Supplementary Figures

Nagpal et al.

Modified Mediterranean-Ketogenic diet modulates gut microbiome and short-chain fatty acids in association with Alzheimer's disease markers in subjects with mild cognitive impairment

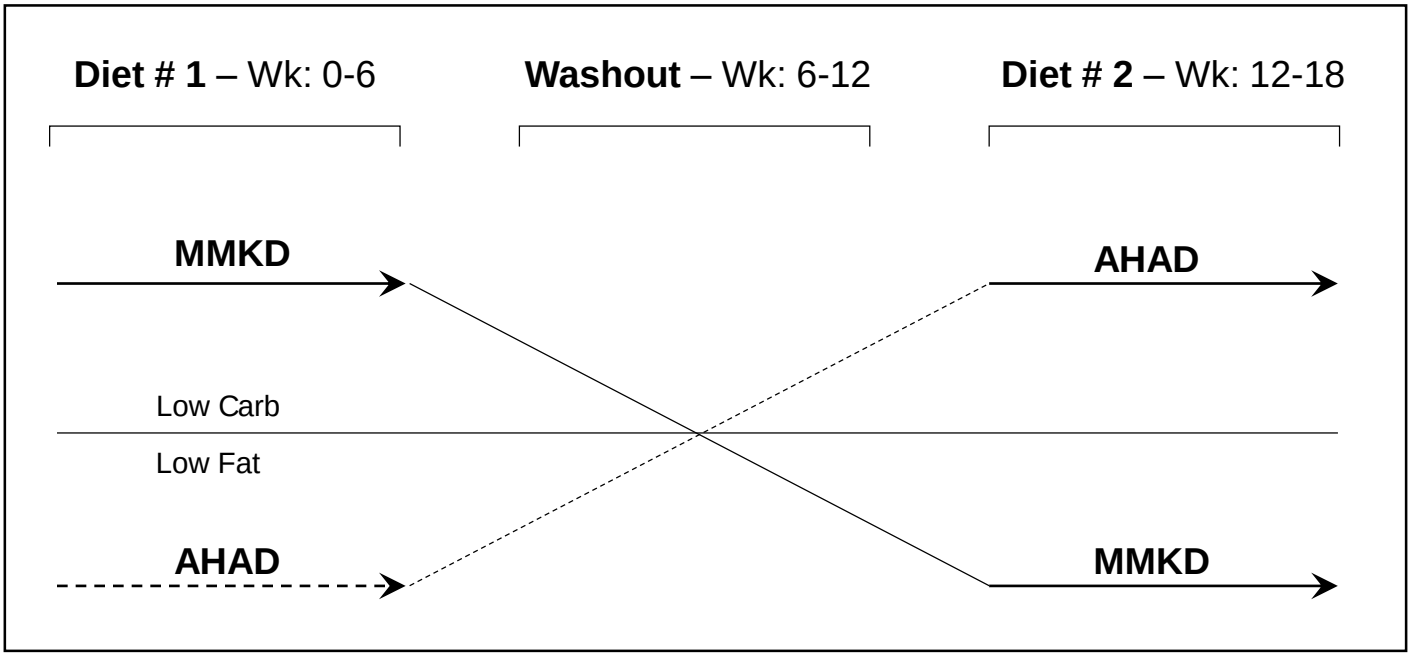
Suppl. Table 1. General characteristics of the participants enrolled in the study.

