

# **Effect of *Bifidobacterium infantis* NLS Super Strain in highly symptomatic celiac disease patients on long-term gluten-free diet: A pilot study.**

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## Background

- A strict gluten-free diet (GFD) is the only currently recommended treatment for celiac disease (CeD).
- 30-50% of treated patients have persistent or relapsing GI symptoms.
- *Bifidobacterium infantis* NLS super strain (NLS-SS) alleviated symptoms in newly diagnosed CeD patients consuming gluten<sup>1</sup> through modulation of innate immunity<sup>2</sup>.

1-Smecuol et al. J Clin Gastro 2013; 2-Pinto-Sánchez J Clin Gastro 2017



## Aim



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To explore the effect of a three-week course of *B. infantis* NLS-SS on persistent or relapsed GI symptoms in patients with CeD following a long-term GFD.

## Methods

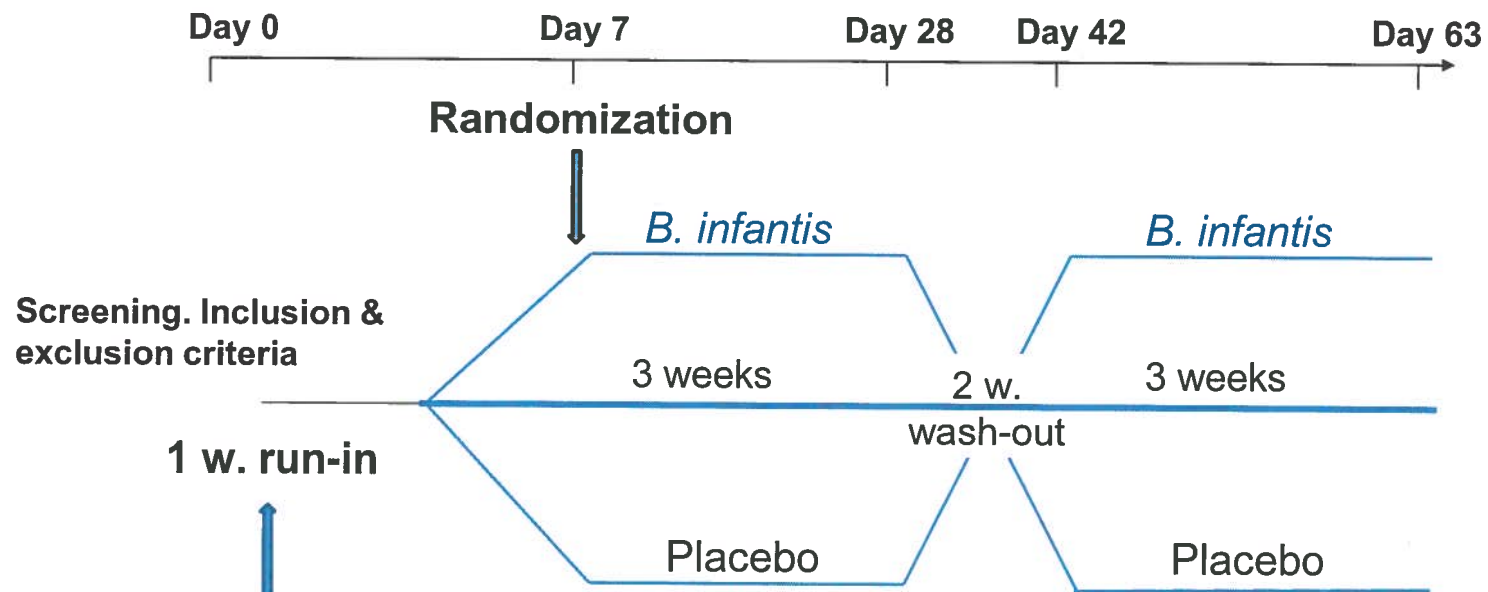
- **Active treatment:** *B. infantis* NLS-SS: 2 capsules t.i.d.;  $2 \times 10^9$  CFU/capsule.
- **Placebo:** rice flour, dehydrated potato powder, cellulose powder, and hydroxypropyl-methylcellulose, 2 capsules t.i.d. (GF).
- **Main outcome measurement:** changes ( $\Delta$ ) in CSI (global score and 2 subscales)<sup>1</sup> for each treatment comparing final vs. baseline assessments.
- **Secondary endpoints:** 1- Changes in CSI in patients with abnormal antibody concentrations (tTG IgA, DGP IgA). 2- GIP excretion according to treatment. 3- Change in fecal microbiota. 4- Adverse events.

