

The effects of an agrarian diet intervention on inflammation and gut microbiome composition in HIV-infected individuals in Colorado

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Background & Introduction

In the United States, 1.2 million people are infected with HIV and a high percentage are men who have sex with men (MSM)[1]. HIV comorbidities include cardiovascular disease, metabolic disease, and chronic inflammation, which are all associated with gut microbiome dysbiosis. Less systemic inflammation in HIV+ individuals is related to reduced mortality risk [2]. The gut microbiome composition of HIV+ individuals and HIV- MSM in the US is predominantly *Prevotella* rich and *Bacteroides* poor (PrevR/BactP) [3]. The Western diet (WD), common in the US, differs from the agrarian diet (AD) consumed by healthy *Prevotella*-rich populations in Malawi and Venezuela [4]. This implies that HIV+ and HIV- MSM may consume inadequate nutrients for their gut bacteria. Therefore, we performed a clinical trial to assess the effects of an AD on HIV-infected individuals.

Hypothesis:

An agrarian diet for PrevR/BactP HIV+ individuals and HIV- MSM individuals will have beneficial health effects as measured by inflammatory markers.

Table 1. Standard Diet Composition of Western and Agrarian Diets

Diet Composition	Western	Agrarian
Protein	15% (62g)	15% (66.75g)
Carbohydrates	55% (228g)	70% (311.5g)
Fat	30% (124.5g)	15% (66.75g)
Fiber	18g	45g
Sugar	114g	67g
Sodium	3650g	1325g
Energy	2000kcal	2000kcal
Processed foods	Yes	No

Methods

A four-week clinical trial on 90 HIV+ and HIV- individuals. Data collected at baseline (T1), and after 2 (T2) and 4 (T3) weeks.

Food preparation:

Weeks 1 - 2: nutrition core prepared

Weeks 3 - 4: study participants counseled/prepared food at home

Data collected:

✓ demographics ✓ questionnaires: sexual behavior, gastrointestinal symptoms and dietary information ✓ metabolic markers (triglycerides, LDL, HDL, insulin, glucose, leptin, adiponectin) ✓ immune markers (IL6) ✓ HIV-specific data (CD4+ and CD8+ cell counts, CD4+ nadir, viral load, etc) ✓ gut microbiome (16S rRNA gene)

Data analysis:

16S rRNA gene sequencing analysis was performed using QIIME 2. Linear mixed effects (LME) modeling was used to address individual subject variation when looking for relationships and changes over time.

