

A short-term enteral nutrition protocol for management of adult Crohn's Disease

– A Pilot Trial



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Introduction:

- Crohn's disease (CD), is one of two main forms of inflammatory bowel disease (IBD).
- Enteral nutrition therapy (exclusive or partial; EEN or PEN, respectively) is an established therapy for management of CD in pediatric populations. It is often administered via naso-gastric tube.
- Use of EEN or PEN for the management of CD in adults is less common.
- Therefore, we conducted an exploratory study to determine the feasibility of a 4-week, semi-elemental formula-based, oral nutrition program for management of adult CD.
- As secondary endpoints, we collected longitudinal data on disease activity, physical and mental health scores, and gut microbiota composition over the course of the intervention.

Methods:

- Open-label, 4-week intervention study.
- Commercially available, semi-elemental, enteral nutrition formula (Peptamen® 1.5, vanilla).
- The formula was consumed orally at or above a volume required to meet 80% of estimated calorie needs.
- Crohn's disease activity index (CDAI) and Harvey-Bradshaw Index (HBI) scores calculated at baseline and end of week 4.
- Patient experience on the semi-elemental EEN regimen was assessed using an investigator generated questionnaire.
- The PROMIS (v1.0) Emotional Distress-Depression – Short Form 4a and PROMIS (v1.2) Global Health Physical 2a were used to measure emotional distress and physical health, respectively.

Statistical Analysis

- Paired t-tests were used to compare continuous variables.
- Gut microbiota composition was characterized using high throughput 16S rRNA gene sequence analysis.

Results

- 4/5 (80%) of enrolled participants tolerated, and successfully completed, the intervention.
- Scores reflecting overall experience on the EEN regimen improved from 3.25 to 4 (out of 5) from week 1 to week 4, but did not reach statistical significance ($p=0.2$).
- Mean HBI and CDAI scores trended towards an improvement (10 vs 6.2 and 216 vs 137, respectively; $p>0.05$).
- Mean PROMIS emotional distress scores improved from 8.25 to 6.5 ($p=0.06$) while physical global health scores did not change.

An oral 4-week semi-elemental formula is a feasible nutrition delivery program for management of adult CD

Figure 1: Longitudinal summary of gut microbiota composition by individual participant