1- Leffler DA, et al. CGH 2009



# Design

Prospective, randomized, cross-over, double blind, placebo-controlled trial



- Written consent.
- Clinical evaluation
- **GSRs**, CSI
- Serology



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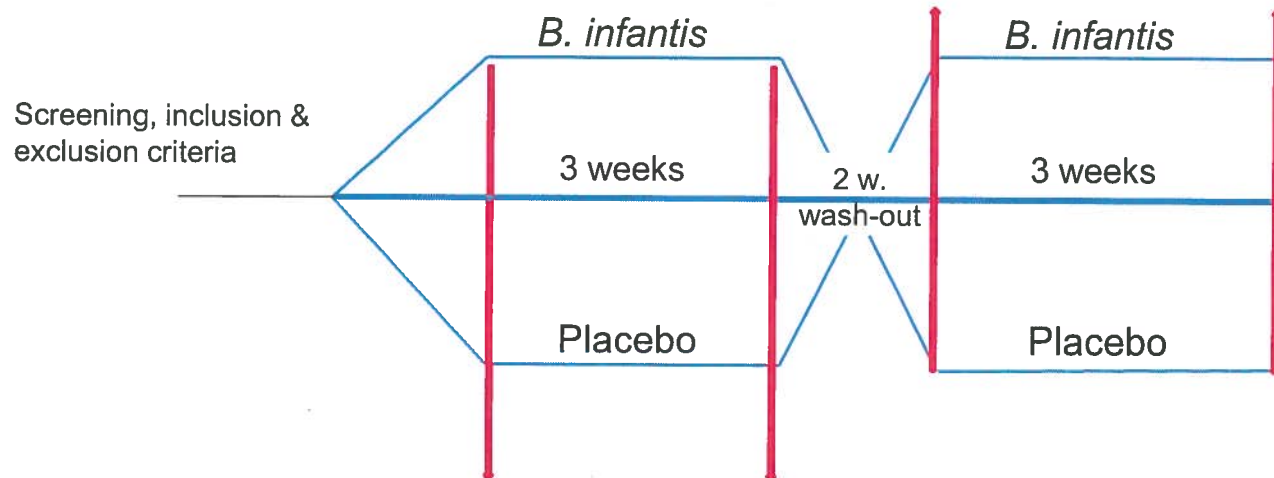
# Outcome measures



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- Clinical/ Dietary asses.
  - **CSI**
  - **Fecal microbiota**
- Clinical/ Dietary asses.
  - **CSI**
  - **Fecal microbiota**
  - **Adverse events**

