

## SUPPLEMENTARY TEXT 6

### RESULTS OF THE APPLICATION OF THE iBBiG APPROACH ON THE NU-AGE DATASET

The application of the iBBiG approach on the NU-AGE data identified 6 overlapping taxonomic modules that had a high mutual co-occurrence (obtained by maximizing the internal entropy) within the dataset. These were referred to as modules 'A' to 'F' (**Supplementary figure 9a**). Based on their detection trends in the overlapping modules, the OTUs could be classified as belonging to either a single (e.g. module A) or a combination of any of the six modules. This resulted in 36 OTU classifications (including one 'not classified' group). In a similar manner, a given sample could be classified into one of 15 classifications (and one 'not classified' group) based on the detection of the various modules in that sample. The classifications of each OTU and sample obtained in the iBBiG approach is listed in **Supplementary Tables 3 and 4**. Each of the six modules were characterized by different number of OTUs, specific trends of prevalence across individuals, as well as distinct patterns of taxonomic composition (**Supplementary figures 9b-c**). We also identified differential associations of each of these modules with frailty, especially with modules B and D being significantly enriched in the individuals with reduced frailty from baseline to post intervention, as compared to the module C, which was enriched in those with increasing frailty (**Supplementary figures 9d**). This indicates module 'C' to be similar to the long-stay-like modules we identified in ELDERMET individuals using the iBBiG approach(16). However, module 'C' was not only associated with a significant enrichment in individuals with increased frailty, but also an increase in representation of the set of DietNegative OTUs (**Supplementary figure 9d**). The observation that adherence to the diet could specifically select against taxa associated with frailty indicates the likelihood that the Mediterranean diet successfully modulated the gut microbiome in a manner predicted to be negatively associated with frailty. A major objective of the NU-AGE dietary intervention was the reduction of frailty and inflamm-ageing in the elderly. Therefore, we next investigated in detail the association of adherence-associated taxa with frailty as well as with the inflammation status of the individuals.