Supplementary Tables

Supplementary Table S1. Carry-over analysis of genus abundances. Genera detected in the intention-to-treat cohort which were not present in microbiota profiles of the per-protocol cohort were assigned NA.

Supplementary Table S2. Cross-over analysis of observed richness, estimated richness, evenness (J), and diversity (Shannon). Carry-over of the richness effect detected was assessed.

Supplementary Table S3. Sample enterotyping (A). Volunteers excluded from the per-protocol cohort are underlined. A summarizing overview of enterotype prevalences and shifts is provided in (B) and (C), both for the per-protocol (1) as well as for the intention-to-treat cohort (2).

Supplementary Table S4. Cross-over analysis of genus (A), family (B), and phylum (C) relative abundances. Genera detected in the intention-to-treat cohort which were not present in microbiota profiles of the per-protocol cohort were assigned NA.

Supplementary Table S5. Pearson correlations between the magnitude of inulin-induced shifts (end riI vs. end I) in relative abundances of treatment-responsive genera and initial numbers (end riI) (A). Pearson correlations between the magnitudes of inulin-induced shifts of different responsive genera (B).

Supplementary Table S6. Cross-over analysis of genus relative abundances of some taxa with reported susceptibility toward prebiotic stimulation.

Supplementary Table S7. Cross-over analysis of fecal metabolite relative abundances. . Metabolites detected in the intention-to-treat cohort which were not present in metabolite profiles of the per-protocol cohort were assigned NA.

Supplementary Table S8. Spearman correlation between magnitudes of dodecanal concentration and genus abundance shifts (consecutive samples: V3-V2, V4-V3, V5-V4, Figure 1).

Supplementary Table S9.

Spearman correlations between dodecanal relative abundance and changes in dietary-, stool- or PaC-QoL parameters.

Supplementary Table S10. Spearman correlations between variation of *Bifidobacterium*, *Anaerostipes*, and *Bilophila* relative abundances and changes in dietary parameters.

Supplementary Table S11.

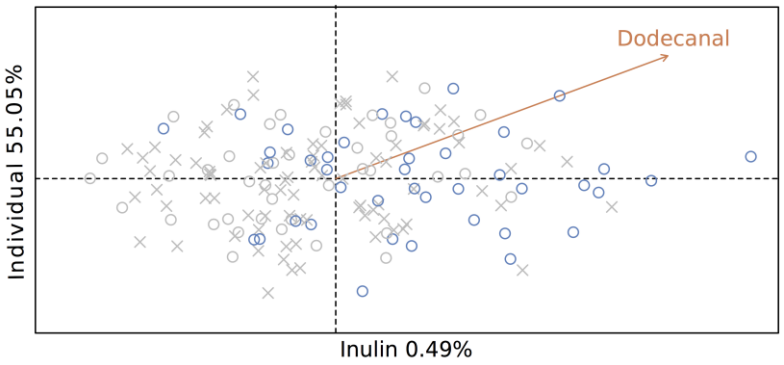
Spearman correlations between variation of *Bifidobacterium, Anaerostipes*, and *Bilophila* relative abundances and changes in stool- or PaC-QoL parameters.

Supplementary Table S12.

Baseline personal characteristics of subjects.

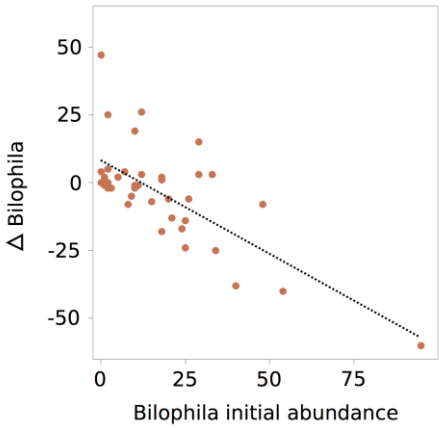
SUPPLEMENTARY FIGURES

Figure S1. Principal Coordinates Analysis with Bray Curtis distance on metabolite data with inulin as a constraining factor.



