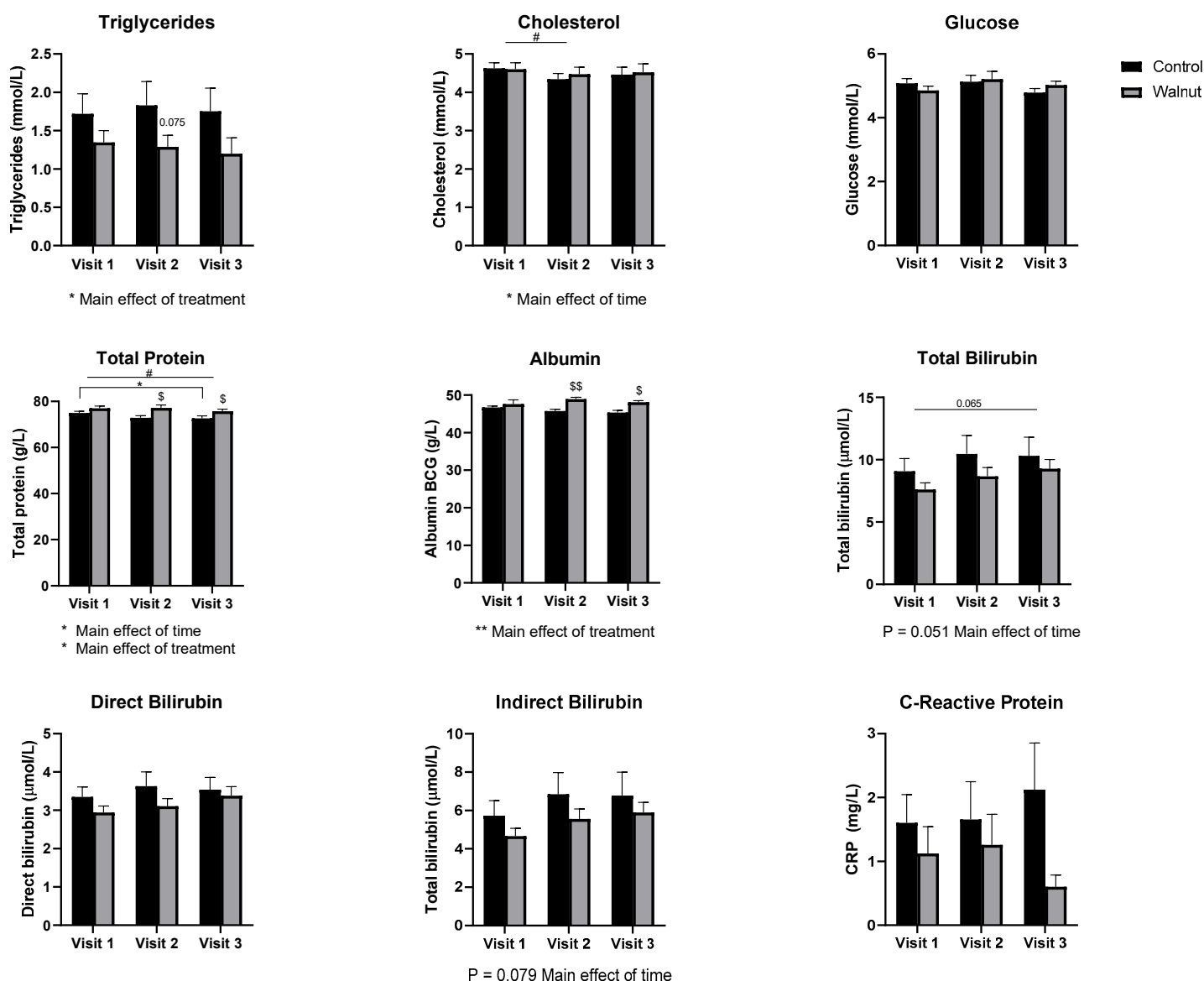
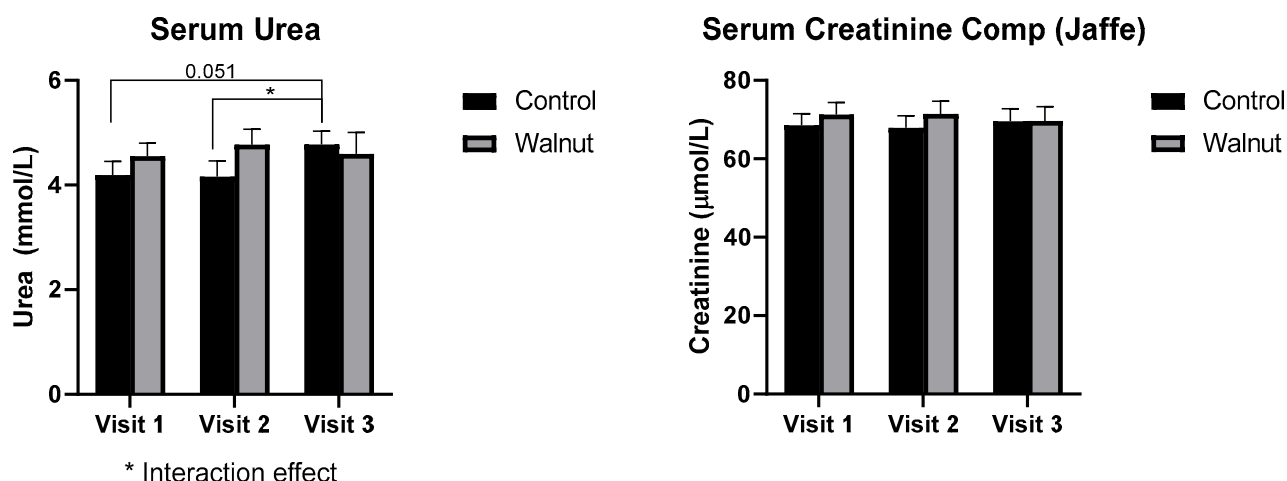


