

# The role of penile microbiome in explaining differential mucosal inflammatory cytokines between men who have sex with men and men who have sex with women.

Debarghya Nandi<sup>1</sup>, Dulal Bhaumik<sup>1</sup>, Duncan Okal, Fredrick Otieno<sup>3</sup>, George N’gety, Eve Obondi, Robert C. Bailey<sup>1</sup>, Supriya D. Mehta.<sup>1</sup>

<sup>1</sup> Division of Epidemiology and Biostatistics, University of Illinois at Chicago School of Public Health, Chicago, IL, USA

<sup>2</sup> Department of DNA Services, University of Illinois at Chicago, Chicago, IL, USA <sup>3</sup> Nyanza Reproductive Health Society, Kisumu, Kenya.

## Background

- Men who have sex with men (MSM) are disproportionately affected by HIV/STI as compared to men who have sex with women(MSW).
- This is hypothesized to be due to different burdens of mucosal inflammation.

## Aim

- We evaluate if there is any significant association of penile microbial composition with mucosal inflammation.

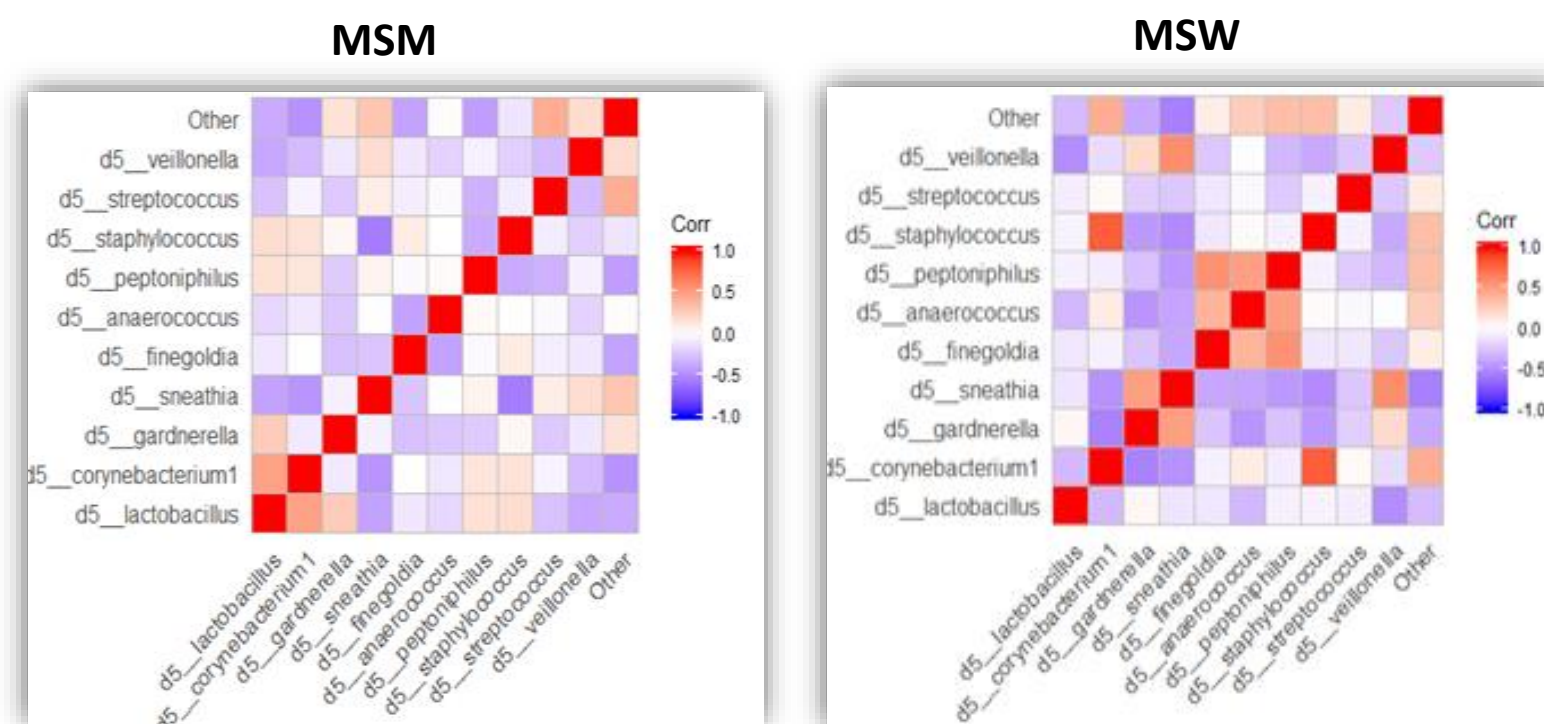
## Design and Methods

- Samples were collected from 43 HIV (-) MSM and 43 HIV(-) MSW residing in Kisumu, Kenya.
- Subjects were matched on age and circumcision status.
- Penile microbiome was assessed via shallow meatal swab, with 16s rRNA amplicon sequencing of the V3-V4 regions.
- Urinary cytokine concentrations were measured using Luminex.