Results

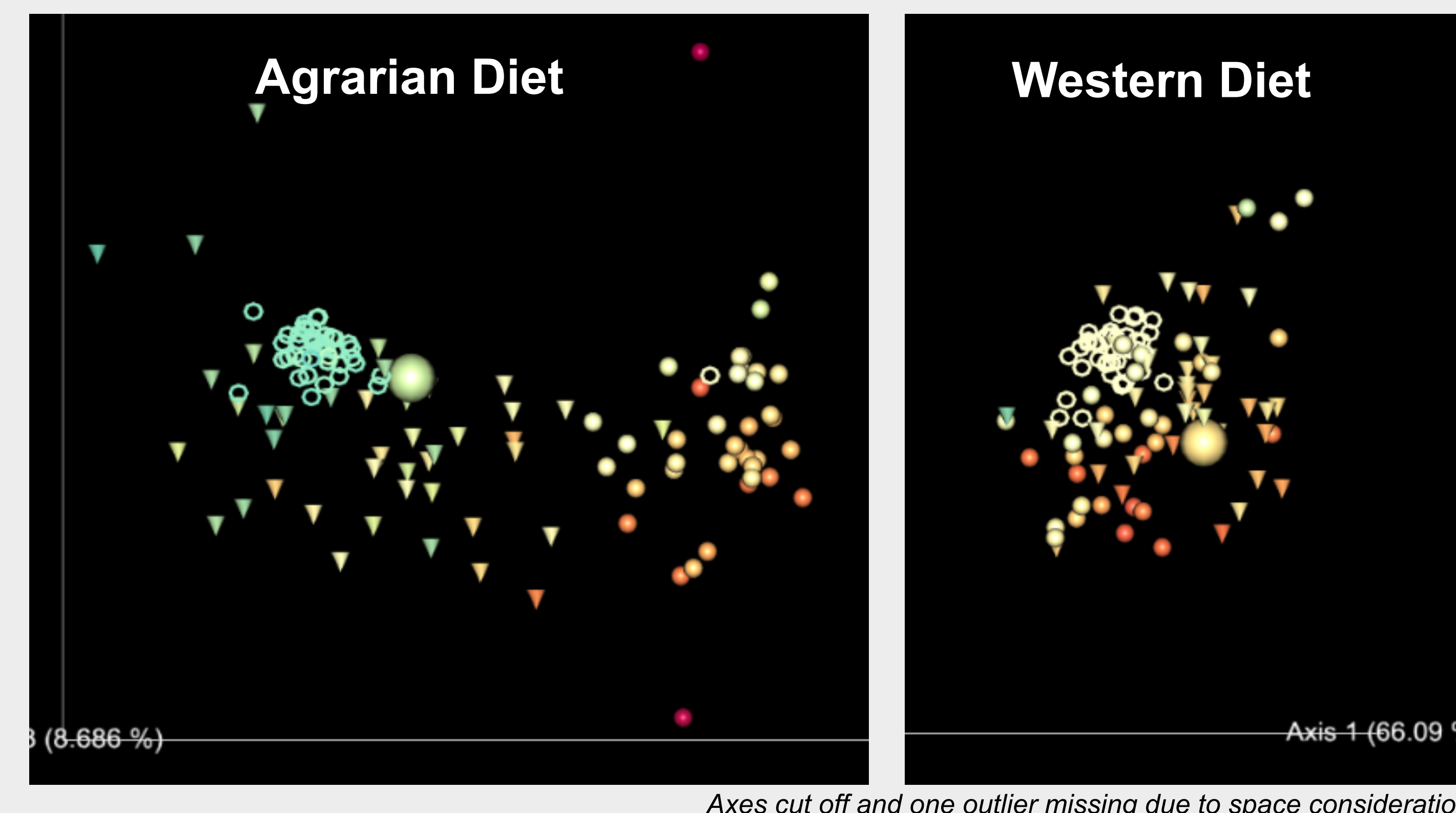


Figure 1. Principal Coordinates Analysis (PCoA) of dietary components for individuals on an agrarian (left) and Western (right) diet. Euclidean distance matrix created from protein, fat, carbs, fiber, sodium, and sugar (all per 1000kcal). T1—sphere, T2—ring, and T3—cone. Large spheres are standard AD (left); standard WD (right).

Most subjects started on a WD and those placed onto an AD shifted toward an AD composition.

At baseline, IL6 was significantly elevated (6.7 pg/mL) in HIV+ individuals, and HIV- individuals high risk for HIV (8.3 pg/mL), compared to HIV- low risk individuals (3.1 pg/mL) (Wilcoxon tests, FDR-adjusted: $q = 0.01$ and $q = 0.02$, respectively).