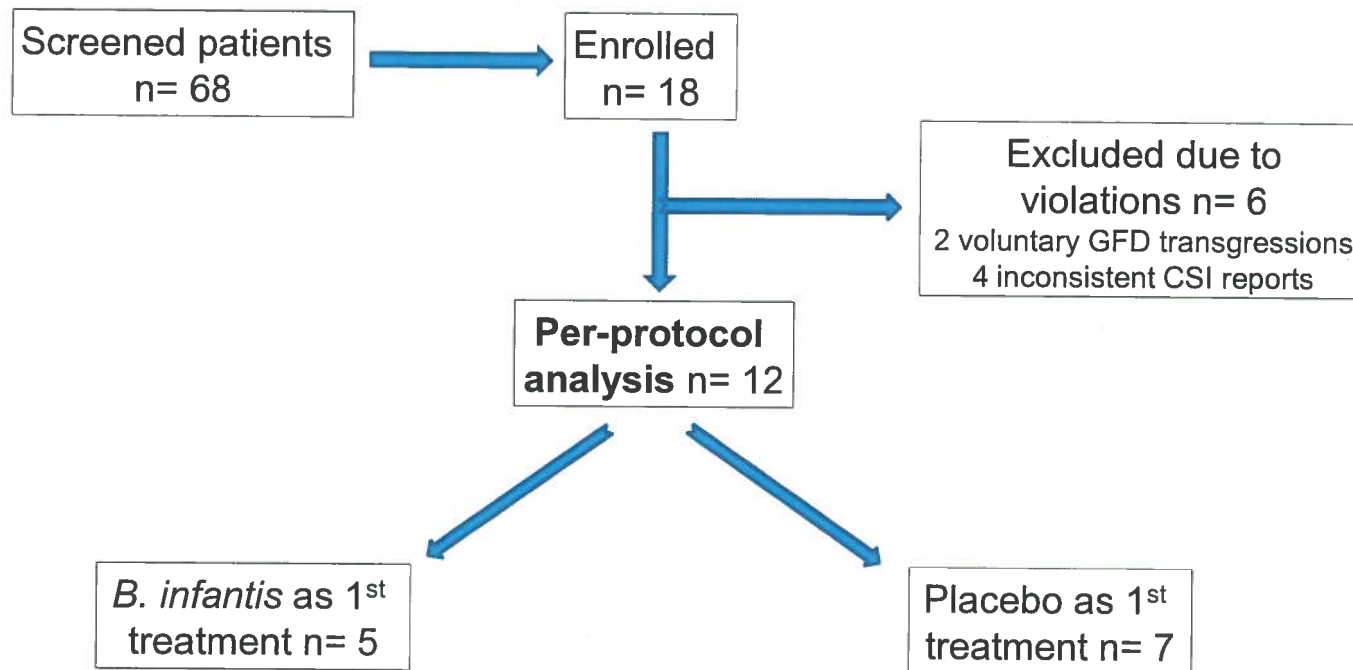


- Clinical & dietary asses.
- **CSI**
- **Fecal microbiota**
- **Biochemistry**

- Clinical/ Dietary asses.
- **CSI**
- **Fecal microbiota**
- **Adverse events**

# Results

## Flow chart



## Clinical characteristics

Per protocol analysis

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N (female)	12 (11)