## Results

### Correlation heatmap of top 10 penile microbiome taxa

Brightness of colors (red for positive and blue for negative) depict strength of correlation.

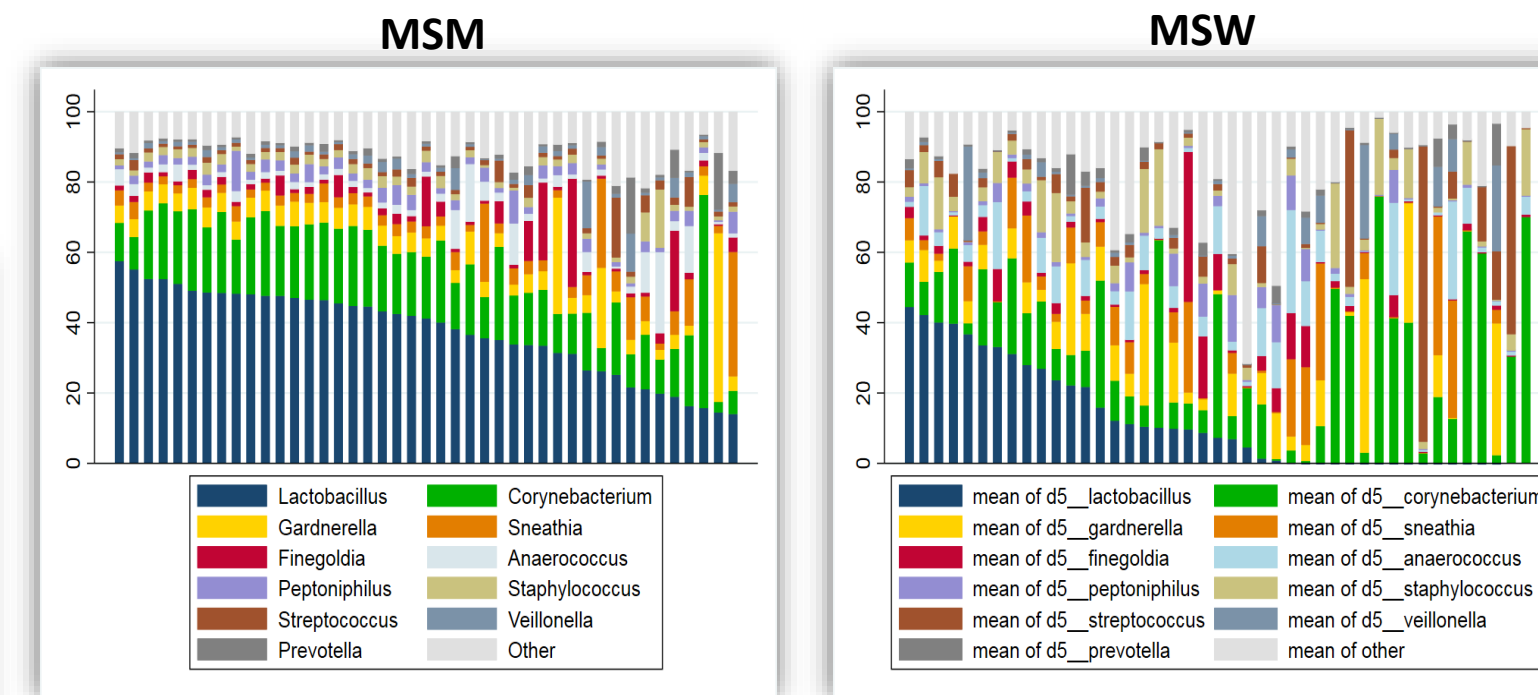


### Taxa importance from Random Forest Classification of MSM vs MSW

Taxa	IMPORTANCE
d5_lactobacillus	33.16
d5_corynebacterium1	4.48
d5_gardnerella	3.22
d5_sneathia	7.79
d5_finegoldia	2.65
d5_anaerococcus	0.73
d5_peptoniphilus	5.98
d5_staphylococcus	11.37
d5_streptococcus	9.63
d5_veillonella	16.56
Other	4.37