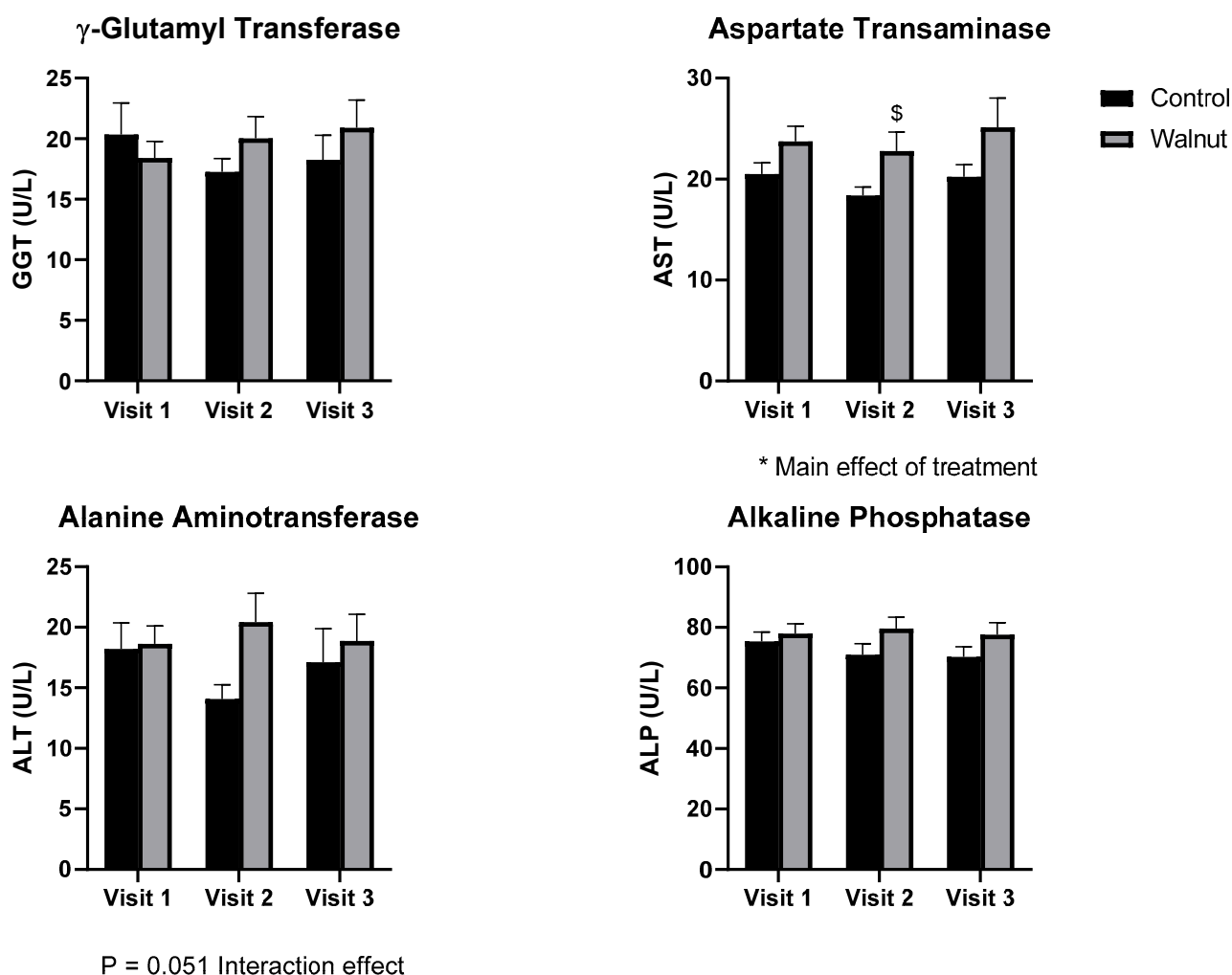
**Figure S1.** The effects of walnut consumption on perceived happiness, self-worth, relationships, independent living, senses and pain before, during and after the university examination period in the 8 dimension-Assessing Quality of Life Questionnaire. Clinical Visit 1 occurred during the first half of the university semester, Visit 2 occurred during the university examination period, and Visit 3 occurred at the end of the university semester. Mixed effects analyses followed by Bonferroni multiple comparisons. \* Denotes a difference in control means compared to the immediately preceding visit unless otherwise indicated by lines, \* =  $p < 0.05$ ; @ denotes a difference in walnut means compared to the immediately preceding visit unless otherwise indicated by lines, @ =  $p < 0.05$ , @@ =  $p < 0.01$ ; # denotes a difference in main effect of time (visit), # =  $p < 0.05$ . Visit 1: control  $n = 34$ ; walnut  $n = 33$ . Visit 2: control  $n = 30$ ; walnut  $n = 29$ . Visit 3: control  $n = 29$ ; walnut  $n = 30$ . Small differences in sample size are due to participant withdrawals and incomplete responses to the questionnaire. Analyses performed on responses from all 3 cohorts.



**Figure S2.** The effects of walnut consumption on biomarkers of general health in blood serum before, during and after the university examination period. Clinical Visit 1 occurred during the first half of the university semester, Visit 2 occurred during the university examination period, and Visit 3 occurred at the end of the university semester. Mixed effects analyses followed by Bonferroni multiple comparisons. \* (Below graph) Denotes significant main effects, \* =  $p < 0.05$ , \*\* =  $p < 0.01$ . \* (On graph) Denotes a difference in control means compared to the immediately preceding visit unless otherwise indicated by lines, \* =  $p < 0.05$ ; \$ Denotes a difference in means between the control and treatment (walnut) group at by visit, \$ =  $p < 0.05$ , \$\$ =  $p < 0.01$ ; # denotes a difference in main effect of time (visit), # =  $p < 0.05$ . Mixed effects analyses followed by Bonferroni multiple comparisons. CRP, C-reactive protein. Refer to Table 2 in main text for group sample numbers for each biomarker.