Age yr. (Median; IQR)	53 (43-57)
Age from Dx. Yr. (Median; IQR)	7 (4-10)
CSI (Median score; IQR)	34 (30-46)
Serology (Median; IQR) [AU/mL] [n +ve cases]	
IgA tTG	13.5 (7.5-19.0) [3/12]
IgA DGP	15.0 (10.0-23.0) [3/12]

(IQR): Inter-quartile range



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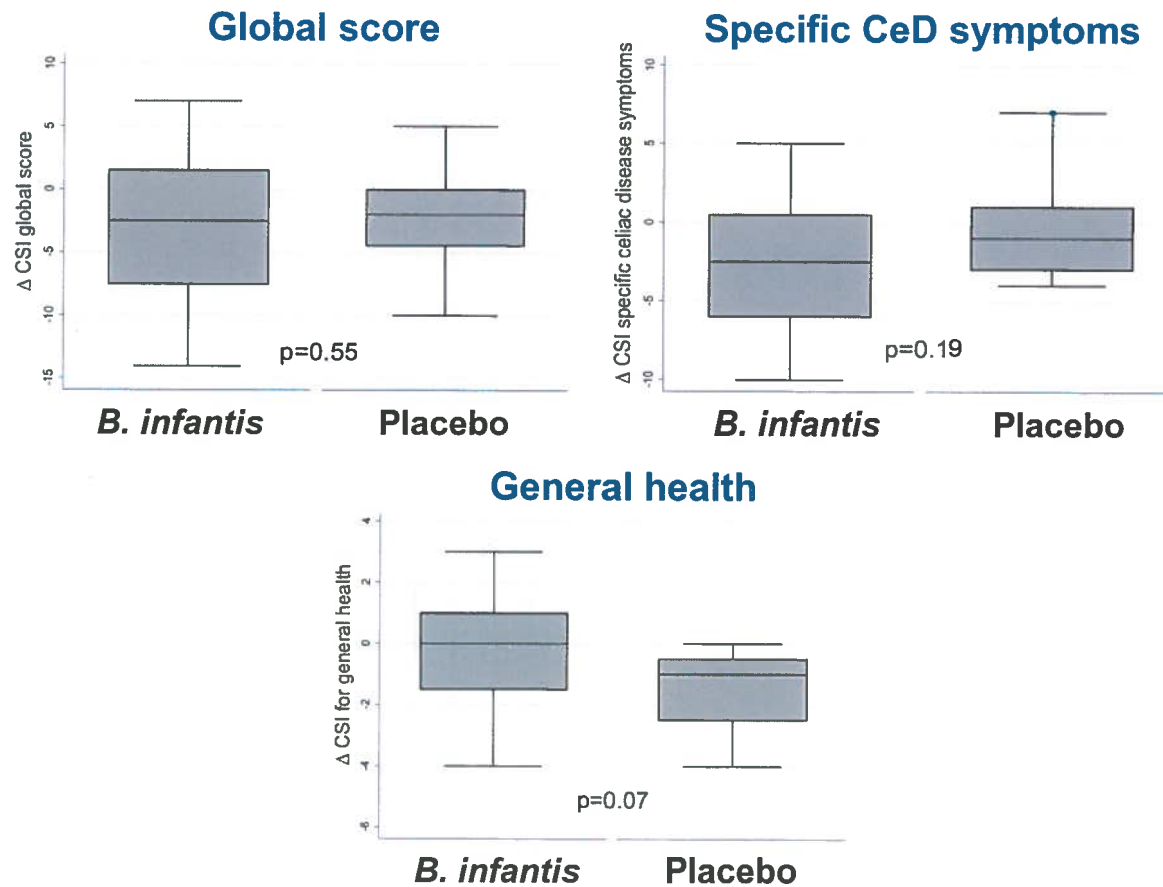