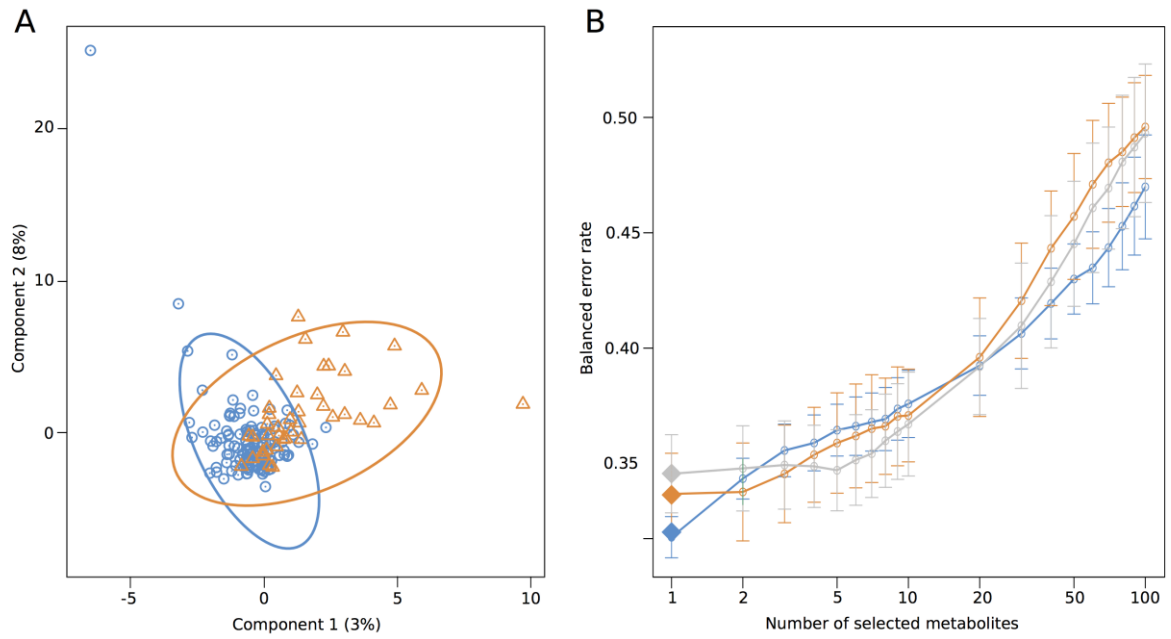
Ordination was performed on samples taken at the end of intervention (o) as well as run-in periods (x). The non-significant effect of inulin supplementation (blue, permutation test, p-value = 0.11) is calculated to account for 0.49% of between-sample metabolome variation while individual variation contributes 55,05%. The one metabolite responsive to prebiotic treatment (Dodecanal, wilcoxon test, q-value < 10^{-3}) was plotted on the ordination.

Figure S2. Magnitude of inulin-induced shifts associates with initial numbers for *Bilophila*.



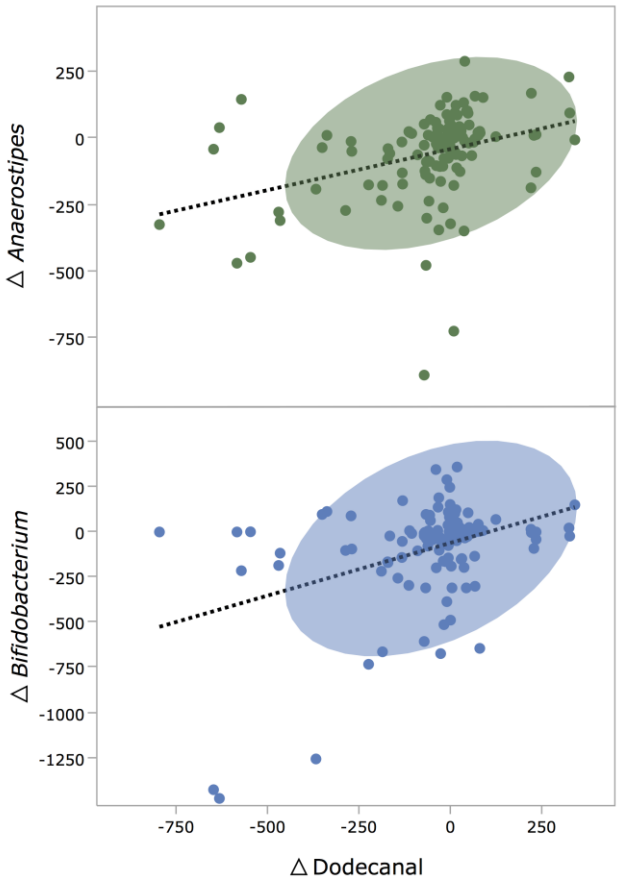
Correlation between the magnitude of inulin-induced shifts in relative abundances (end riI vs. end I; Δ *Bilophila*) and initial numbers (end riI) for *Bilophila* (Pearson, r = -0.71, p-value < 10^{-6}).

