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Background

- The prevalence of obesity is rising among people living with HIV
- Both obesity and HIV infection are associated with immune dysregulation and may work synergistically to increase the risk of inflammation-associated sequelae.
- Disruption of gut bacterial communities may be one of the key drivers of this inflammation; however, the combined effects of HIV and obesity on the microbiome have not been explored.

Materials & Methods

- Participants (N=381) with archived rectal swabs collected between 2014 and 2017 were selected from an ongoing cohort of diverse young men who have sex with men (The mSTUDY, NIDA U01 DA036267).
- Thirty-nine participants were HIV+ and obese (H+O+), 143 were HIV+ and non-obese (H+O-), 64 were HIV- and obese (H-O+), and 135 were HIV- and non-obese (H-O-).
- Microbiome composition was assessed by targeted sequencing of the V4 region of the 16S rRNA gene followed by exact sequence inference with DADA2.
- Analyses included permutational (PERMANOVA) with Bray-Curtis distance to test for differences in overall composition and zero-inflated negative binomial (ZINB) models to test for differential abundance of specific genera.
- All analyses utilized inverse probability of treatment weighting to control for a large set of clinical and behavioral factors including demographics, ART use, sexual behavior, positive rectal STI test by PCR, smoking, and self-reports of methamphetamine, marijuana, and alcohol use.

H-O-Characteristic **H-**135 28, 27 Age (mean, median) Race/Ethnicity 39% Black non-Hispanic 47% Hispanic 14% Other non-Hispanic 24, 24 BMI (mean, median) Log₁₀ viral load (mean, median) CD4 cells/mm³ (mean, median) Used methamphetamine in past 6 months 23% 64% Used marijuana in past 6 months Number of sex partners in past 6 months (mean, median) **Positive for rectal STI** 13%

Table 1: Participant characteristics, N = 381 MSM in Los Angeles



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Joint Effects of HIV and Obesity on the Microbiome of Young Men who have Sex with Men

ANOVA multivariate

) +	H+O-	H+O+
	143	39
, 29	33, 33	36, 36
%	38%	36%
%	49%	51%
)	13%	13%
, 33	24, 24	35, 33
	1.6, 1.3	1.5, 1.3
	621, 603	643, 632
%	60%	41%
%	54%	47%
4	8, 5	6, 3
)	16%	8%



Figure 1:Rectal microbial composition, ordination of Bray-Curtis distances, and Chao1 diversity of study participants. (A) Average microbial composition within each HIV and obesity category, adjusted for behavioral and clinical confounders using inverse probability of treatment weighting. Bacterial genera representing less than 1% of the overall relative composition or present in less than 20% of the samples were grouped into "Other." (B) Ordination of Bray-Curtis distances between samples using principal coordinates analysis. PCoA = Principal coordinate axis. Ellipses are 95% confidence regions for each group assuming points follow a multivariate t distribution. (C) Boxplots of Chao1 index vales. Boxes represent the lower, median, and upper quartile of the data and whiskers are 1.5*interquartile range.

- Men averaged 31 years old, 49% were Hispanic and 39% were non-Hispanic Black (Table 1).
- Significant variability in microbial composition was explained by the combination of HIV and obesity (R² for the marginal contribution of the H+/O+ group = .008, p = .001; Figure 1B).
- , with little difference by obesity (Figure 1C).
- H+O+ participants had the highest ratios of *Prevotella* to described in HIV and obesity independently (Figure 2B).
- H+O+ participants had lower levels of *Bacteroides* and effect of HIV and obesity on these genera (Figure 3).
- Dietzia and Finegoldia were reduced and Faecalibacterium compared to H-O- controls, suggesting that HIV and obesity

Results

HIV+ individuals generally showed higher diversity than HIV-

Bacteroides, a pro-inflammatory enterotype that has been

Veillonella than all other groups, suggesting a synergistic

was enriched in H+O+ compared to H+O- and H-O+, but not may have some antagonistic effects on these genera (Figure 3).



Figure 2: Ratios of Firmicutes to Bacteroidetes and Prevotella to Bacteroides. Firmicutes to Bacteroidetes ratio: (A) Boxplots of log ratios. Boxes represent the lower, median, and upper quartile of the data and whiskers are 1.5*interquartile range. (B) Mean differences in ratios and Wald 95% confidence intervals, adjusted for behavioral and clinical confounders using inverse probability of treatment weighting (IPTW). Prevotella to Bacteroides ratio: (C) Boxplots of log ratios. (D) IPTW-adjusted mean differences in ratios and 95% confidence intervals.

- alone.
- inflammatory consequences.



Figure 3: Combined effects of HIV and obesity on individual bacterial genera. Heatmap of results of zero-inflated negative binomial models comparing genus-level bacterial counts. Statistically significant results (false discovery rate-adjusted p < .1) are colored with intensity proportional to effect size; "no effect" indicates adjusted p > .1.



Conclusions

• In a diverse sample of young men who have sex with men, microbial composition was altered by the combination of HIV and obesity over and above the contributions of each condition

• Our findings may help explain higher levels of generalized inflammation among people living with both HIV and obesity • Interactions between conditions altering the microbiome, such as HIV and obesity, should be taken into consideration when designing interventions to address dysbiosis and reduce its