No differences in  $\Delta$  CSI global score, and sub-dimensions (specific CeD symptoms or general health dimensions) in the overall population (n=12)



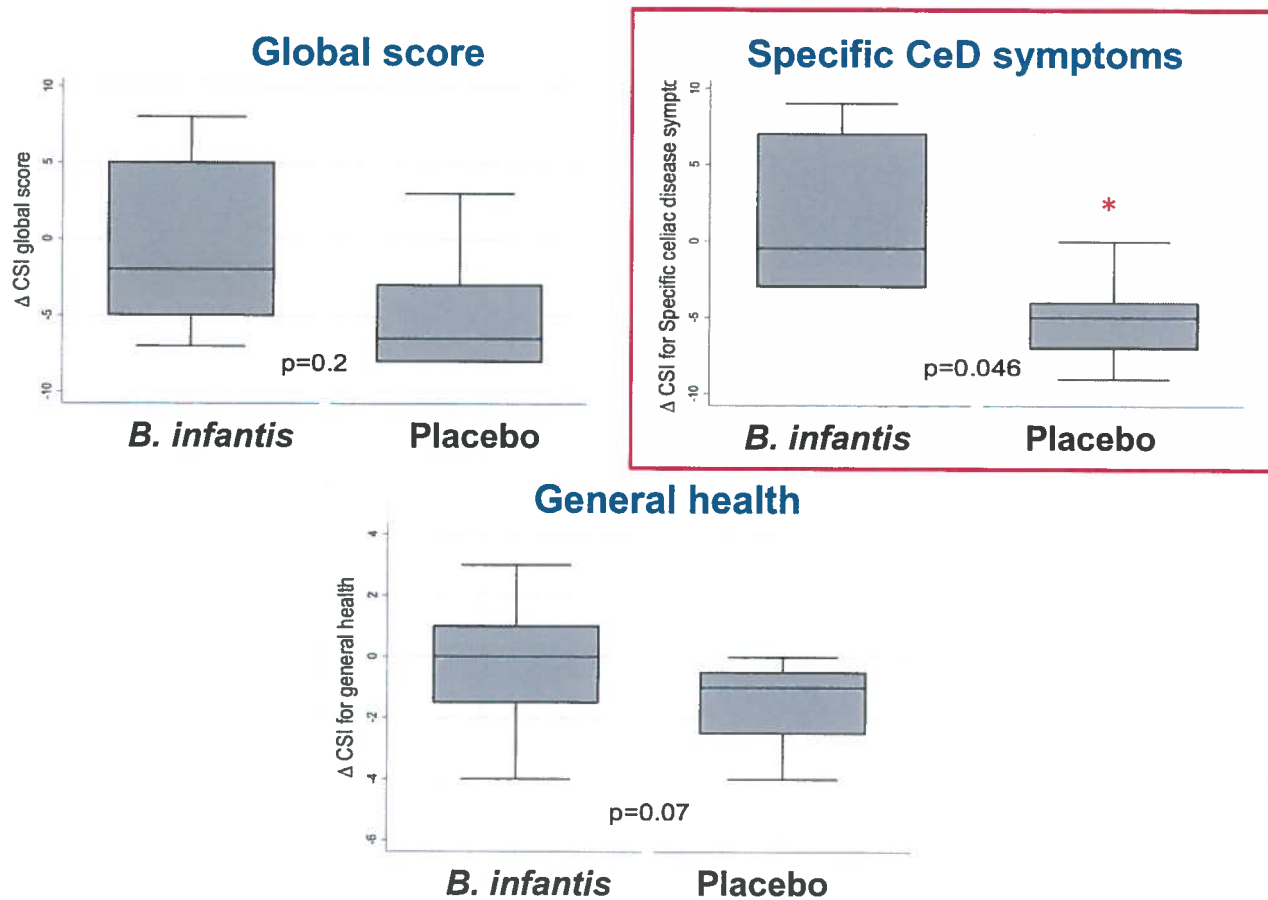
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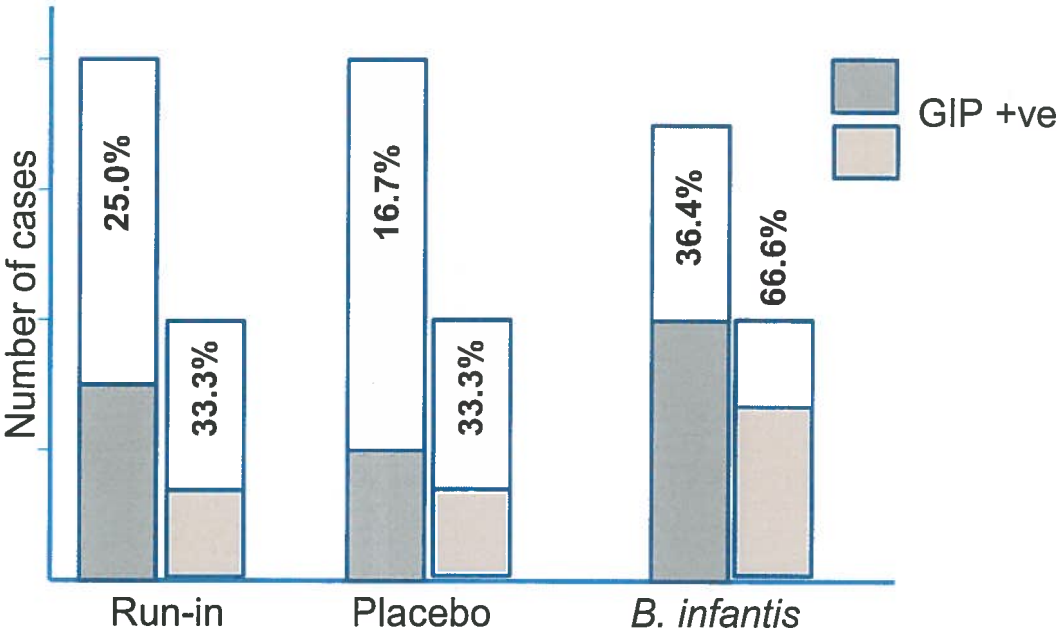
Improvement in  $\Delta$  CSI specific CeD symptom dimension in patients with more severe baseline CSI (>median) (n=6).



