Table S1 Content of macronutrients, wholegrain, dietary fibres, resistant starch, arabinoxylan and alkylresorcinol homologs in the study products

	Energy[1] (MJ/100g)	**Protein[1] (g/100g)**	**Fat[1] (g/100g)**	**CHO[1] (g/100g)**	**WG[1] (g/100g)**	**Total DF[1] (g/100g)**	**RS[2] (g/100g)**	**AX[2] (g/100g)**	**Total AR[2] (µg/g)**	**AR C15:0[2] (µg/g)**	**AR C17:1[2] (µg/g)**	**AR C17:0[2] (µg/g)**	**AR C19:1[2] (µg/g)**	**AR C19:0[2] (µg/g)**	**AR C21:1[2] (µg/g)**	**AR C21:0[2] (µg/g)**	**AR C23:1[2] (µg/g)**	**AR C23:0[2] (µg/g)**	**AR C25:1[2] (µg/g)**	**AR C25:0[2] (µg/g)**
Wholegrain products																				
Rolled Oats	1.43	13	6.5	56	100	10	6.1	2.5	0	0	0	0	0	0	0	0	0	0	0	0
Oat flakes	1.65	12	6	68	84	9	8.1	2.2	0	0	0	0	0	0	0	0	0	0	0	0
Wholegrain rye kernel bread	0.8	6	1	35	50	8	5.3	18.4	934.2	13.4	33.0	173.5	76.4	213.8	60.3	176.9	29.3	74.5	21.4	61.7
Wholegrain wheat buns	0.97	9.5	2.5	38	50	9	4.8	9.1	352.1	1.5	2.6	16.3	18.0	104.5	14.1	152.1	0.0	30.7	0.0	12.2
Wholegrain wheat pasta	1.45	14	2	65	55	7	2.6	5.4	313.3	0.0	0.0	2.3	3.8	37.1	11.4	172.0	6.5	58.6	0.0	21.4
Wholegrain wheat kernels	1.41	11	2.5	61	100	12	7.8	7.3	652.7	3.2	4.1	25.3	28.0	185.3	21.3	289.9	0.0	65.0	0.0	30.6
Wholegrain bulgur	1.49	11	1.5	65	100	13	3.2	4.5	376.9	4.1	4.5	18.6	22.2	121.2	13.7	153.7	0.0	27.7	0.0	11.3
Wholegrain rye crisp bread	1.45	9	1.5	66	90	15	7.2	9.5	1120.8	16.4	40.1	202.5	93.1	263.1	71.9	211.8	35.4	87.7	23.0	75.9
Refined grain products																				
Wheat-rice flakes	1.61	14	1.5	76	-	2.5	4.6	1.5	130.6	1.5	1.6	5.5	6.5	37.0	4.8	56.7	0.0	11.8	0.0	5.1
Oat flakes	1.65	12	6	68	84	9		2.2	0	0	0	0	0	0	0	0	0	0	0	0
Maslin rye bread[3]	1.06	9	5	38	-	5	3.7	8.8	597.8	9.5	21.1	114.3	48.1	136.4	39.9	112.9	20.0	47.9	12.6	35.3
Wheat buns	1	9	1.5	45	-	2.5	3.6	6.5	25.7	0.0	0.0	1.3	0.9	6.2	0.8	10.6	0.6	3.6	0.0	1.7
Wheat pasta	1.5	12	2	71	-	3.5	2.7	2.3	48.9	0.0	0.1	0.2	0.6	4.8	1.8	26.3	1.2	10.3	0.0	3.8
Pearled spelt kernels[3]	1.45	13	3	61	-	7.5	3.8	4.6	433.1	1.7	2.9	13.7	20.9	107.8	19.8	213.3	0.0	52.8	0.0	0.0
Bulgur	1.4	12	2.5	63	-	-	2.8	3.3	70.1	0.0	0.0	0.5	1.1	8.6	2.9	35.4	1.6	14.1	0.0	5.9
Crisp bread	1.75	12	10	65	-	6	6	2.8	74.4	0.0	0.0	3.2	3.5	21.5	1.3	34.2	0.0	7.6	0.0	3.1

Abbreviations: AR, alkylresorcinols, AX, arabinoxylan; CHO, carbohydrates; DF, dietary fibres; RS, resistant starch; WG, wholegrain

[1] Derived from package labelling

[2] Experimental measured values

[3] The higher alkylresorcinol content in this product is due to a higher flour extraction rate than standard refined flour, but the product still does not contain all parts of the cereal grain and counts as a refined cereal product.