Figure S3. Sparse Partial Least Square Discriminant Analysis confirms the discriminant power of dodecanal.



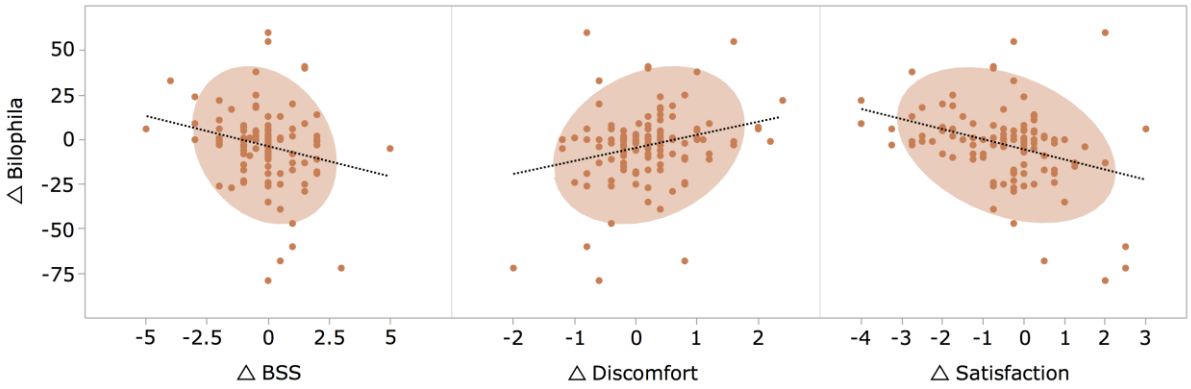
(A) Separation of the prebiotic (orange) and non-prebiotic (blue) samples in the first plane based on the optimized sPLS-DA model including three components. (B) Error rates are lowest when only one variable is selected for the first component (blue), namely Dodecanal. The second component (green) optimally consists out of two metabolites, Tetradecanal and Pentadecanal, while the third component (grey) only needs the inclusion of 1,3,5-trimethyl-benzene for optimal performance. Stability frequency scores of the variables of each component of the final model (indicating how often the variables of a component are selected across the different cross validation folds with 1, always and 0, never) were determined to be 1 for Dodecanal, 0.94 for Tetradecanal, 0.46 for Pentadecanal and 0.39 for 1,3,5-trimethyl-benzene.

Figure S4. Magnitude of dodecanal concentration shifts correlates with *Anaerostipes* and *Bifidobacterium* abundance variation.



Correlation between magnitudes of dodecanal concentration shifts (consecutive samples; Δ Dodecanal) and *Anaerostipes* and *Bifidobacterium* abundance variation (Δ *Anaerostipes* and Δ *Bifidobacterium*; Spearman, rho = 0.50, p-value < 0.0001 and rho = 0.29, p-value < 0.05, respectively) with zones indicating 95% confidence level. Shifts were assessed as the difference of consecutive samples over the course of the study using all 165 samples (V3-V2, V4-V3, V5-V4, Figure 1).

Figure S5. *Bilophila* abundances correlate with stool consistency and quality-of-life parameters.



Correlation between *Bilophila* abundance shifts (consecutive samples; Δ *Bilophila*) and differences in stool consistency measured by the Bristol Stool Scale (Δ BSS; spearman rho = -0.22, q-value < 0.05), as well as differences in PaCQoL scores for physical discomfort (Δ Discomfort; spearman rho=0.20, p-value < 0.05), and treatment satisfaction (Δ Satisfaction; spearman rho=-0.30, q-value < 0.01), with zones indicating 95% confidence level. Shifts were assessed as the difference of consecutive samples over the course of the study using all 165 samples (V3-V2, V4-V3, V5-V4, Figure 1).