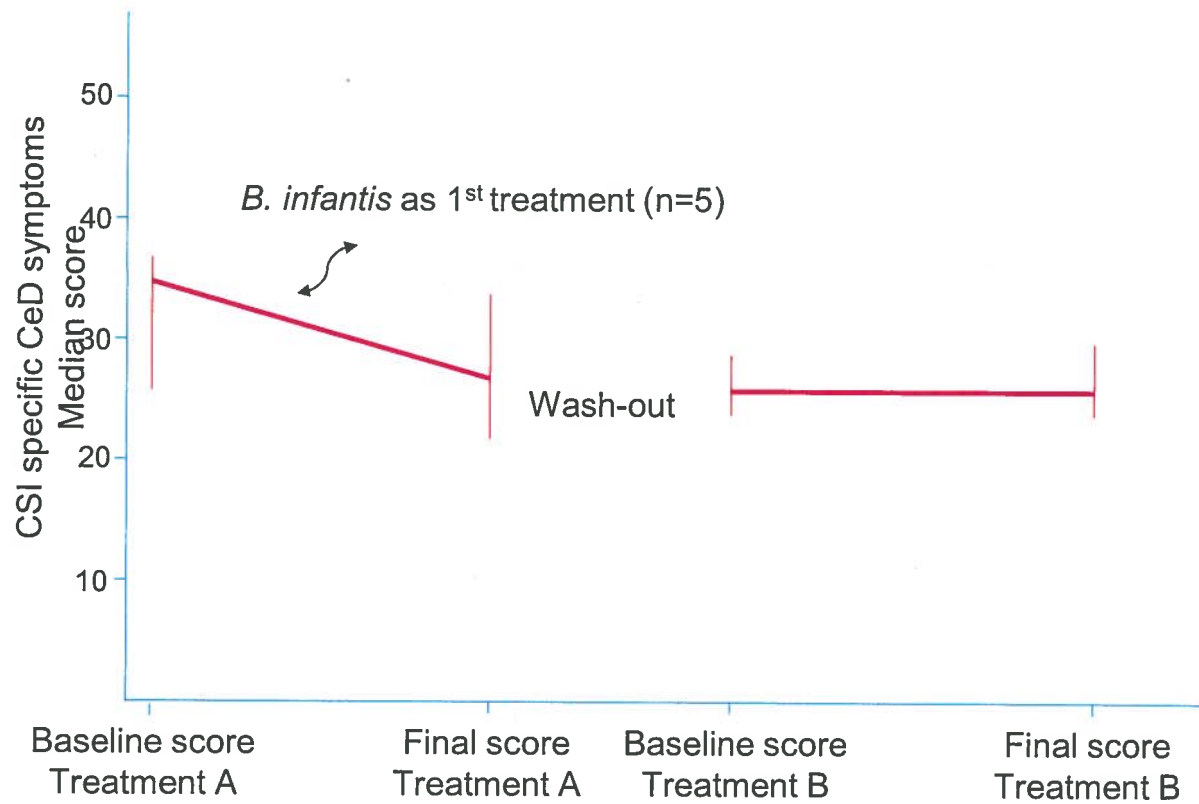
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The clinical effect was detected despite no significant differences in dietary transgressions (+ stool and/or urine GIP tests) in patients on probiotics.



# Evidence of carryover effect in patients with *B. infantis* as 1<sup>st</sup> treatment



(Median & IQR)

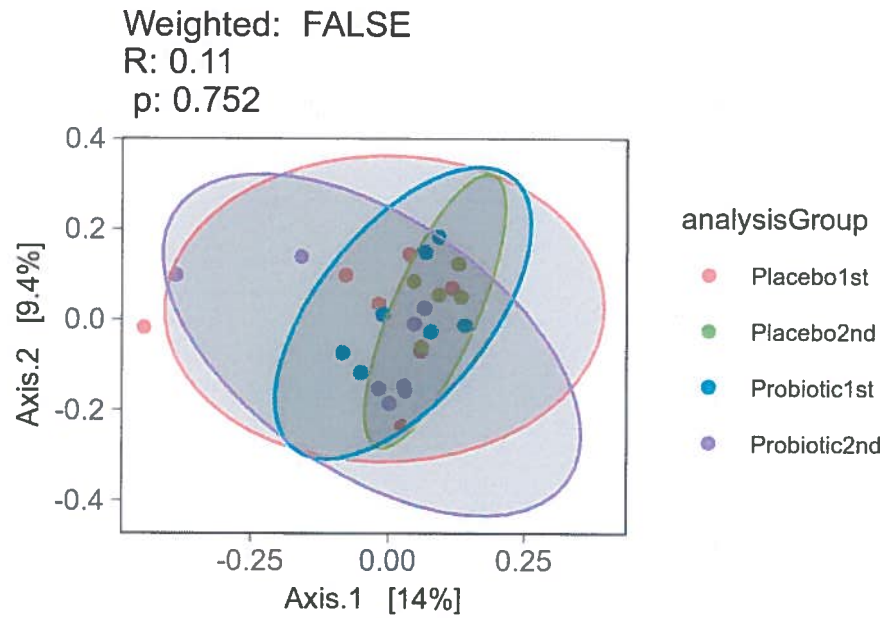
# Overall fecal microbiota profiles in each treated group