**Figure S3.** The effects of walnut consumption on biomarkers of general kidney function in blood serum before, during and after the university examination period. Clinical Visit 1 occurred during the first half of the university semester, Visit 2 occurred during the university examination period, and Visit 3 occurred at the end of the university semester. Mixed effects analyses followed by Bonferroni multiple comparisons. \* (Below graph) Denotes significant main effects, \* =  $p < 0.05$ . \* (On graph) Denotes a difference in control means compared to the immediately preceding visit unless otherwise indicated by lines, \* =  $p < 0.05$ . Creatinine composition evaluated using the Jaffe method. Urea – Visit 1: control  $n = 29$ , walnut  $n = 26$ ; Urea – Visit 2: control  $n = 26$ , walnut  $n = 25$ ; Urea – Visit 3: control  $n = 24$ , walnut  $n = 19$ . Creatinine Comp. – Visit 1: control  $n = 30$ , walnut  $n = 37$ ; Creatinine Comp. – Visit 2: control  $n = 26$ , walnut  $n = 27$ ; Creatinine Comp. – Visit 3: control  $n = 24$ , walnut  $n = 23$ . Small differences in sample size are due to technical issues with blood collection and withdrawals from subsequent visits. Analyses performed on samples from all 3 cohorts.



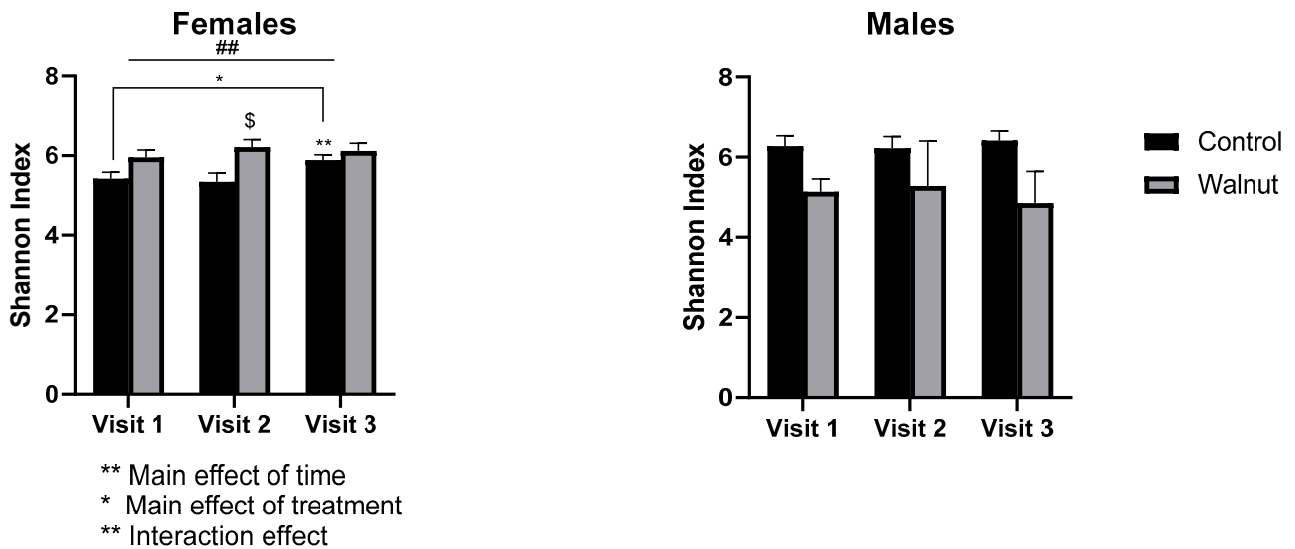
**Figure S4.** The effects of walnut consumption on biomarkers of general liver function in blood serum before, during and after the university examination period. Clinical Visit 1 occurred during the first half of the university semester, Visit 2 occurred during the university examination period, and Visit 3 occurred at the end of the university semester. Mixed effects analyses followed by Bonferroni multiple comparisons. \* (Below graph) Denotes significant main effects, \* =  $p < 0.05$ . \$ Denotes a difference in means between the control and treatment (walnut) group at visit 2, \$ =  $p < 0.05$ . GGT,  $\gamma$ -glutamyl transferase; AST, aspartate transaminase; ALT, alanine aminotransferase; ALP, alkaline phosphatase. GGT – Visit 1: control n = 30, walnut n = 37; GGT – Visit 2: control n = 26, walnut n = 27; GGT – Visit 3: control n = 24, walnut n = 22. AST. – Visit 1: control n = 30, walnut n = 37; AST – Visit 2: control n = 26, walnut n = 23; AST – Visit 3: control n = 24, walnut n = 21. ALT. – Visit 1: control n = 31, walnut n = 37; ALT – Visit 2: control n = 26, walnut n = 26; ALT – Visit 3: control n = 24, walnut n = 22. ALP. – Visit 1: control n = 30, walnut n = 37; ALP – Visit 2: control n = 25, walnut n = 27; ALP – Visit 3: control n = 24, walnut n = 23. Small differences in sample size are due to technical issues with blood collection and withdrawals from subsequent visits. Analyses performed on samples from all 3 cohorts.

**Table S1.** The effects of walnut consumption on total polyphenol content and antioxidant capacity of blood plasma before, during and after the university examination period. Clinical Visit 1 occurred during the first half of the university semester, Visit 2 occurred during the university examination period, and Visit 3 occurred at the end of the university semester. Mixed effects analyses followed by Bonferroni multiple comparisons comparing the control and walnut group at each clinical visit are shown. GAE, gallic acid equivalent; AA, ascorbic acid; TEq, Trolox equivalent. †.