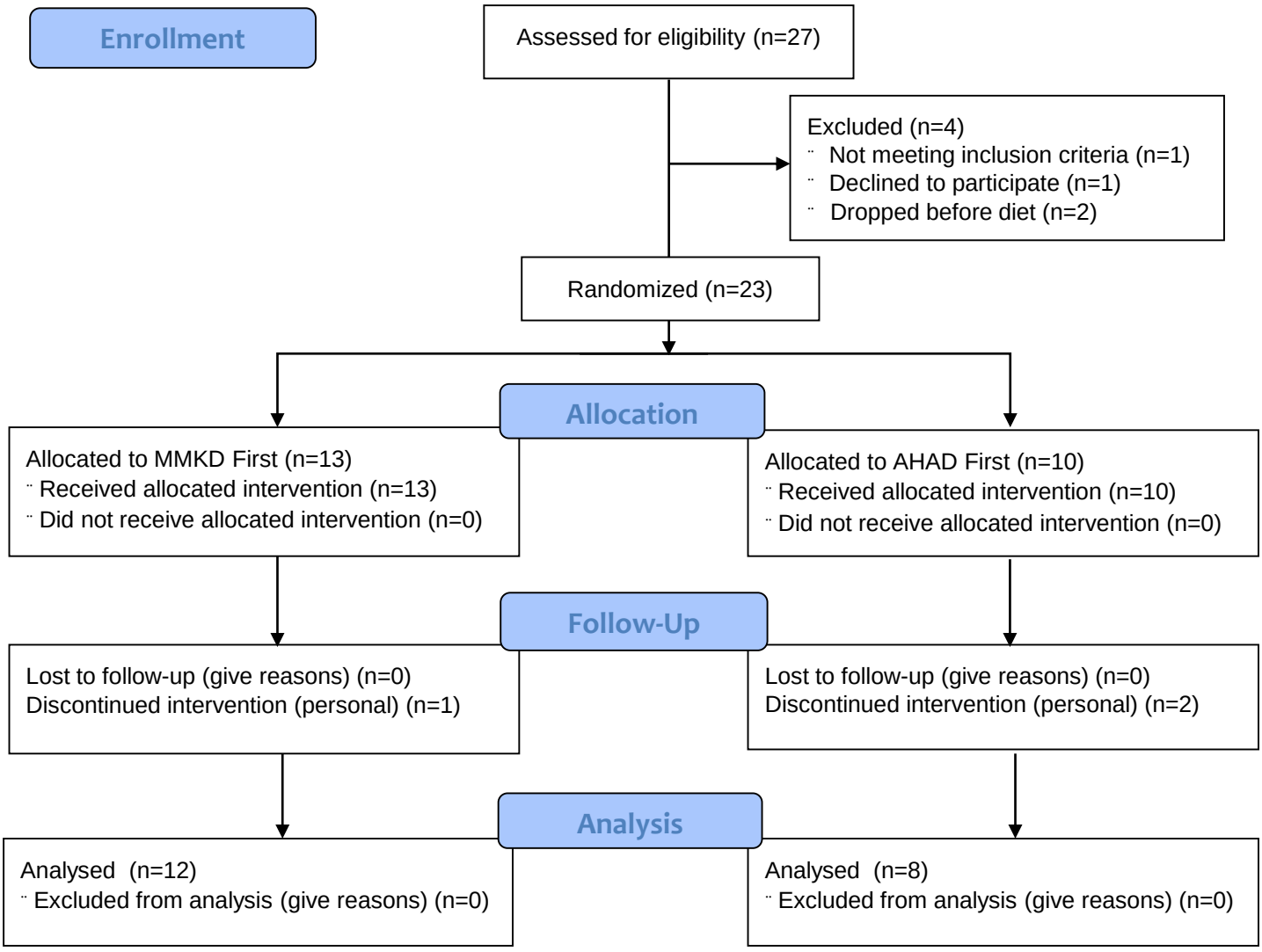
StudyID	E4	MCI	FirstDiet	Age	Sex	Race	EDUC (yrs)
1263001	0	1	MMKD	62	M	W	12
1263002	0	0	AHAD	62	M	W	19
1263007	0	1	MMKD	64	F	W	17
1263011	0	0	AHAD	63	F	W	14
1263013	0	0	MMKD	72	F	W	18
1263016	1	0	AHAD	65	F	W	12
1263017	0	0	MMKD	66	M	W	18
1263018	1	1	MMKD	65	F	AA	16
1263019	0	1	MMKD	57	F	AA	13
1263020	0	1	MMKD	59	F	AA	12
1263023	0	0	AHAD	63	F	AA	14
1263024	0	1	MMKD	60	F	W	16
1263026	1	1	MMKD	84	F	W	18
1263027	1	1	MMKD	57	F	W	18
1263028	0	1	AHAD	62	M	W	20
1263034	1	1	AHAD	70	F	AA	16
1263039	1	1	MMKD	67	M	W	19