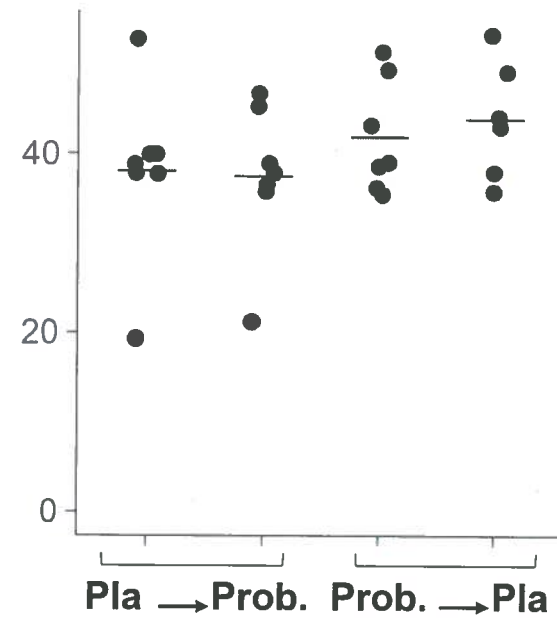
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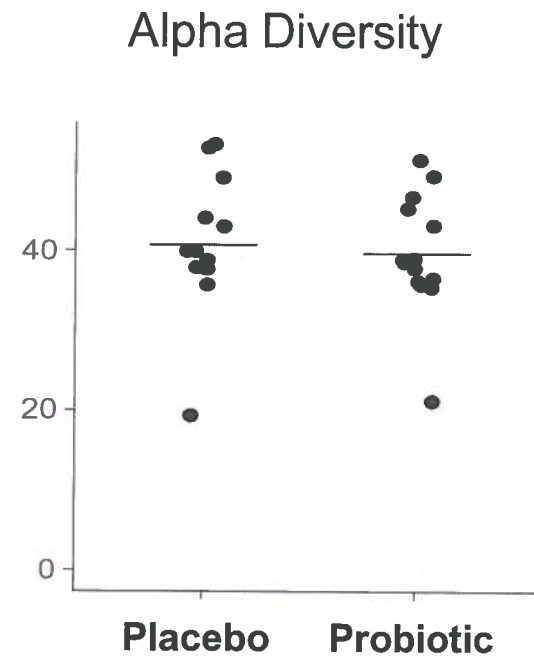
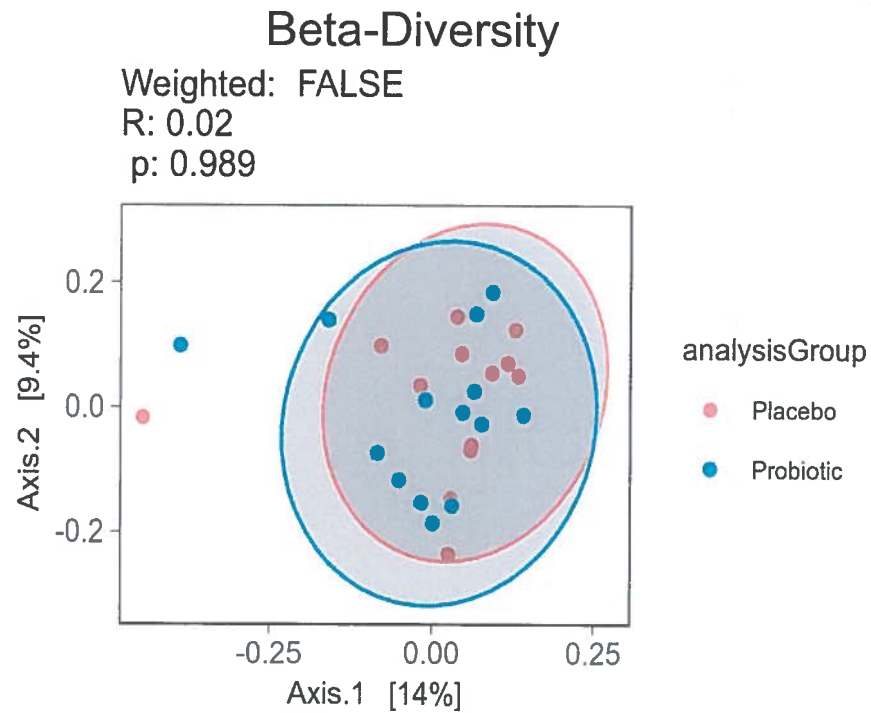
## Beta-Diversity