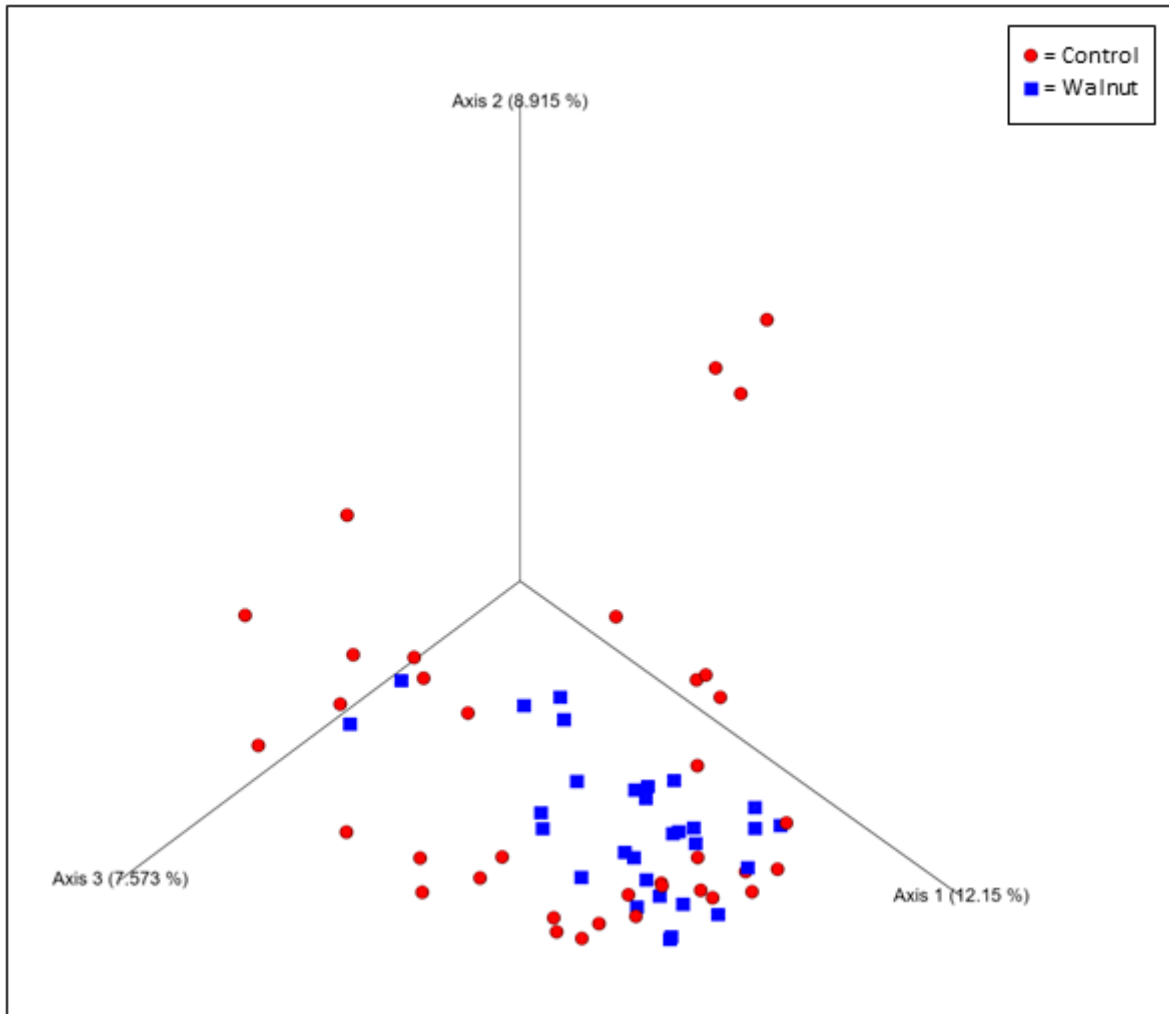
	Control diet			Walnut diet			P value (Control versus Walnut)		
	Visit 1	Visit 2	Visit 3	Visit 1	Visit 2	Visit 3	Visit 1	Visit 2	Visit 3
Total polyphenol content ( $\mu\text{g}$ GAE/ml)	1608.941 $\pm$ 47.00 (n = 25)	1513.031 $\pm$ 45.39 (n = 24)	1706.030 $\pm$ 106.67 (n = 20)	1700.123 $\pm$ 77.27 (n = 24)	1662.863 $\pm$ 41.94 (n = 25)	1585.512 $\pm$ 62.99 (n = 18)	0.9592	0.0578	>0.9999
Ferric reducing ability of plasma ( $\mu\text{g}$ AA/ml)	1421.256 $\pm$ 15.84 (n = 26)	1357.246 $\pm$ 49.12 (n = 26)	1372.314 $\pm$ 28.37 (n = 21)	1437.826 $\pm$ 19.19 (n = 25)	1423.333 $\pm$ 20.24 (n = 25)	1431.871 $\pm$ 22.51 (n = 19)	>0.9999	0.6667	0.3256
Oxygen radical absorbance capacity ( $\mu\text{mol}$ TE/mg)	12394.230 $\pm$ 351.93 (n = 26)	12275.203 $\pm$ 462.36 (n = 26)	12696.725 $\pm$ 426.95 (n = 21)	12211.568 $\pm$ 393.09 (n = 25)	11765.261 $\pm$ 485.19 (n = 25)	485.190 $\pm$ 643.28 (n = 19)	>0.9999	>0.9999	0.9858

Small differences in sample size are due to technical issues with blood collection and withdrawals from subsequent visits. Analyses only performed on samples from cohort 1 and 2.