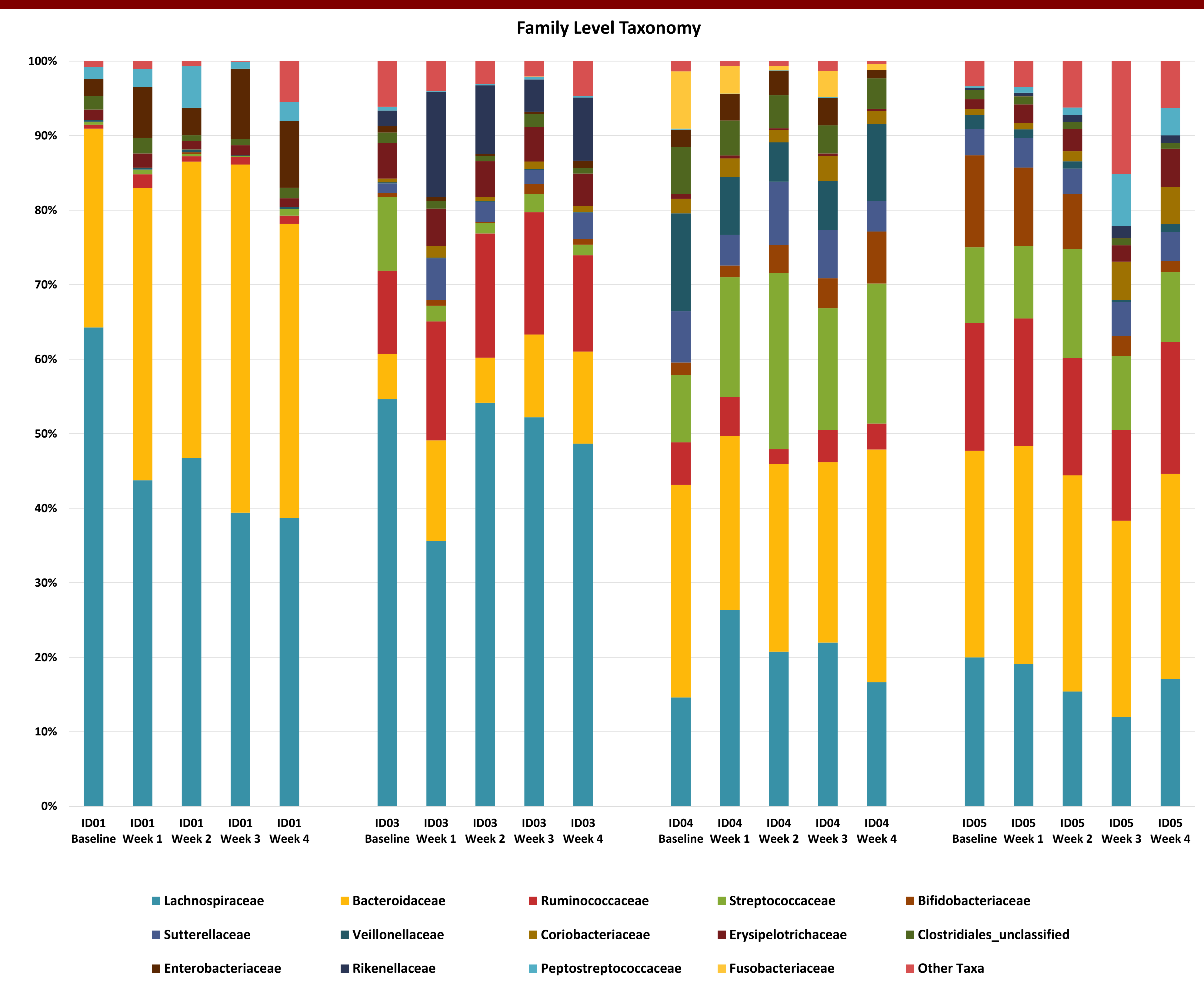
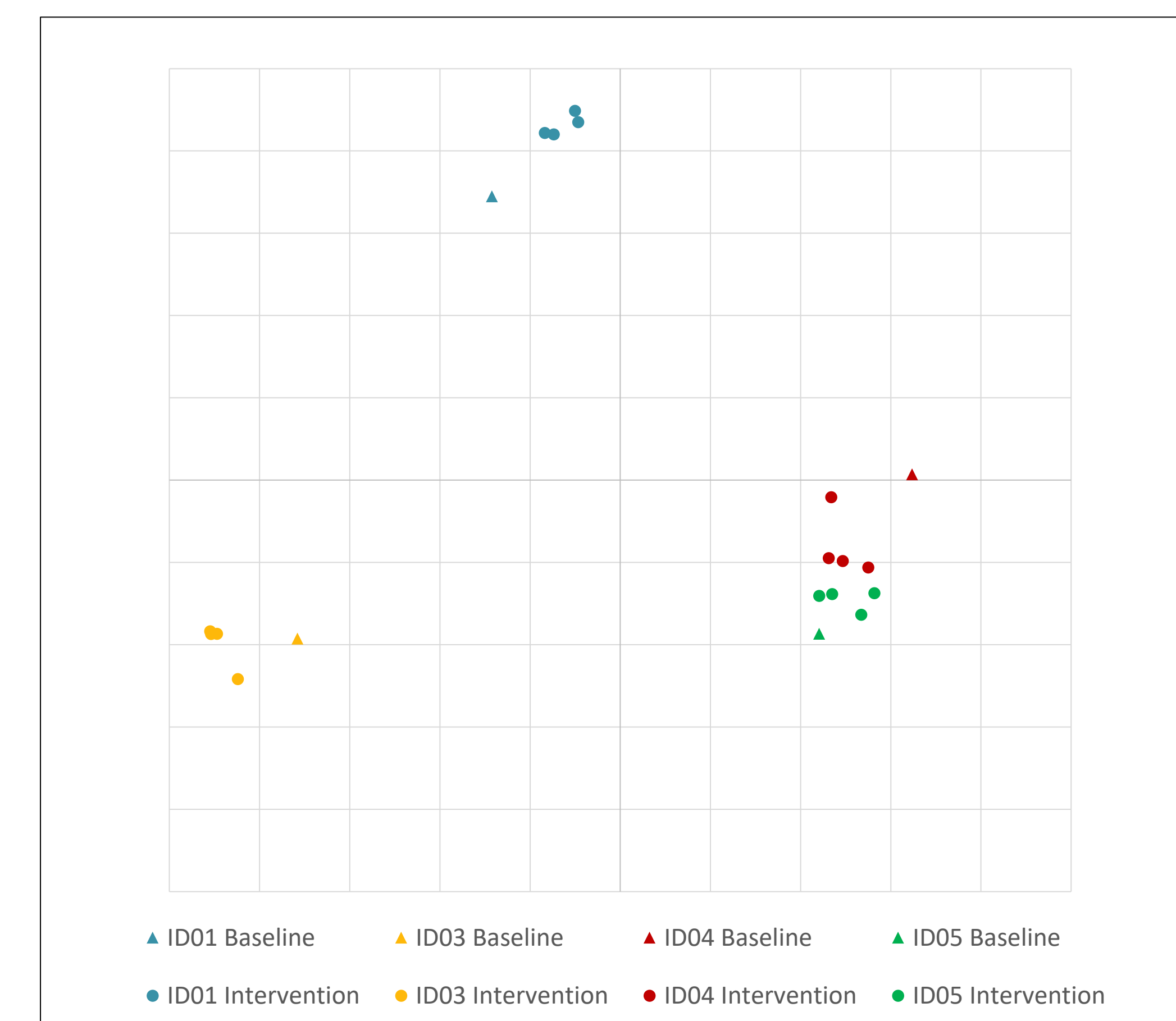


Figure 2: Principal Coordinate Analysis (PCoA) plot of longitudinal beta diversity by participant



Microbiota findings (Figures 1 and 2)

1. Gut microbiota changes have been proposed as a possible mechanism of action of exclusive enteral nutrition therapy on gut inflammation.
2. There was no difference in Shannon diversity index between subjects (mean=3.2) or between pre- and post-intervention ($p=0.1$).
3. Linear discriminant analysis effect size (LEfSe) analysis identified one differentially abundant genus, *Flavinofactor*, which was associated with post-intervention samples (LDA score 3.7).

Conclusion

1. These findings demonstrate the feasibility of utilizing a 4-week semi-elemental formula-based, oral nutrition delivery program for management of adult CD and provides important estimates on the effect size of this intervention for future studies.
2. While we observed trends towards clinical improvement, the study was not powered to detect changes.
3. We also identified *Flavinofactor* as the only differentially abundant genus discriminating post samples from pre samples, which might suggest a potential role in CD, however further work with a larger sample size is needed to elucidate the role of gut microbiota in the therapeutic efficacy of EEN.