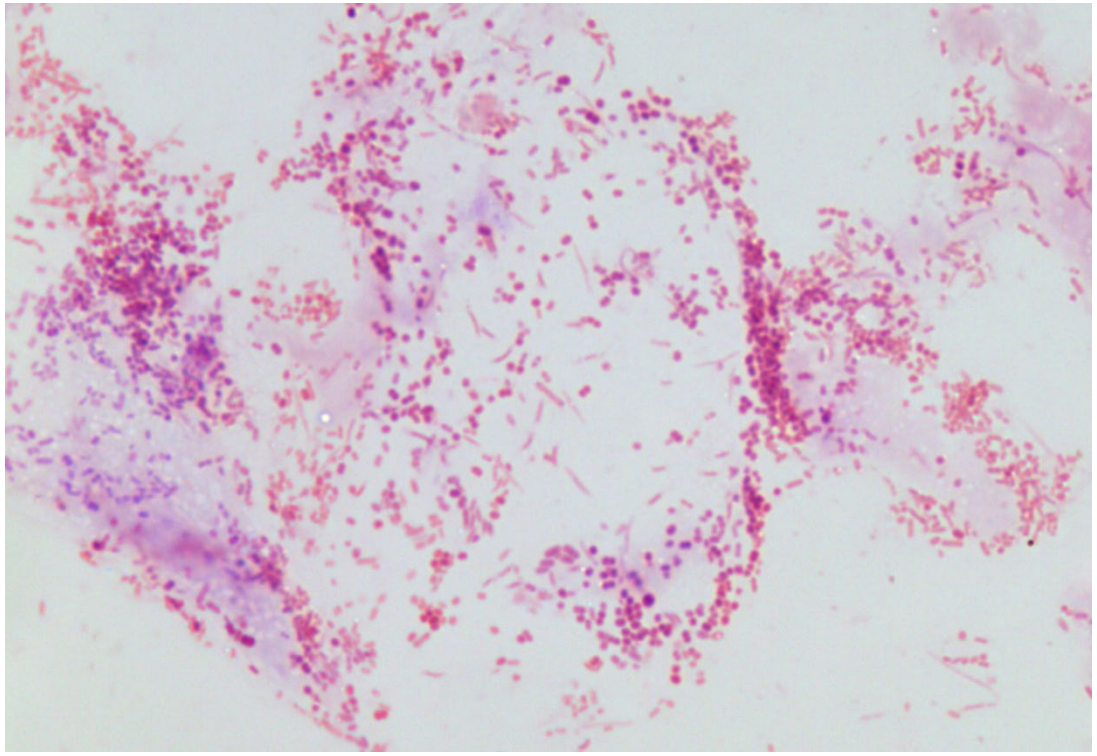
Low-inflammation microbiota

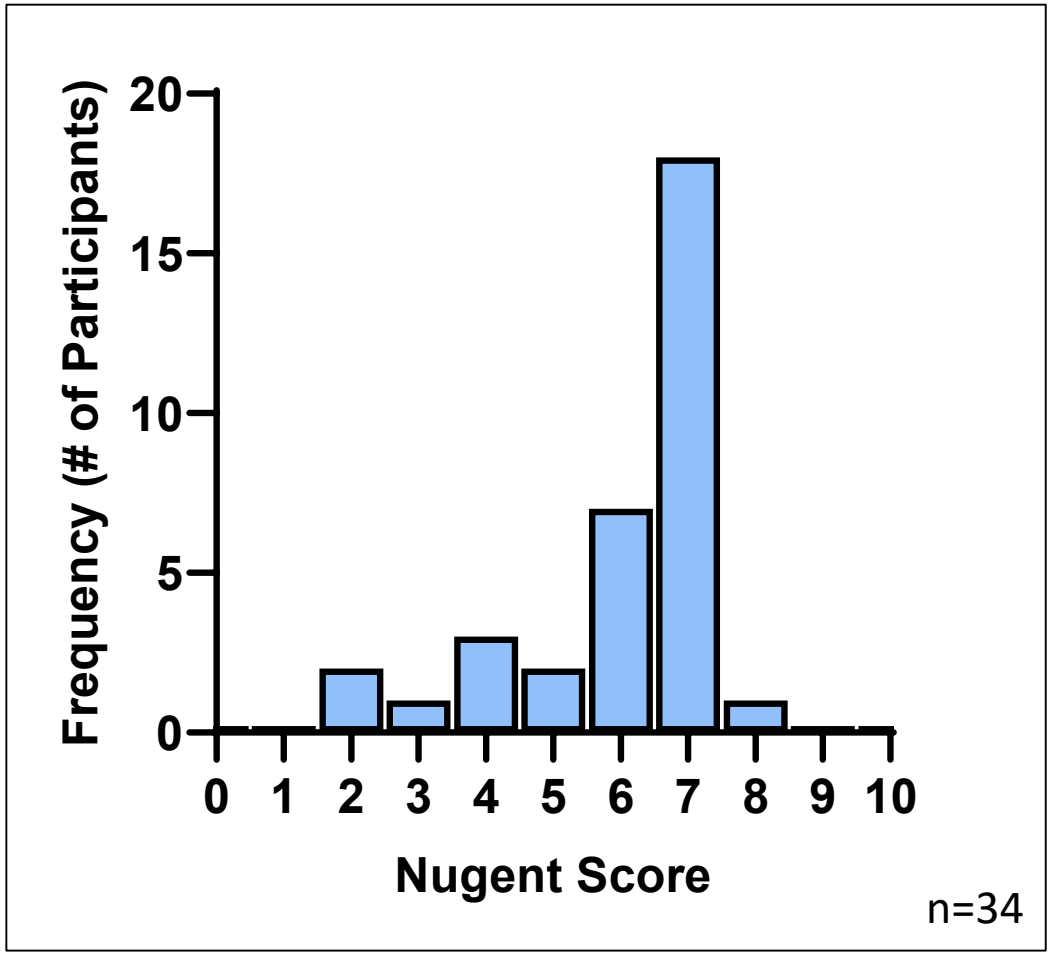
Nugent Score = 7

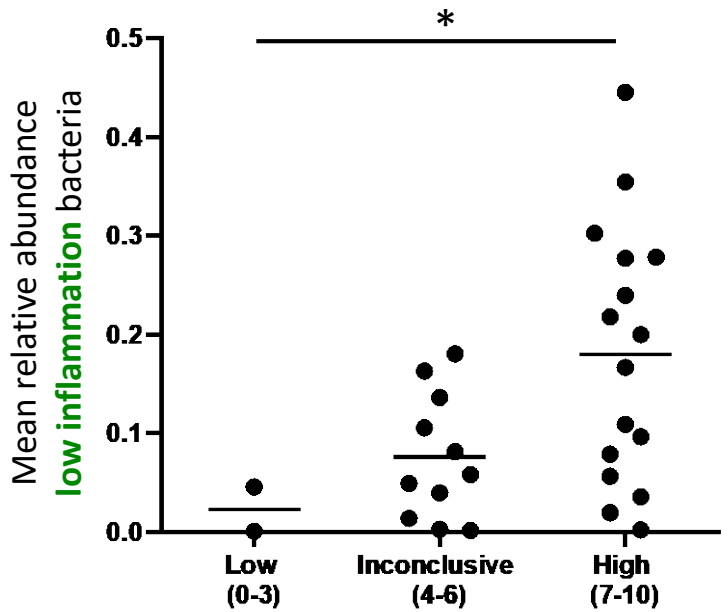


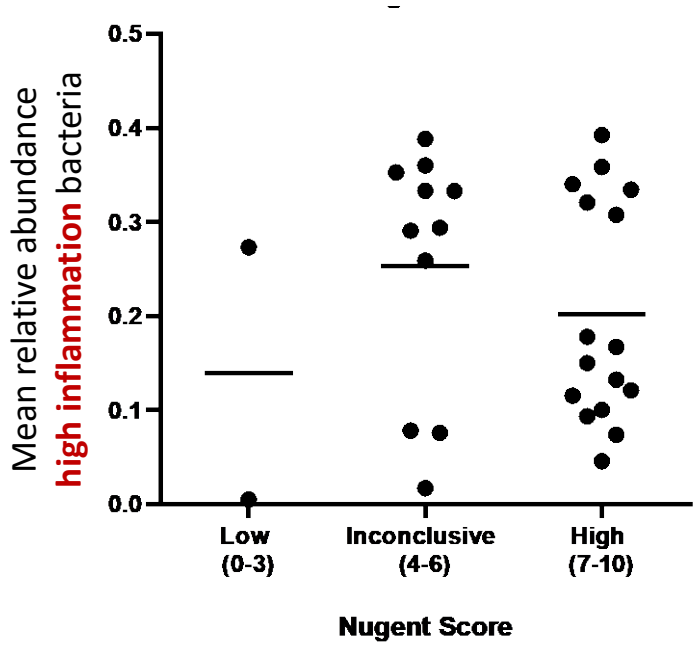
High-inflammation microbiota

Nugent Score = 7

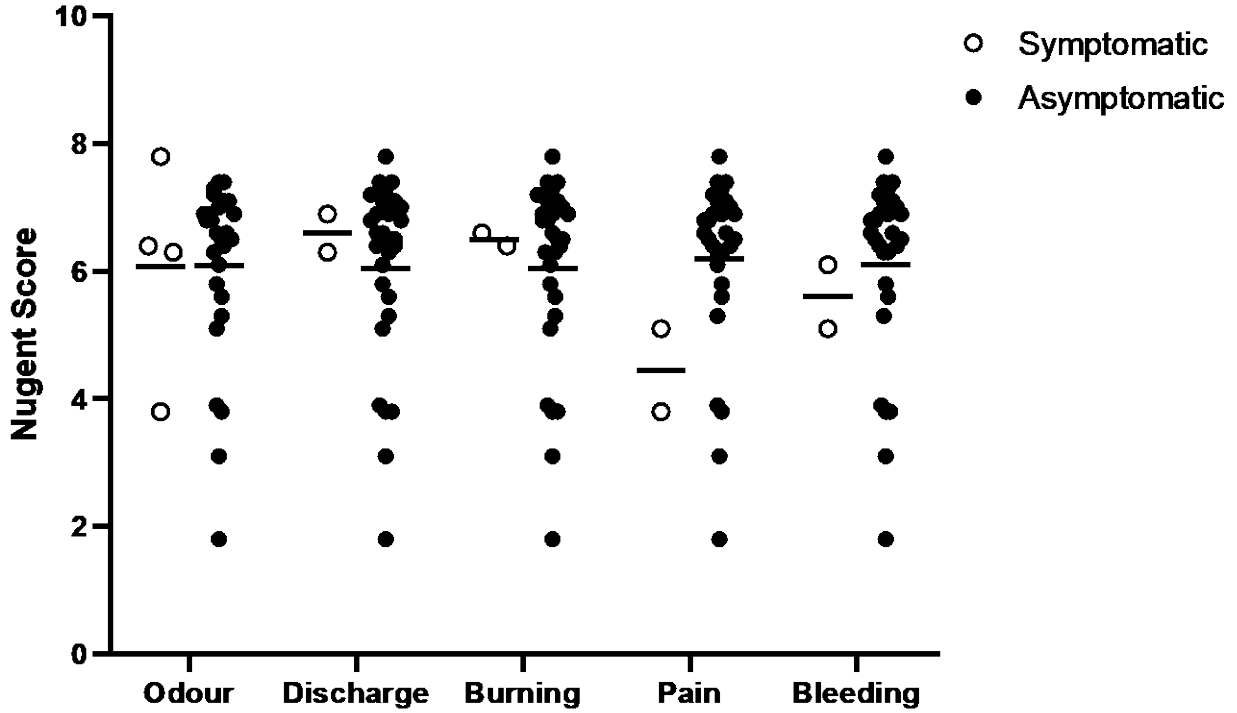



Frequency (# of Participants)
20
15
10
5
0
0 1 2 3 4 5 6 7 8 9 10
Nugent Score
n=34





Symptoms ≠ High Nugent



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Sequence-based

- Hologic: *L. gasseri, L. crispatus, L. jensenii, G. vaginalis, Atopobium vaginae*

Key Takeaways

- Neovaginal epithelium retains skin-like microstructure
- Neovagina bacteriome is different from natal vagina, and very diverse
  - → Distinct low- and high-inflammation communities
  - → Nugent scoring and other BV diagnostics not useful
  - → Efficacy of metronidazole?
  - → What's determining bacterial communities?? Need longitudinal studies
    - But douching *looks* okay

Western University · Canada

Jessica Prodger
Hannah Wilcox
Reeya Parmar
Ainslie Shouldice
Jorge Rojas-Vargas

Greta Bauer

University of Maryland

Jacques Ravel
Bern Monari
Pawel Gajer

WCHRI Women's College Hospital Healthcare Revolutionized

Emery Potter
Yonah Krakowsky
Gresha Shah

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

NIH National Institute of Allergy and Infectious Diseases

Canada Research Chairs / Chaires de recherche du Canada

TransBiota
The Trans Microbiota Initiative