Summary

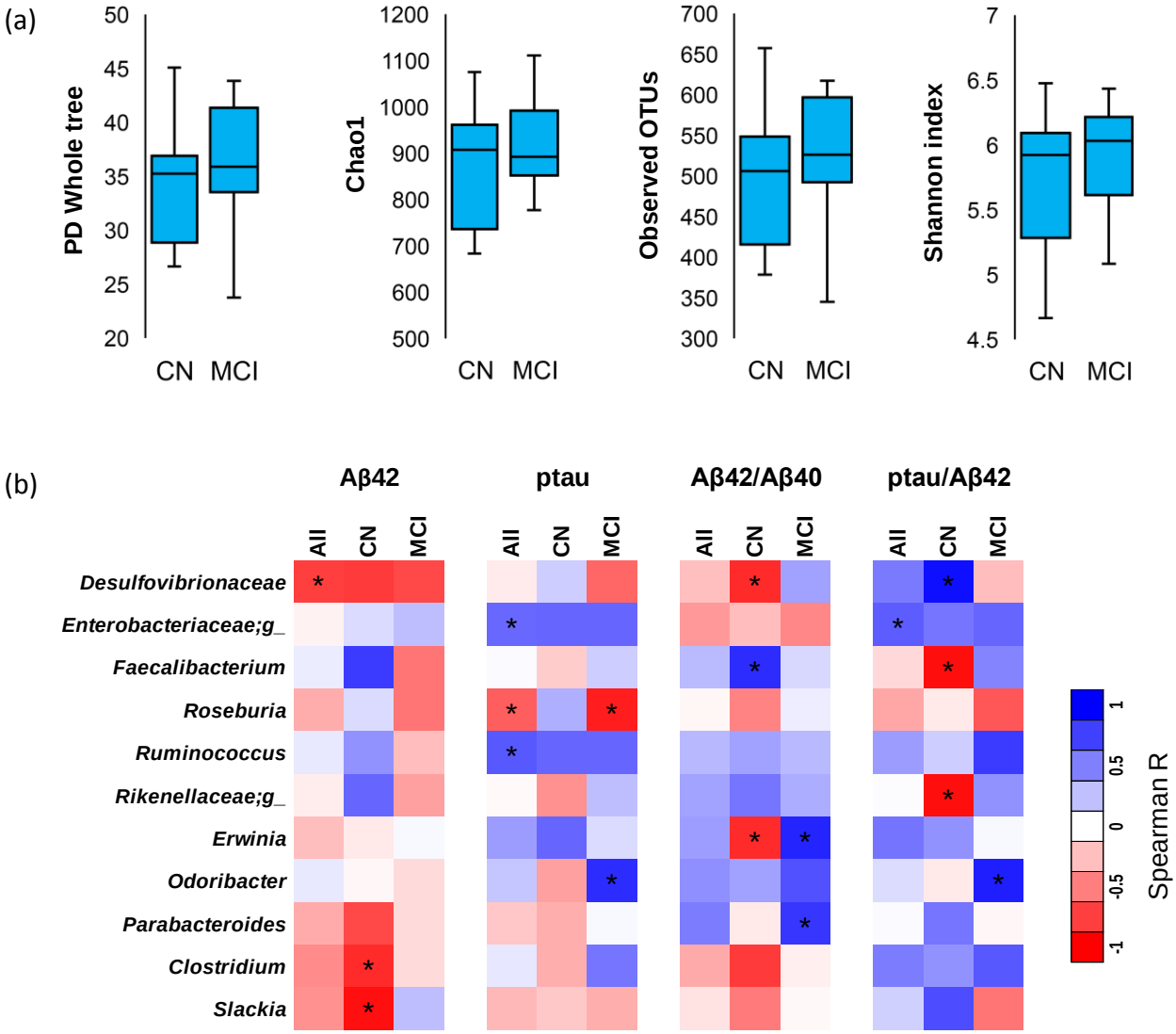
Total number of subjects	17
Age, years (mean±SD)	64.6 ± 6.4
Sex (F/M)	12/5
N, Mild cognitive impairment (MCI)	11
N, APOE ε4 (E4) genotype	6
N, African-American/White	5/12

Suppl. Fig. 1. Study design.