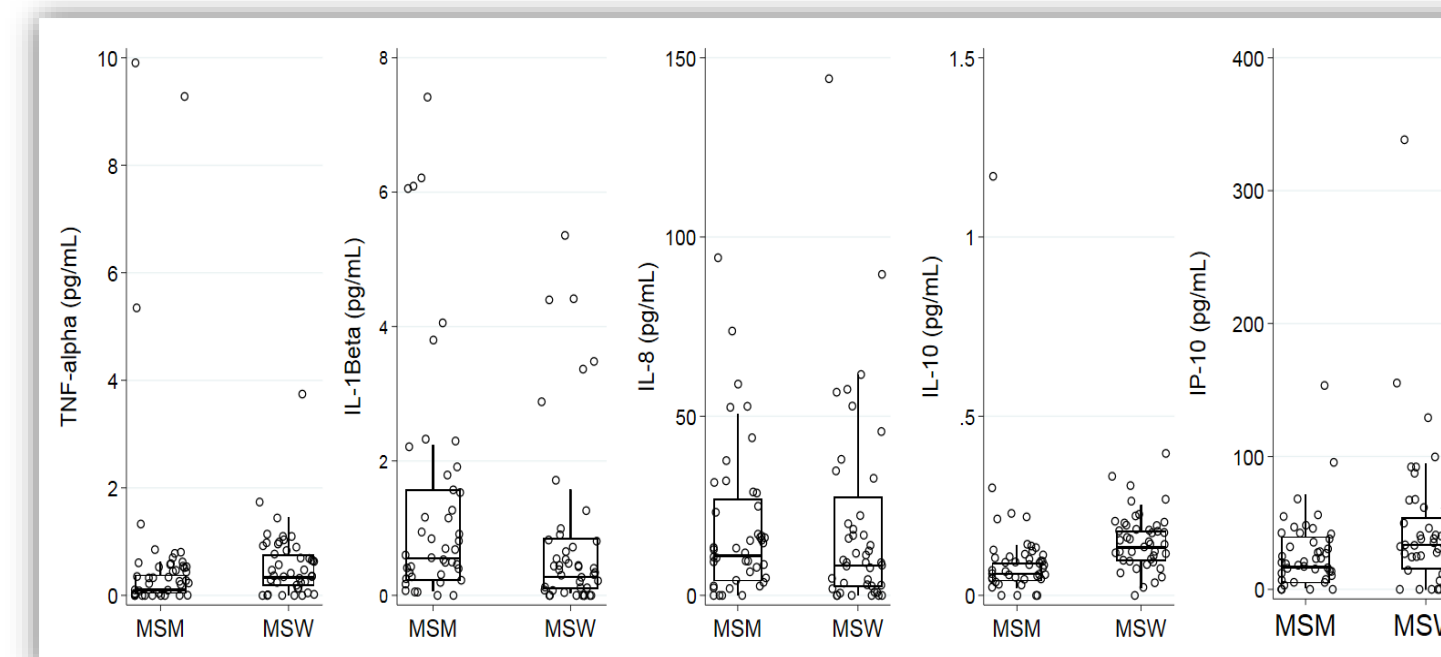
*Lactobacillus*, *Veillonella* and *Staphylococcus* were selected by Random Forest as top features based on gini information.

### Relative Abundance of top 10 penile microbial taxa



*Lactobacillus*, *Corynebacterium1* and *Gardnarella* were observed to be most abundant for MSM and MSW.

### Summary of urinary cytokine concentrations by MSM/ MSW status.



A statistically significant difference in mean was observed for all cytokine groups except for *IL-8*. *Wilcoxon Rank-Sum* was used for this test at  $\alpha = 0.05$ .

## Statistical Approach

- Filter MSM and MSW genus level taxa to remove taxa with < 1% of total sequence reads.
- Normalize samples by dividing by total number of reads(RA) and use the Centered Log Ratio Transform(CLR).
- Random Forest with 5 –fold CV to identify genus level taxa differing between MSM and MSW.
- Linear regression to model cytokines as a function of the genus level taxa.

## Discussion

### Prediction of status

- Composition and influence of taxa has been observed to be significantly different for MSM and MSW.

### Cytokine concentration

- All cytokines except IL-8 were significantly elevated for MSW as compared to MSM.

### Association of taxa with cytokines

- Microbiome composition did not account for difference in TNF-  $\alpha$ , IP – 10 or IL-10 between MSM and MSW.

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