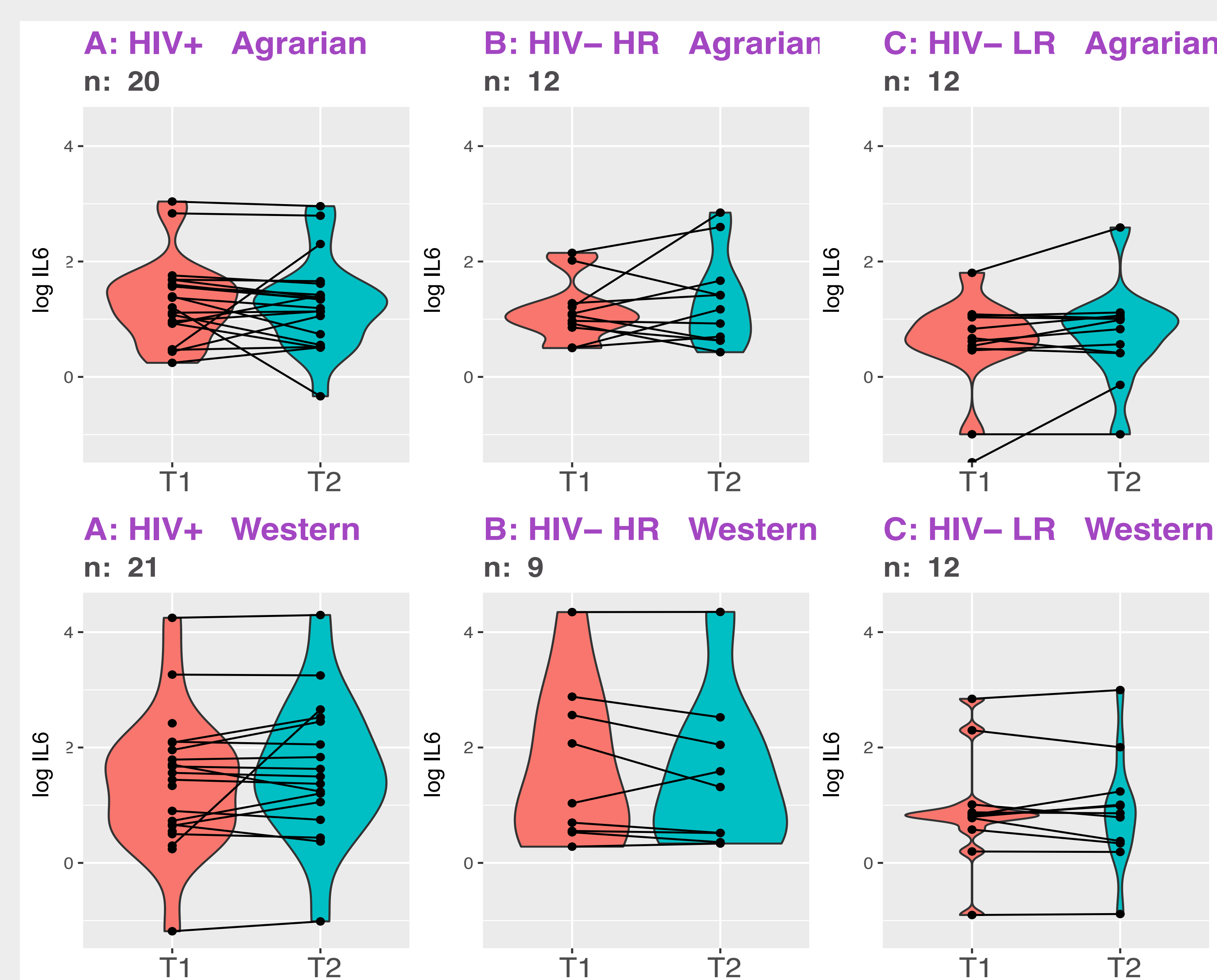


Figure 2. Systemic inflammation (Log IL6) at baseline (T1) and after two weeks (T2) of diet. After 2 weeks, HIV+ individuals (83% are MSM) on an AD had a reduction in baseline IL6 by 2.64 pg/mL that was not observed in HIV- individuals and those on a WD (LME $\chi^2(17) = 27.8$, $p=0.047$).