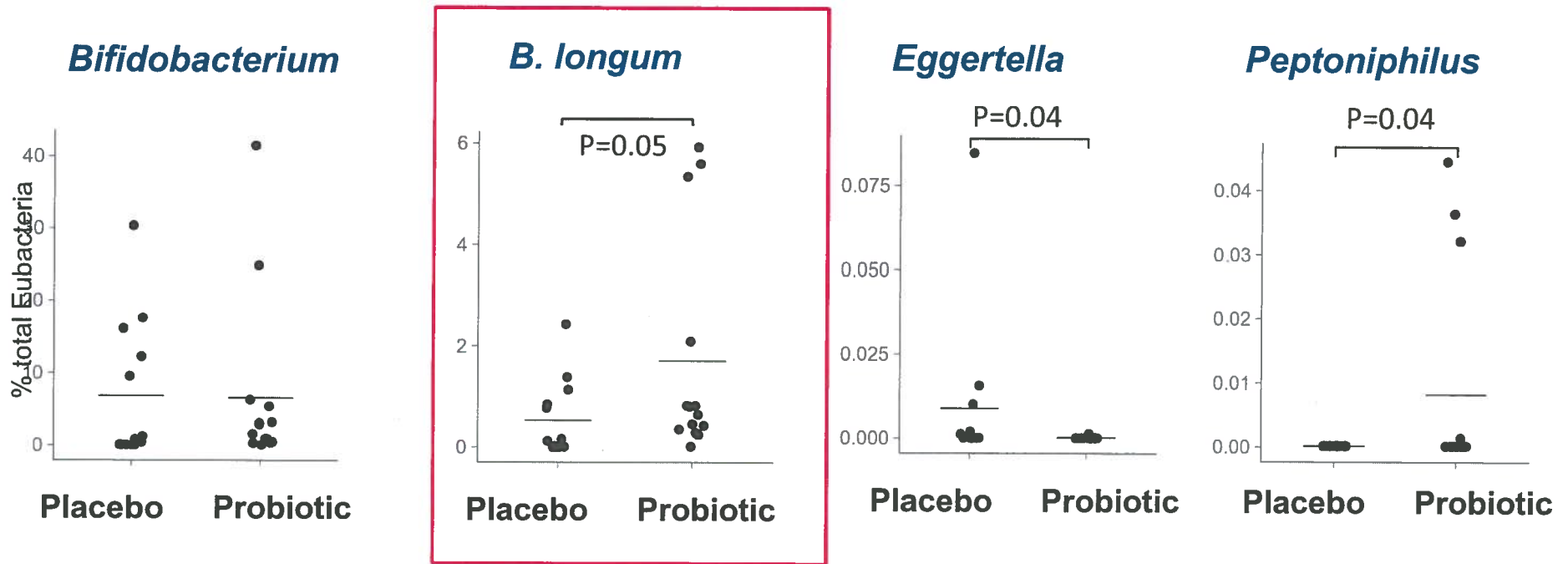
## Alpha Diversity



# Overall microbiota profiles in patients pooled according to receiving probiotics or placebo



# Analysis at genus level in all pooled patients according to receiving probiotics or placebo (Relative Abundance)



## Summary I

- No significant change of CSI scores between groups among the overall study population.
- Patients with highest baseline CSI scores (>median) improved specific CeD symptoms subscale by *B. infantis* but not by placebo.
- There was a non-statistically significant trend for a placebo effect in the general health subscale of CSI.



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## Summary II

- No effect of GFD transgressions or effect associated to the antibody levels on CSI score (data not shown).
- There was a non-statistically significant carryover effect in those consuming *B. infantis* as 1<sup>st</sup> treatment.
- Some differences in fecal bacterial genera are found between treatment groups, notably higher abundance of *Bifidobacterium (longum)* in probiotic treated.
- No adverse events were reported during trial.



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## Conclusions



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- *B. infantis* NLS-SS may improve specific CeD symptoms in GFD-treated patients with higher symptomatic burden irrespective of transgressions.
- Our results suggest higher fecal *Bifidobacterium (longum)* relative abundance in probiotic-treated patients.
- Whether this is an immune modulatory consequence of *B. infantis* NLS-SS treatment remains to be determined in larger studies.