## $\alpha$ -Diversity



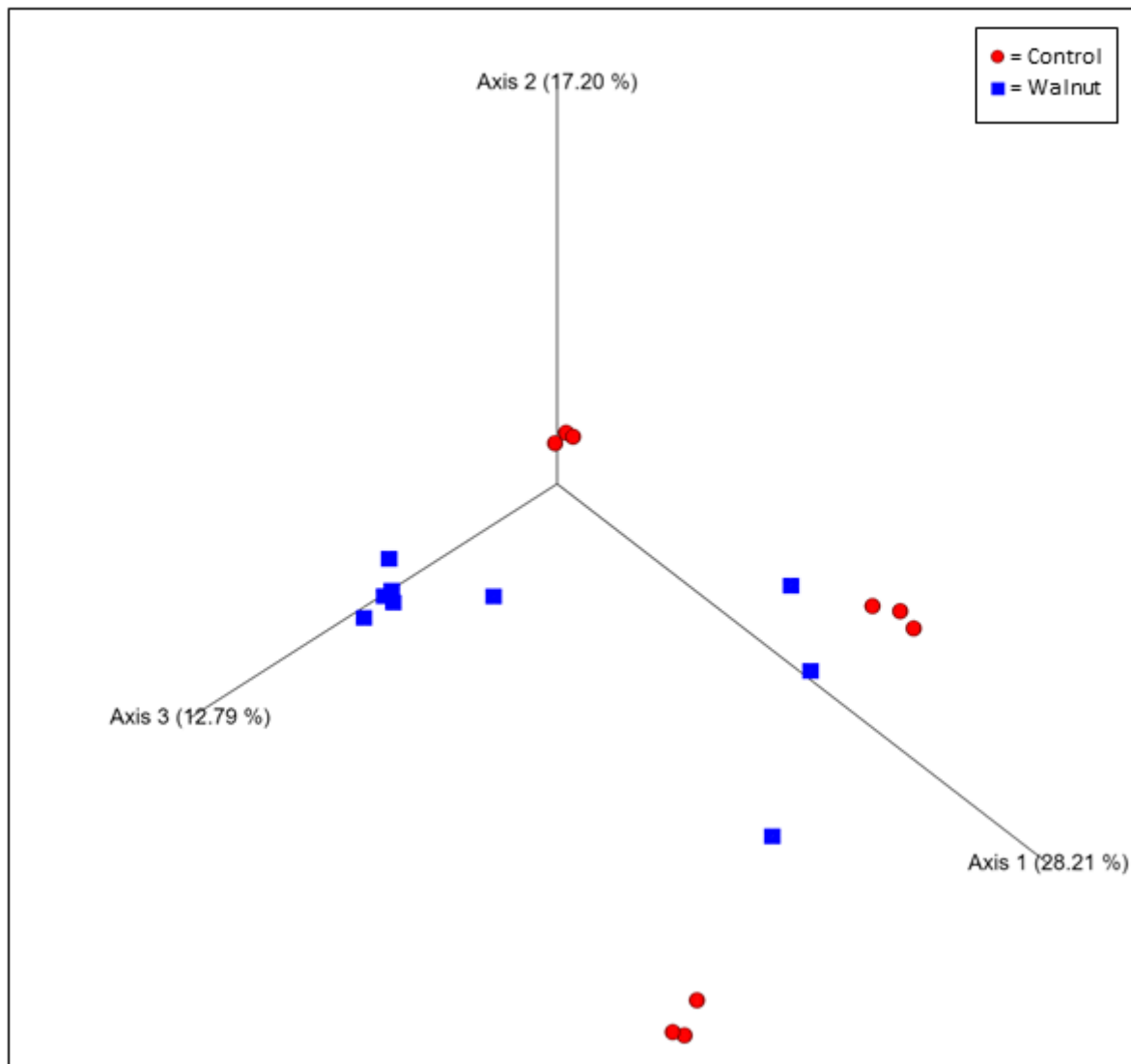
**Figure S5.**  $\alpha$ -Diversity analysis of the gut microbiota in cohort 2 & 3 in females versus males before, during and after the university examination period.  $\alpha$ -Diversity is represented by the Shannon diversity index. Clinical Visit 1 occurred during the first half of the university semester, Visit 2 occurred during the university examination period, and Visit 3 occurred at the end of the university semester. Mixed effects analyses followed by Bonferroni multiple comparisons. \* (Below graph) Denotes significant main effects, \* =  $p < 0.05$ , \*\* =  $p < 0.01$ . \* (On graph) Denotes a difference in control means compared to the immediately preceding visit unless otherwise indicated by lines, \* =  $p < 0.05$ , \*\* =  $p < 0.01$ . \$ Denotes a difference in means between the control and treatment (walnut) group, \$ =  $p < 0.05$ . # denotes a difference in main effect of time (visit), ## =  $p < 0.01$ . Females, Visit 1: control  $n = 14$ ; walnut  $n = 11$ . Visit 2: control  $n = 11$ ; walnut  $n = 10$ ; Visit 3: control  $n = 11$ ; walnut  $n = 9$ . Males, Visit 1: control  $n = 3$ ; walnut  $n = 5$ . Visit 2: control  $n = 3$ ; walnut  $n = 2$ ; Visit 3: control  $n = 3$ ; walnut  $n = 2$ . Results from cohort 2 and 3 are pooled.



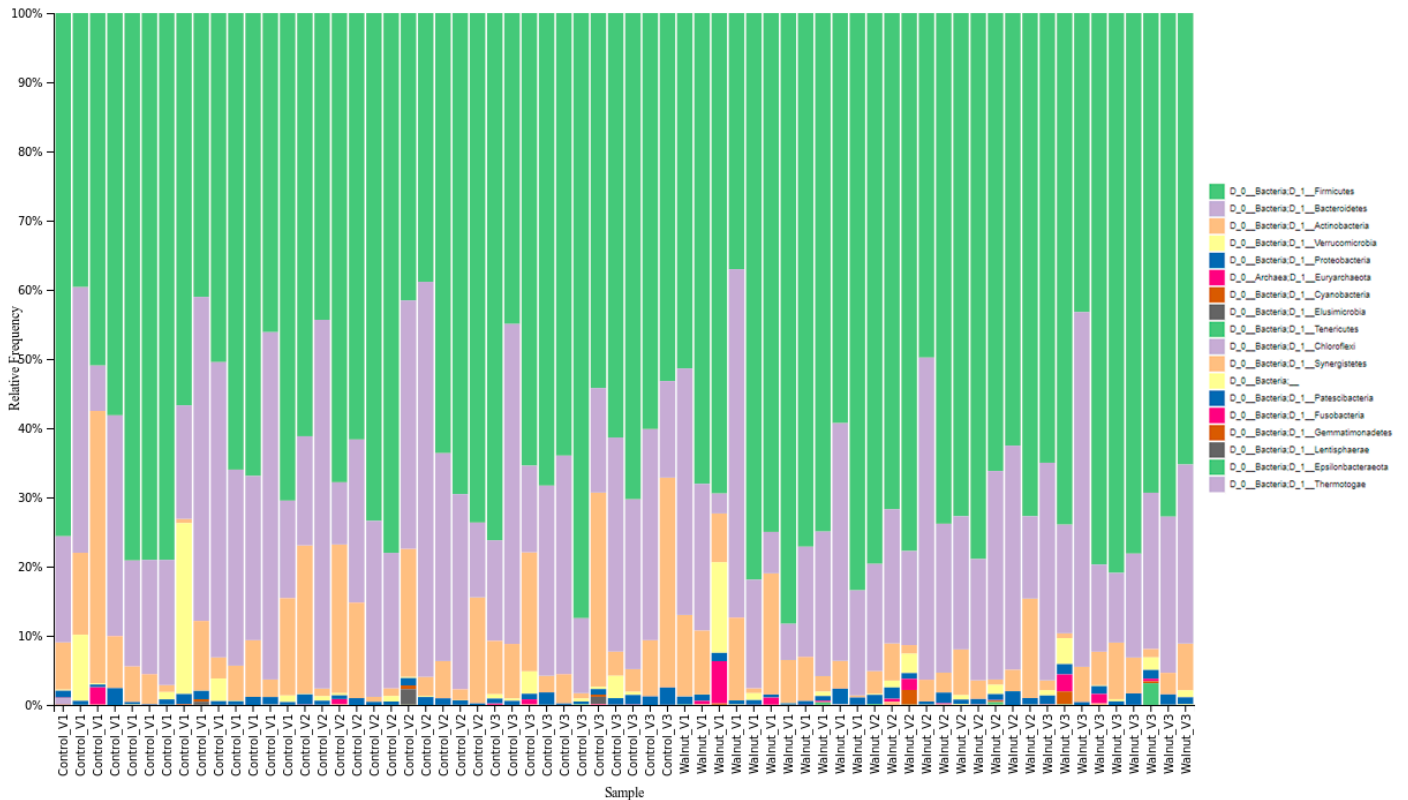
**Figure S6.** Principle coordinate analysis (PCoA) plot of Bray-Curtis dissimilarity in the gut microbiota in cohort 2 & 3 in females. Control, n = 36; Walnut, n = 30. Results from cohort 2 and 3 are pooled.

