

## Statistical plans

All data collected by questionnaires will be entered into database management software (EpiData), double checked by independent researchers, and exported to SPSS statistics version. If data is not normally distributed, their natural logarithms will be used for further analysis. Descriptive statistics will be used to present the background and anthropometric data at the baseline and follow-up assessments as mean and 95% confidence interval (CI) unless otherwise stated.

An intention-to-treat (ITT) analysis will be performed to compare the Probiotics group to Placebo group. The effects of the interventions will be assessed using analysis of variance (ANCOVA) for repeated measures (treatment group  $\times$  time) and baseline difference as a covariate. If the significance of the group by time interaction is  $p < 0.05$ , the effect will be localized utilizing Bonferroni for multiple comparisons. The level of statistical significance chosen for the contrasts will be  $p < 0.05$ . In addition to the ITT analysis, efficacy or active treatment analysis will be done when the compliance of the participation of the intervention is  $\geq 60\%$  of the whole trial [ANCOVA for repeated measures (treatment group  $\times$  time) and baseline difference as a covariate.] The percentage differences (0–3month) will be calculated from duration between baseline and end point measurements for each individual. The comparison of percentage changes in different groups will be performed using ANCOVA (two factor interactions: compliance/noncompliance  $\times$  treatment group) controlled for the baseline value using Bonferroni for multiple comparisons. If the significance of the overall group difference is  $p < 0.05$ , then the effect will be localized by contrast to the Con group. When the 95% CI does not include zero, the difference is regarded as statistically significant at  $\alpha = 0.05$ .

Linear Pearson's correlation, partial correlation, Kendall Tau's, and bivariate, logistic, and multivariate regression analysis will be used for analyzing relationships. In addition, systems biology approaches will be used to develop models which integrate the different types of data and the high-throughput data measured in terms of gut microbiota composition, as well as LPSs and inflammation.