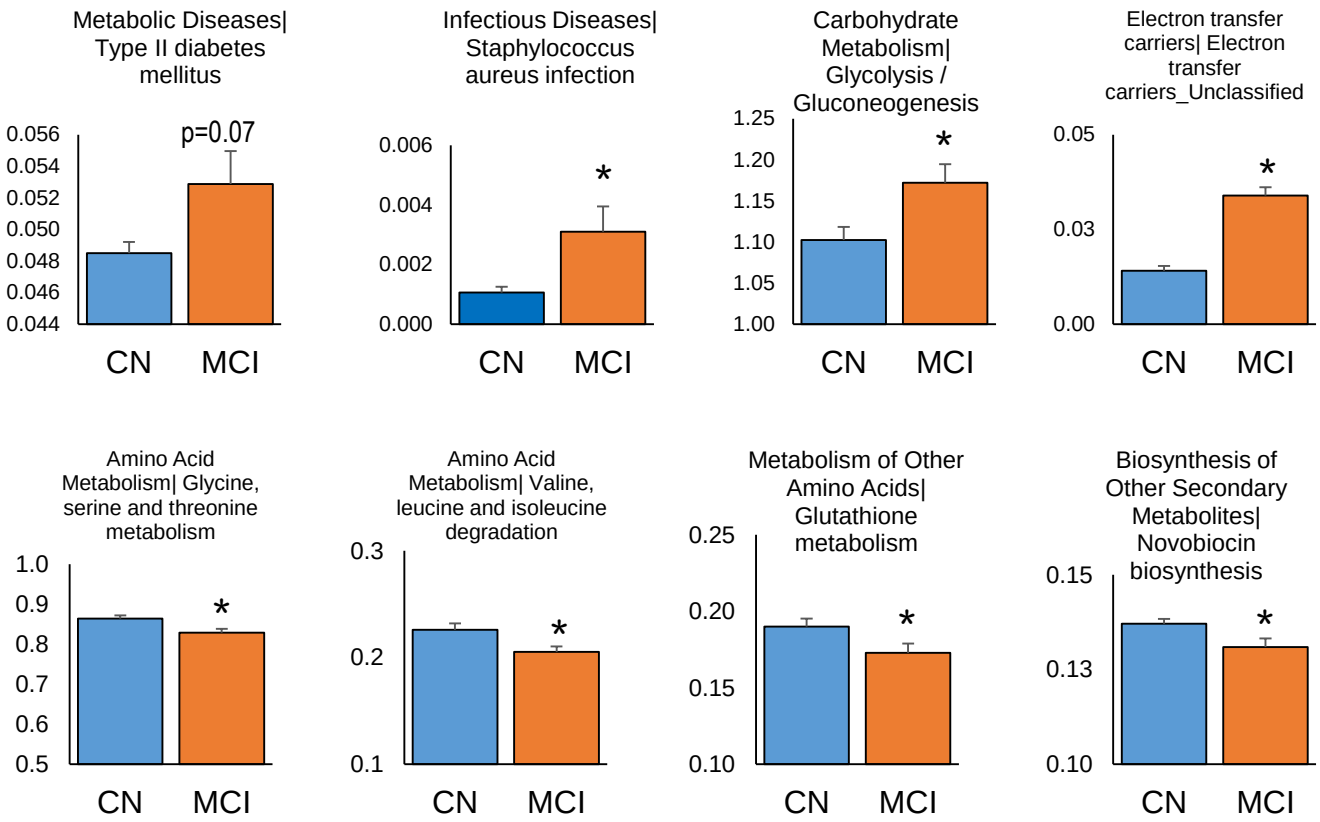




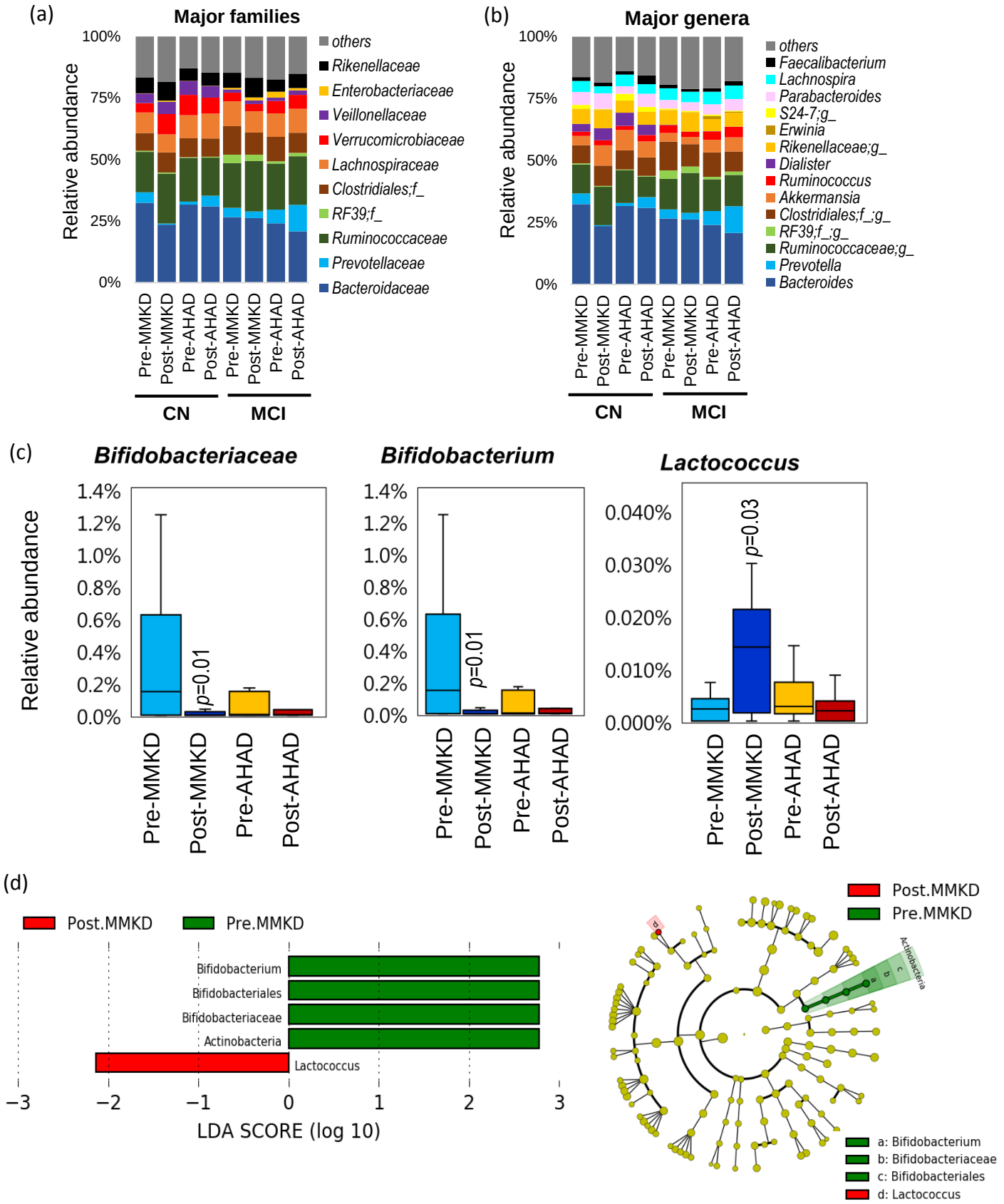
Suppl. Fig. 2. (a) Indices of the gut microbiome alpha-diversity in cognitively normal (CN) subjects versus subjects with mild cognitive impairment (MCI). (b) Association of gut bacterial taxa with cerebrospinal fluid biomarkers of Alzheimer's disease in CN and MCI subjects (*p<0.05).