**Table S2.**  $\beta$ -Diversity analysis of the gut microbiota in cohort 2 & 3 in males before, during and after the university examination period.  $\beta$  - Diversity is represented by the Bray-Curtis dissimilarity index. Clinical Visit 1 occurred during the first half of the university semester, Visit 2 occurred during the university examination period, and Visit 3 occurred at the end of the university semester. Pairwise PERMANOVA comparisons are shown. \* Denotes a difference in control versus walnut means per visit, \* =  $p < 0.05$ . Visit 1: control n = 3; walnut n = 5. Visit 2: control n = 3; walnut n = 2; Visit 3: control n = 3; walnut n = 2. Results from cohort 2 and 3 are pooled.

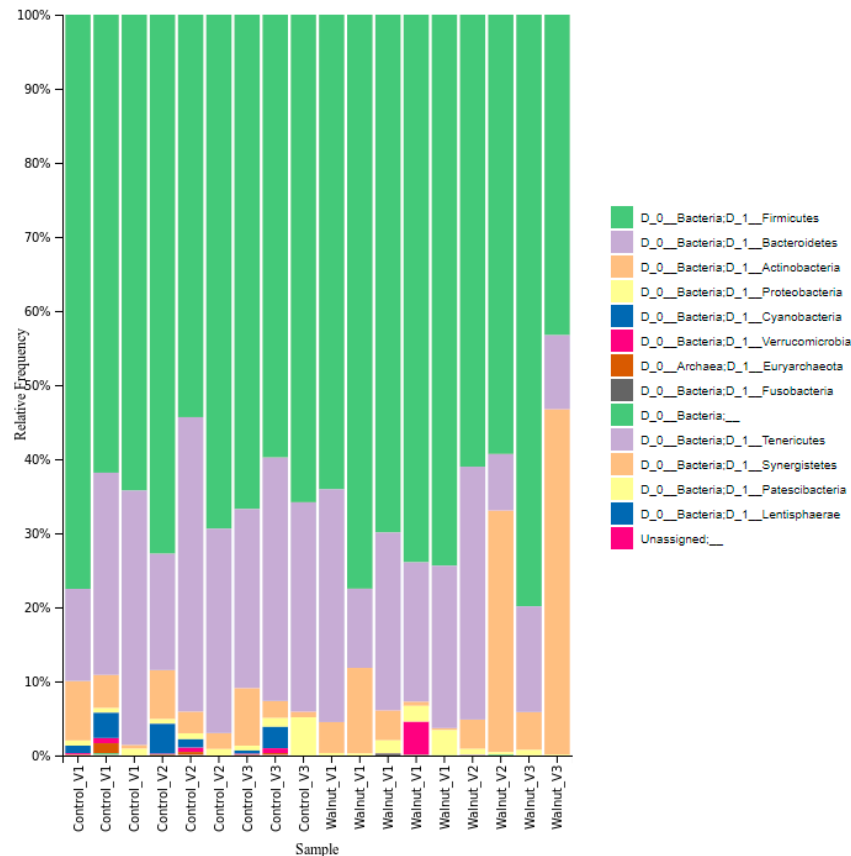
Comparison 1	Comparison 2	Sample size	Permutations	pseudo-F	p-value	q-value
Control Visit 1	Control Visit 2	6	999	0.241876	0.79	1
Control Visit 1	Control Visit 3	6	999	0.23223	0.702	1
Control Visit 1	Walnut Visit 1	8	999	1.355055	0.042 *	0.36
Control Visit 1	Walnut Visit 2	5	999	0.846519	0.815	1
Control Visit 1	Walnut Visit 3	5	999	1.191944	0.304	0.8025
Control Visit 2	Control Visit 3	6	999	0.1401	1	1
Control Visit 2	Walnut Visit 1	8	999	1.436977	0.068	0.36
Control Visit 2	Walnut Visit 2	5	999	0.870726	0.808	1
Control Visit 2	Walnut Visit 3	5	999	1.268063	0.315	0.8025
Control Visit 3	Walnut Visit 1	8	999	1.384651	0.072	0.36
Control Visit 3	Walnut Visit 2	5	999	0.874581	0.799	1
Control Visit 3	Walnut Visit 3	5	999	1.213358	0.321	0.8025
Walnut Visit 1	Walnut Visit 2	7	999	0.576801	0.949	1
Walnut Visit 1	Walnut Visit 3	7	999	0.534501	1	1
Walnut Visit 2	Walnut Visit 3	4	999	0.279272	1	1



**Figure S7.** Principle coordinate analysis (PCoA) plot of Bray-Curtis dissimilarity in the gut microbiota in cohort 2 & 3 in males. Control, n = 9; Walnut, n = 9. Results from cohort 2 and 3 are pooled.



**Figure S8.** Bar plot showing the relative taxonomic frequency of the gut microbiota at the phylum level in females before, during and after the university examination period. Clinical Visit 1 (V1) occurred during the first half of the university semester, Visit 2 (V2) occurred during the university examination period, and Visit 3 (V3) occurred at the end of the university semester. Visit 1: control n = 14; walnut n = 11. Visit 2: control n = 11; walnut n = 10; Visit 3: control n = 11; walnut n = 9. Results from cohort 2 and 3 are pooled.



