

SUPPLEMENTARY TEXT 9

ASSOCIATION OF DIET-ASSOCIATED MICROBIOME TAXA WITH DISEASE PATHOPHYSIOLOGIES, POLY-PHARMACY, AND OTHER HOST-FACTORS

The dataset included 11 diseases containing at least three (of 612) diseased subjects at the baseline. We first investigated the effect of these diseases on the diet-associated taxa at the baseline. Nine of the 11 diseases were associated with lower microbiome indices, significantly so for diabetes, heart attack and inflammatory disorders ($P < 0.05$) and marginally significant for Cancer ($P < 0.097$) (**Supplementary table 6; Supplementary figure 14 a-d**). Individuals with multiple diseases had significantly lower microbiome indices and significantly lower ratios of DietPositive to DietNegative taxa abundances compared to those with single or no disease, indicating that the diet-favoured microbiome components are negatively associated with disease at baseline (**Supplementary figure 14e-f**). However, when we examined partial spearman correlations at baseline, the pattern of association of microbiome index with seven of the 10 inflammatory markers and frailty indices (identified in **figure 4**) remained invariant even after taking into account all confounders including age, BMI, gender, poly-pharmacy and different disease pathophysiologies (**Supplementary figure 15a**). All the above associations were retained (except for leptin) even after considering age, gender, BMI and poly-pharmacy (as confounders) across both the baseline and follow-up time points, further supporting the hypothesis that it is the microbiome response that is linked to the above measures (even after adjusting for all host associated confounding factors) rather than dietary adherence alone (**Supplementary figure 15b**).