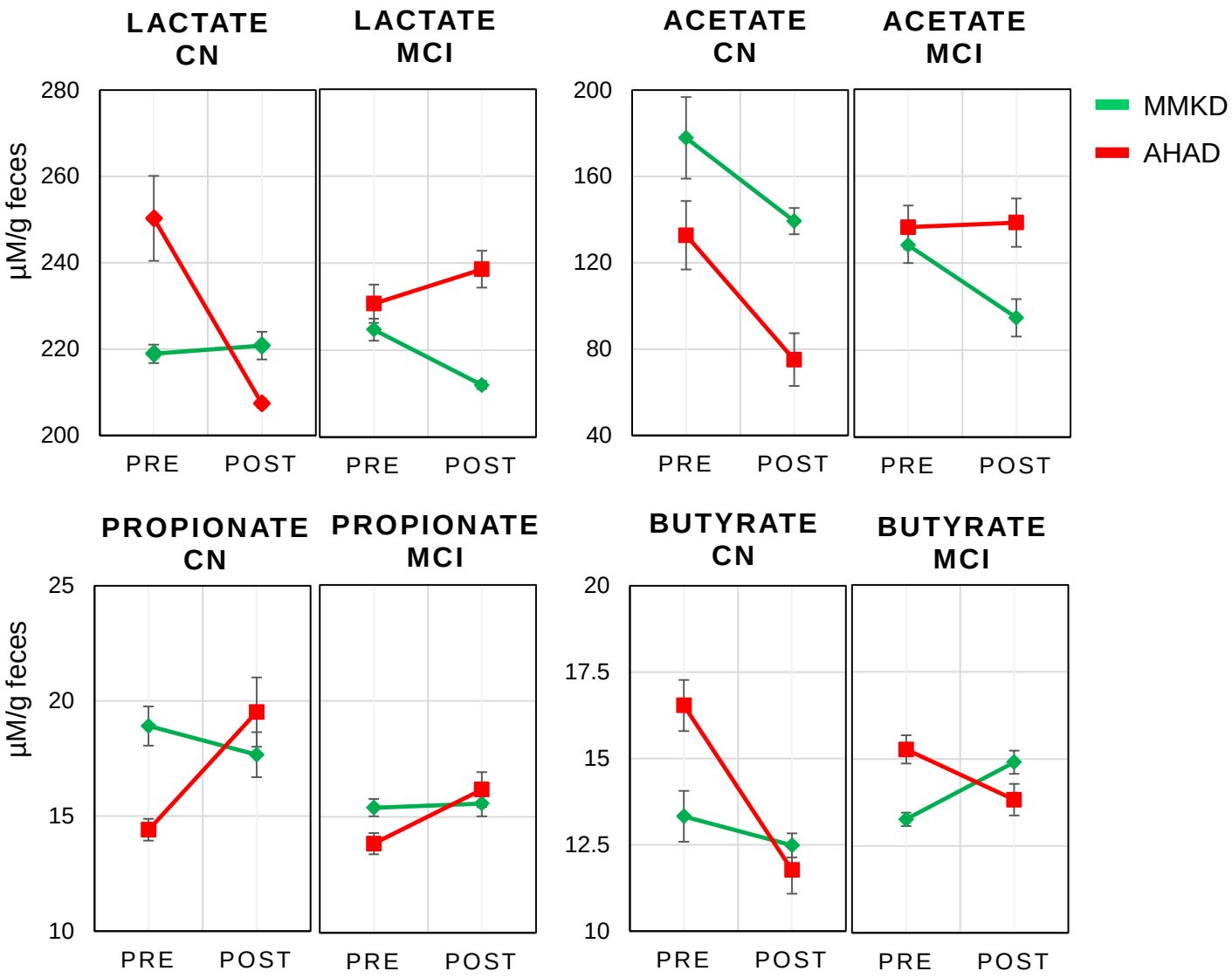
Suppl. Fig. 3. Differences in the functional analysis of the gut microbiome in subjects with MCI versus cognitively normal (CN) subjects. The relative abundance of the functional content (Level 2 and Level 3 KEGG pathway) of the gut microbiome was inferred by using PICRUSt based on the 16S amplicon sequencing data. Only the pathways showing considerable difference between the two groups are shown here (*p<0.05).