**Figure S9.** Bar plot showing the relative taxonomic frequency of the gut microbiota at the phylum level in males before, during and after the university examination period. Clinical Visit 1 (V1) occurred during the first half of the university semester, Visit 2 (V2) occurred during the university examination period, and Visit 3 (V3) occurred at the end of the university semester. Visit 1: control n = 3; walnut n = 5. Visit 2: control n = 3; walnut n = 2; Visit 3: control n = 3; walnut n = 2. Results from cohort 2 and 3 are pooled.



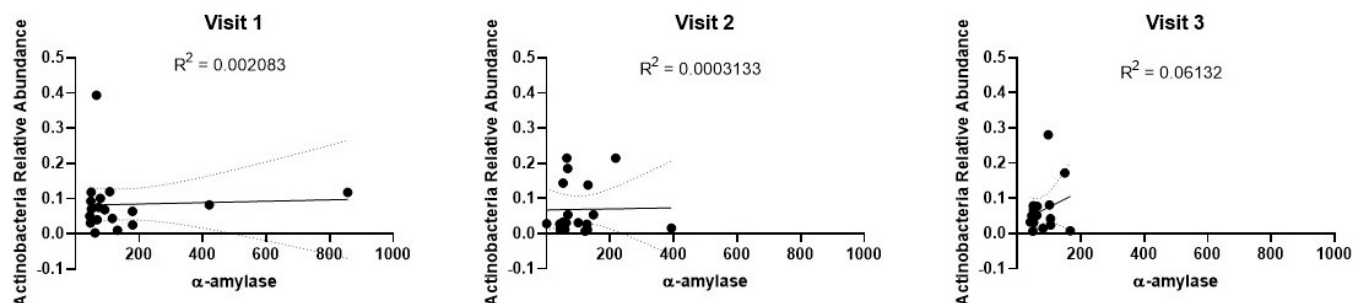


**Figure S10.** Bar plot showing the relative taxonomic frequency of the gut microbiota at the family level in females before, during and after the university examination period. Clinical Visit 1 (V1) occurred during the first half of the university semester, Visit 2 (V2) occurred during the university examination period, and Visit 3 (V3) occurred at the end of the university semester. Visit 1: control n = 14; walnut n = 11. Visit 2: control n = 11; walnut n = 10; Visit 3: control n = 11; walnut n = 9. Results from cohort 2 and 3 are pooled.