Results

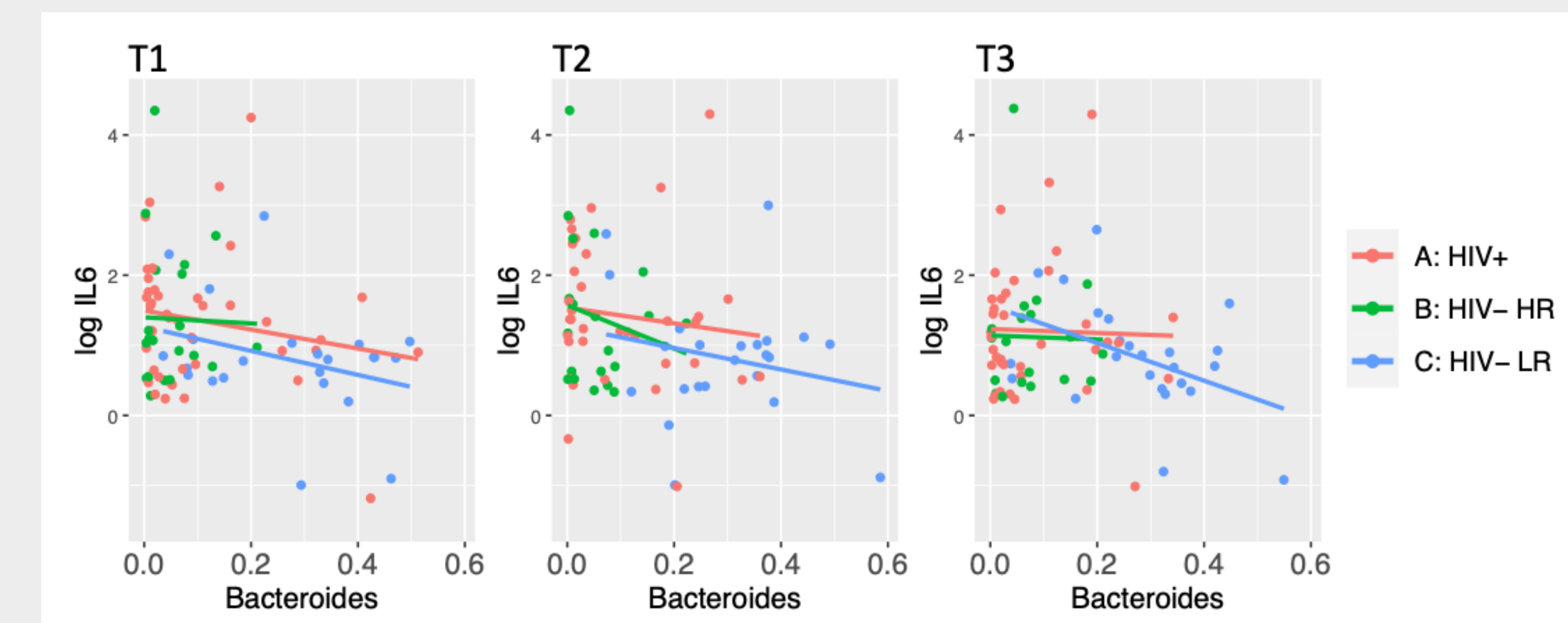


Figure 3. IL6 relationship to *Bacteroides* at all timepoints. Directionality suggests a protective effect (1.97 pg/mL reduction in IL6, LME $\chi^2(1) = 8.7$, $p = 0.003$). There was no relationship to *Prevotella*.

There was an increase in mean *Bacteroides* relative abundance (0.28 to 0.37) after 4 weeks of an AD (LME $\chi^2(17) = 8.7$, $p = <0.001$).

Conclusions

These preliminary results suggest that an agrarian diet can protect from HIV associated systemic inflammation, although more analyses are needed to understand how the gut microbiome (*Prevotella*, *Bacteroides* and enterotype classification) may influence this health benefit.

Future Directions

- Use other immune markers as health outcome (Lipopolysaccharide (LPS)-binding protein (LBP) and c-reactive protein (CRP))
- Assess effect of MSM on our findings
- Explore enterotype classification and possible shifts from baseline
- Explore data imputation methods
- Develop machine learning model using longitudinal data for prediction of health benefit for individual at baseline using mixed effects random forests (MERFS) [5].

References

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