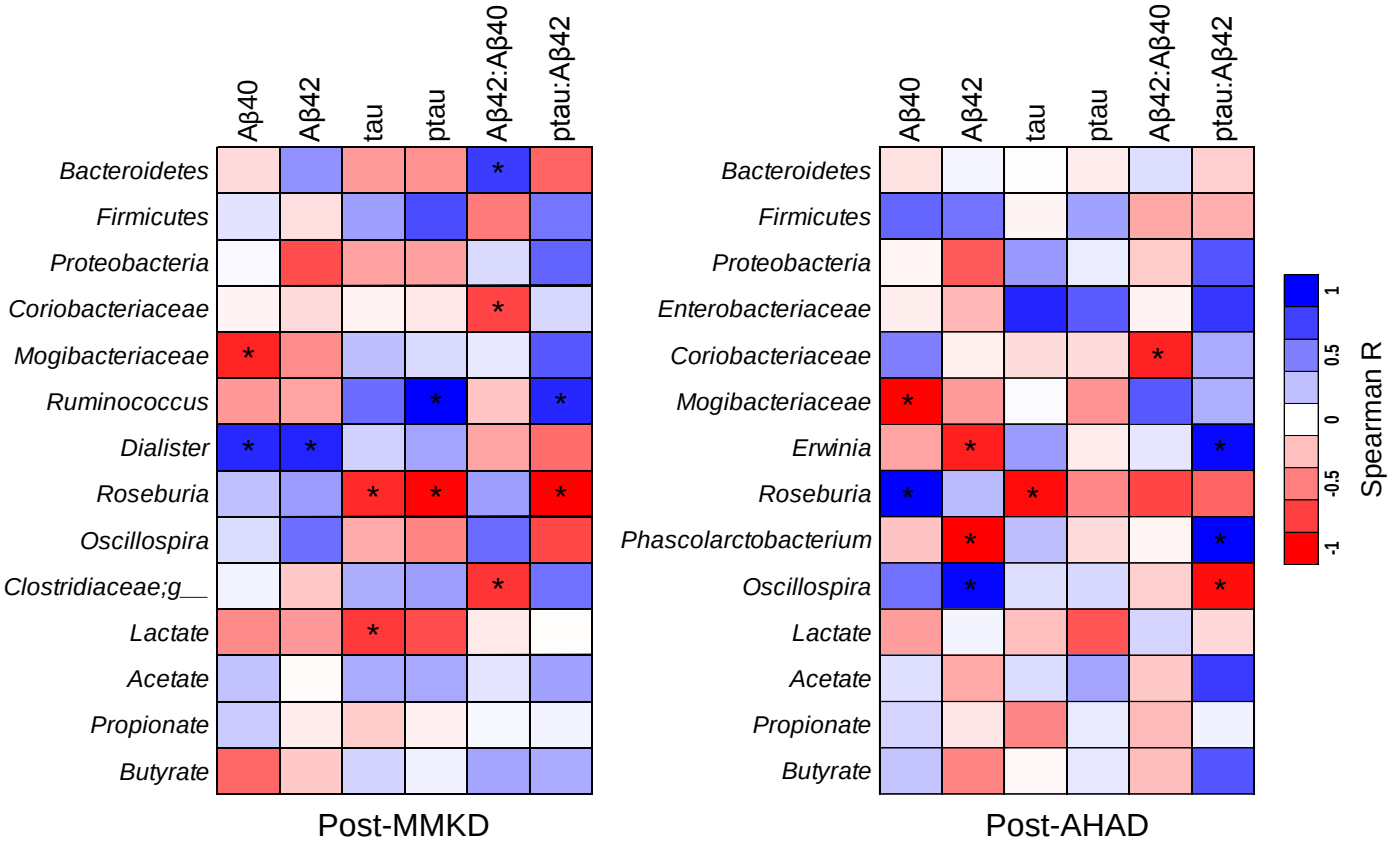
Suppl. Fig.4. Comparison of family- and genus-level gut microbiome composition (a-b) and the relative abundance of selected bacterial taxa (c) at baseline and endpoint of MMKD and AHAD intervention in subjects with mild cognitive impairment (MCI; n=11) versus cognitively normal (CN) counterparts (n=6). (d) Lefse analysis showing bacterial taxa contributing to the microbiome difference between the two diet groups.