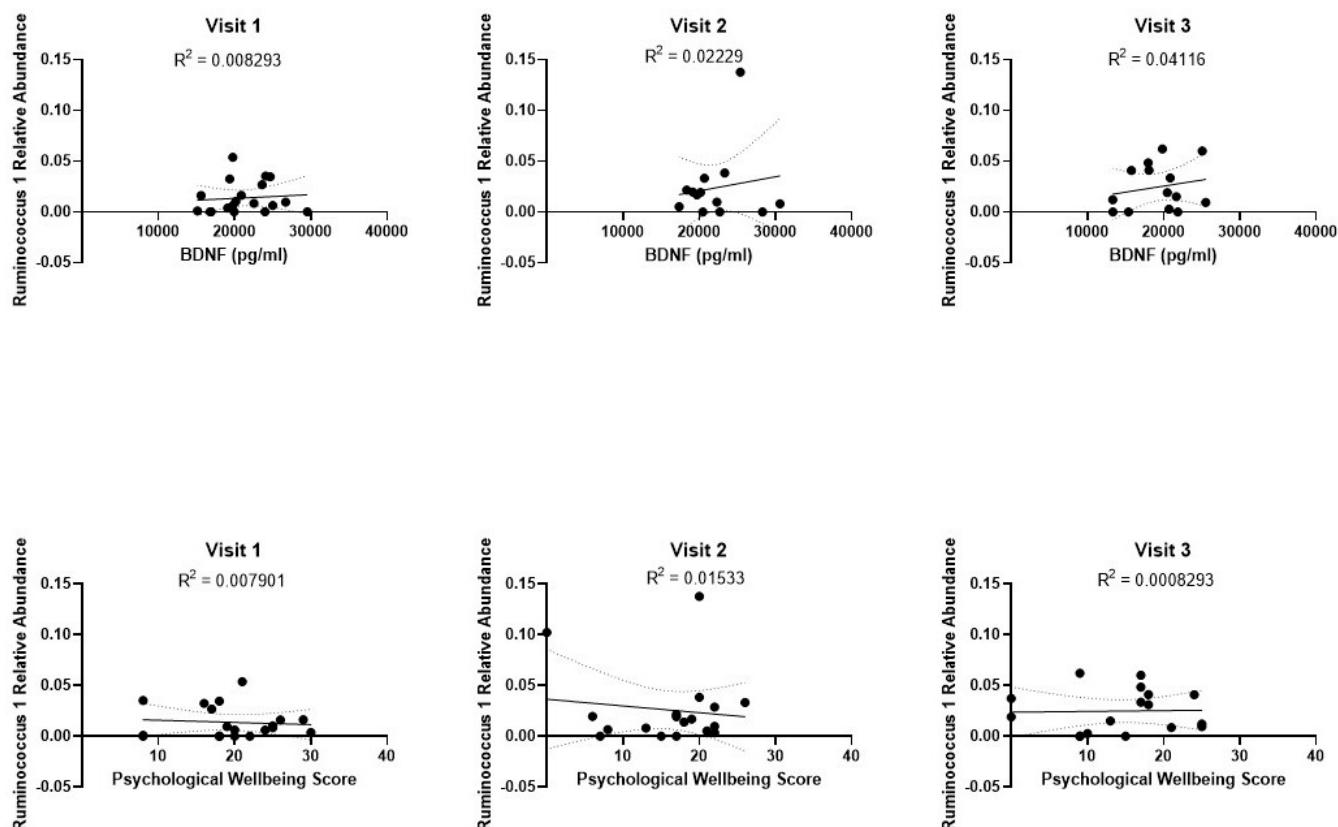


D_0_Bacteria;D_1_Firmicutes;D_2_Clostridia;D_3_Clostridiales;D_4_Lachnospiraceae
D_0_Bacteria;D_1_Firmicutes;D_2_Clostridia;D_3_Clostridiales;D_4_Ruminococcaceae
D_0_Bacteria;D_1_Bacteroidetes;D_2_Bacteroidia;D_3_Bacteroidales;D_4_Prevotellaceae
D_0_Bacteria;D_1_Bacteroidetes;D_2_Bacteroidia;D_3_Bacteroidales;D_4_Rikenellaceae
D_0_Bacteria;D_1_Firmicutes;D_2_Negativicutes;D_3_Selenomonadales;D_4_Veillonellaceae
D_0_Bacteria;D_1_Actinobacteria;D_2_Actinobacteria;D_3_Bifidobacteriales;D_4_Bifidobacteriaceae
D_0_Bacteria;D_1_Firmicutes;D_2_Negativicutes;D_3_Selenomonadales;D_4_Acidaminococcaceae
D_0_Bacteria;D_1_Actinobacteria;D_2_Coriobacterii;D_3_Coriobacteriales;D_4_Coriobacteriaceae
D_0_Bacteria;D_1_Bacteroidetes;D_2_Bacteroidia;D_3_Bacteroidales;D_4_Rikenellaceae
D_0_Bacteria;D_1_Firmicutes;D_2_Clostridia;D_3_Clostridiales;D_4_Christensenellaceae
D_0_Bacteria;D_1_Firmicutes;D_2_Clostridia;D_3_Clostridiales;D_4_Clostridiaceae 1
D_0_Bacteria;D_1_Proteobacteria;D_2_Gammaproteobacteria;D_3_Betaproteobacteriales;D_4_Burkholderiaceae
D_0_Bacteria;D_1_Proteobacteria;D_2_Alphaproteobacteria;D_3_Rhodospirillales;D_4_uncultured
D_0_Bacteria;D_1_Firmicutes;D_2_Erysipelotrichia;D_3_Erysipelotrichales;D_4_Erysipelotrichaceae
D_0_Bacteria;D_1_Bacteroidetes;D_2_Bacteroidia;D_3_Bacteroidales;D_4_Tannerellaceae
D_0_Bacteria;D_1_Firmicutes;D_2_Clostridia;D_3_Clostridiales;D_4_Peptostreptococcaceae
D_0_Bacteria;D_1_Bacteroidetes;D_2_Bacteroidia;D_3_Bacteroidales;D_4_Barnesiellaceae
D_0_Bacteria;D_1_Bacteroidetes;D_2_Bacteroidia;D_3_Bacteroidales;D_4_Muribaculaceae
D_0_Bacteria;D_1_Cyanobacteria;D_2_Melainabacteria;D_3_Gastranaerophilales;__
D_0_Bacteria;D_1_Firmicutes;D_2_Clostridia;D_3_Clostridiales;D_4_Clostridiales vadinBB60 group
D_0_Bacteria;D_1_Actinobacteria;D_2_Coriobacterii;D_3_Coriobacteriales;D_4_Eggerthellaceae
D_0_Bacteria;D_1_Verrucomicrobia;D_2_Verrucomicrobiae;D_3_Verrucomicrobiales;D_4_Akkermansiaceae
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D_0_Bacteria;D_1_Cyanobacteria;D_2_Melainabacteria;D_3_Gastranaerophilales;D_4_uncultured bacterium
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D_0_Bacteria;D_1_Proteobacteria;D_2_Gammaproteobacteria;D_3_Enterobacteriales;D_4_Enterobacteriaceae
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D_0_Bacteria;D_1_Firmicutes;D_2_Clostridia;D_3_Clostridiales;D_4_Peptococcaceae
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D_0_Bacteria;D_1_Firmicutes;D_2_Bacilli;D_3_Lactobacillales;D_4_Lactobacillaceae
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D_0_Bacteria;D_1_Actinobacteria;D_2_Coriobacterii;D_3_Coriobacteriales;D_4_Coriobacteriales Incertae Sedis
D_0_Bacteria;D_1_Firmicutes;D_2_Clostridia;D_3_Clostridiales;D_4_Defluviitaleaceae
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D_0_Bacteria;D_1_Firmicutes;D_2_Bacilli;D_3_Bacillales;D_4_Family XI
D_0_Bacteria;D_1_Tenericutes;D_2_Mollicutes;D_3_Mollicutes RF39;D_4_metagenome
D_0_Bacteria;D_1_Firmicutes;D_2_Clostridia;D_3_DTU014;D_4_uncultured bacterium
D_0_Bacteria;D_1_Proteobacteria;__;__;__
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Unassigned;__;__;__;__
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D_0_Bacteria;D_1_Firmicutes;D_2_Bacilli;D_3_Lactobacillales;D_4_Aerococcaceae

**Figure S11.** Bar plot showing the relative taxonomic frequency of the gut microbiota at the family level in males before, during and after the university examination period. Clinical Visit 1 (V1) occurred during the first half of the university semester, Visit 2 (V2) occurred during the university examination period, and Visit 3 (V3) occurred at the end of the university semester. Visit 1: control n = 3; walnut n = 5. Visit 2: control n = 3; walnut n = 2; Visit 3: control n = 3; walnut n = 2. Results from cohort 2 and 3 are pooled.



**Figure S12.** Correlations between Actinobacteria relative abundance and salivary  $\alpha$ -amylase in females before, during and after the university examination period. Clinical Visit 1 occurred during the first half of the university semester, Visit 2 occurred during the university examination period, and Visit 3 occurred at the end of the university semester. Simple linear regression. Visit 1: control n = 14; walnut n = 11. Visit 2: control n = 11; walnut n = 10; Visit 3: control n = 11; walnut n = 9. Results from cohort 2 and 3 are pooled.



**Figure S13.** Correlations between *Ruminococcus 1* relative abundance, serum BDNF and Psychological Wellbeing Scores from the MHC in females before, during and after the university examination period. Clinical Visit 1 occurred during the first half of the university semester, Visit 2 occurred during the university examination period, and Visit 3 occurred at the end of the university semester. Simple linear regression. Visit 1: control n = 14; walnut n = 11. Visit 2: control n = 11; walnut n = 10; Visit 3: control n = 11; walnut n = 9. BDNF, mature brain-derived neurotrophic factor. MHC, Mental Health Continuum. Results from cohort 2 and 3 are pooled.