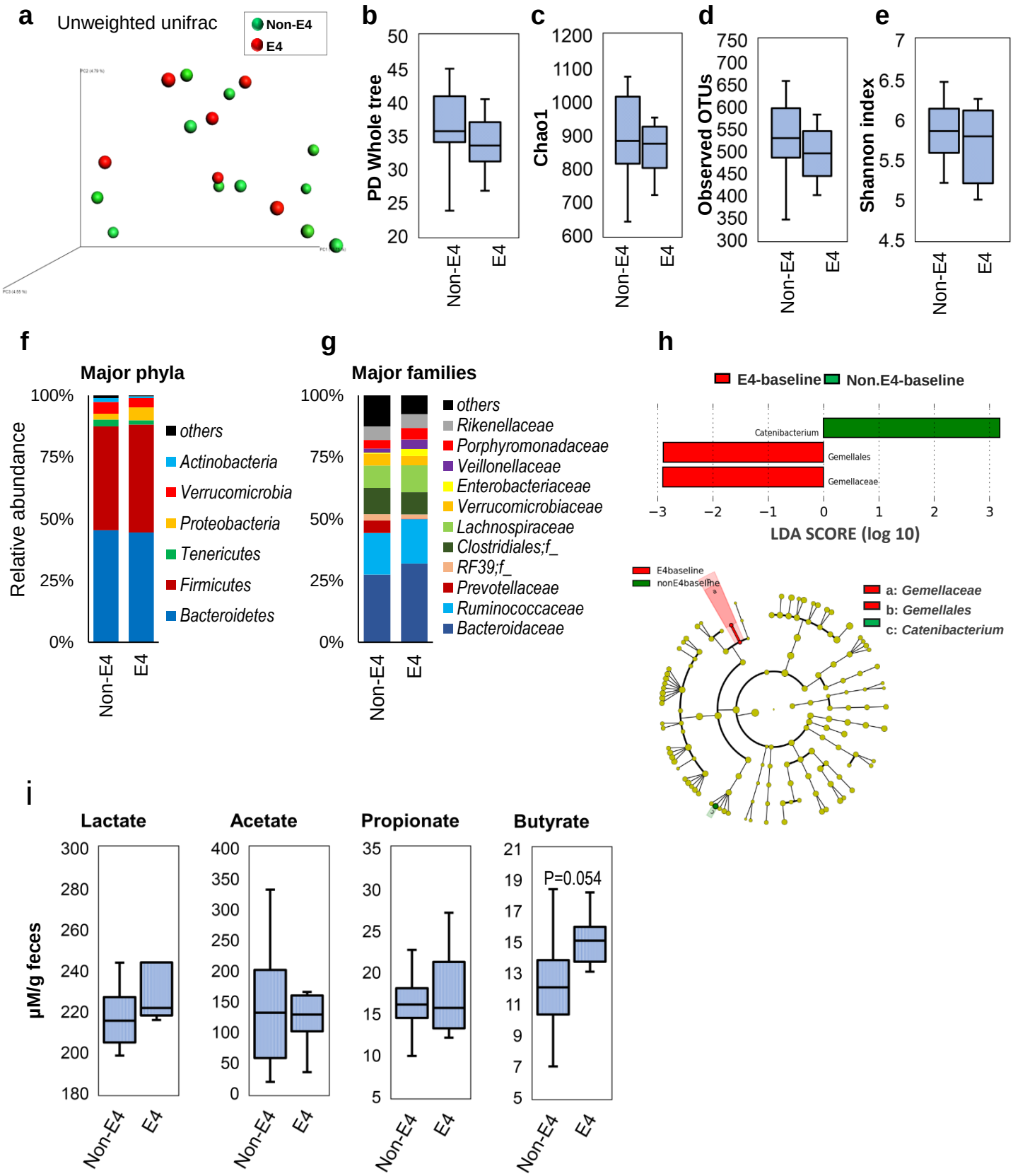
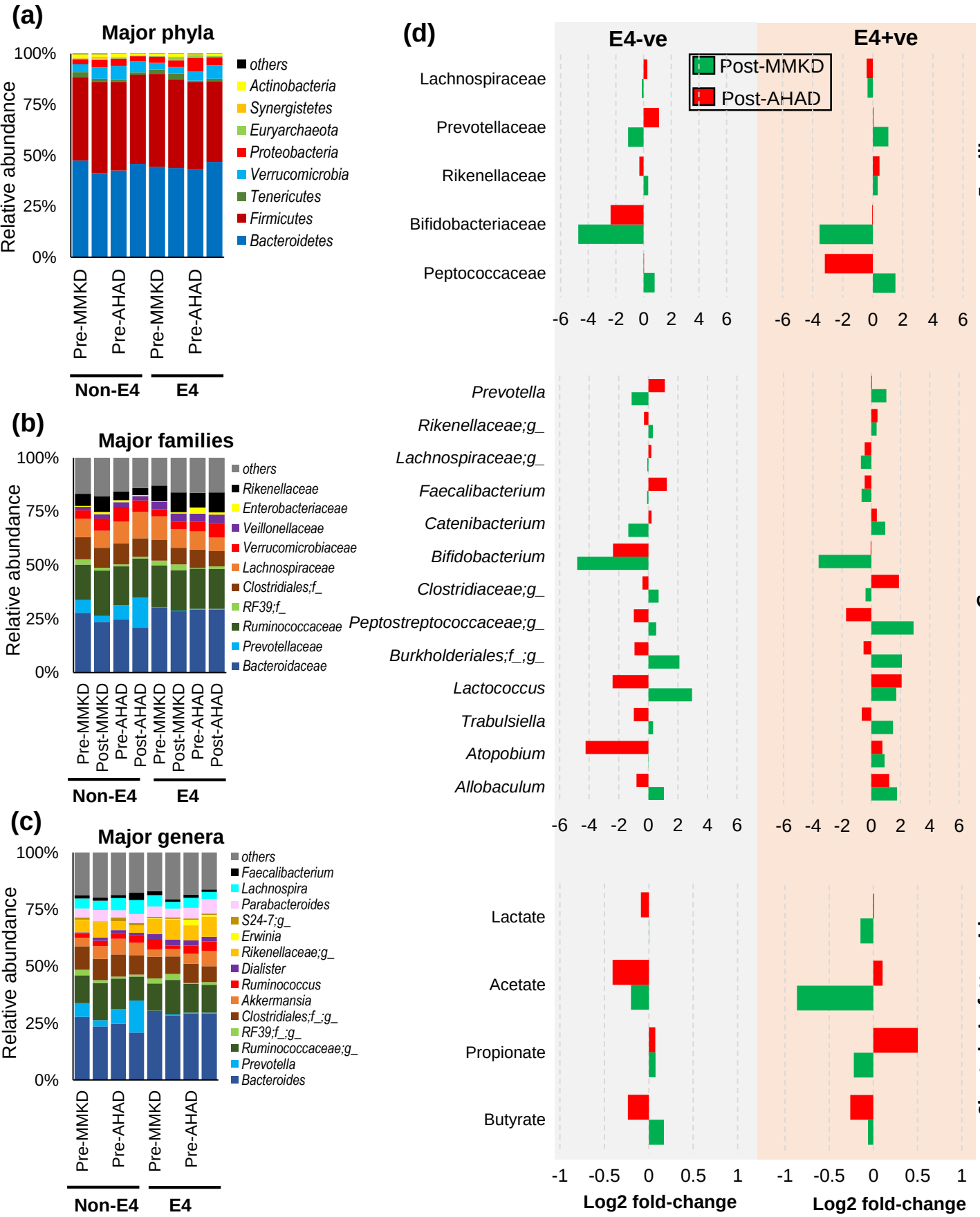
Suppl. Fig. 5. Fecal concentration of lactate and short-chain fatty acids at baseline and endpoint of MMKD and AHAD intervention in subjects with mild cognitive impairment (MCI; n=11) versus cognitively normal (CN) counterparts (n=6).



Suppl. Fig. 6. Association of gut bacterial taxa and fecal organic acids with cerebral spinal fluid biomarkers of Alzheimer's disease in all subjects combined (n=17) (*p<0.05).



Suppl. Fig. 7. Beta-diversity, (a) alpha-diversity indices (b-e), genus- and family-level gut microbiome composition (f-g), and fecal concentration of organic acids (i) in MCI subjects with or without EpoE-4 (E4) genotype. (h) Lefse analysis showing bacterial taxa contributing to the microbiome difference between the two groups.



Suppl. Fig. 8. Gut microbiome composition at phylum-, family- and genus level (a-c) at baseline and endpoint of MMKD and AHAD intervention in subjects with or without EpoE-4 (E4) genotype. (d) Mean Log_2-fold change in major bacterial taxa and fecal organic acids during the two diets.