Table S2 Baseline characteristics of study completers (mean ± SD)

	All (n=50)	Men (n=18)	Women (n=32)
Age (y)	48.6 ± 11.1	46.2 ± 11.8	49.9 ± 10.7
BMI (kg/m2)	28.9 ± 3.6	29.1± 2.7	28.9 ± 4.0
Waist circumference	101.4 ± 8.6	105.4 ± 7.0	99.2 ± 8.8
Body weight (kg)	86.1 ± 13.0	93.8 ± 11.5	81.7 ± 11.8
Body fat mass (kg)	28.9 ± 9.3	22.9 ± 6.3	32.3 ± 9.1
Fat free mass	57.2 ± 11.9	70.9 ± 7.4	49.5 ± 4.6
Systolic BP (mmHg)	126 ± 13	130 ± 12	124 ± 13
Diastolic BP (mmHg)	81 ± 8	82 ± 8	81 ± 9
HOMA-IR	3.0 ± 1.7	3.0 ± 1.4	2.9 ± 1.8
Fasting plasma glucose (mmol/L)	5.7 ± 0.6	5.8 ± 0.4	5.6 ± 0.7
Fasting serum TAG	1.2 ± 0.5	1.3 ± 0.5	1.2 ± 0.5
Fasting serum HDL cholesterol	1.3 ± 0.3	1.2 ± 0.2	1.4 ± 0.3

Abbreviations: BP, blood pressure; HOMA, Homeostatic model assessment for insulin resistance; FFA, free-fatty acids;

Table S3 Study product consumption for all participants during wholegrain and refined grain periods (mean±SD)

Wholegrain products	Product intake (g/day)	Product intake (%)	Refined grain products	Product intake (g/day)	Product intake (%)
Rolled Oats	27.8 ± 15.4	11%	Wheat-rice flakes	28.3 ± 14.9	11%
Oat flakes	11.7 ± 9.0	5%	Oat flakes	7.2 ± 5.7	3%
Wholegrain rye kernel bread	72.5 ± 25.7	30%	Maslin rye bread	80.5 ± 30.1	32%
Wholegrain wheat buns	60.7 ± 18.1	25%	Wheat buns	68.6 ± 20.5	27%
Wholegrain wheat pasta	20.5 ± 8.4	8%	Wheat pasta	19.5 ± 10.0	8%
Wholegrain wheat kernels	12.5 ± 8.5	5%	Pearled spelt kernels	15.4 ± 8.0	6%
Wholegrain bulgur	19.8 ± 10.8	8%	Bulgur	19.6 ± 7.9	8%
Wholegrain rye crisp bread	18.1 ± 8.6	7%	Crisp bread	16.2 ± 8.3	6%

Intervention products substituted all dietary cereal products during the studies and were consumed *ad libitum*

Table S4 Average monosaccharide composition of the refined grain and wholegrain products (values are presented as mean ± SD)

Monosaccharide	Refined grain products (mg/g dry matter)	Wholegrain products (mg/g dry matter)	Fold difference (wholegrain/control)
Fucose	0.0±0.0	0.1±0.0	2.1
Arabinose	11.4±0.2	19.9±1.5	1.8
Rhamnose	Nd	Nd	-
Galactose	4.3±0.1	5.1±0.4	1.2
Starch glucose	769.2±11.7	740.3±32.7	1
Non-starch glucose	55.0±2.0	64.9±3.4	1.2
Xylose	17.1±0.3	29.2±2.9	1.7
Mannose	1.9±0.1	2.5±0.3	1.3
Galacturonic acid	5.8±0.1	1.7±0.2	0.3
Glucoronic acid	Nd	0.5±0.1	-
Ash	21.5±1.1	21.5±1.1	1

Nd, not detected

Monosaccharide composition analysis was performed in triplicates

Table S5 Diet composition of the subjects before and during the interventions

Food group[1]	**Baseline diet**	**Refined grain diet**	**Wholegrain diet**
	Mean (CI 95%)	*Mean (CI 95%)*	*Mean (CI 95%)*
Milk and milk products	286 (231-342)	284 (228-341)	284 (222-347)
Cheese and cheese products	37 (31-43)	34 (26-42)	31 (23-39)
Cereals and starch products	246 (222-270)	291 (274-309)^{a}	288 (268-309)^{a}
Vegetables	190 (144-236)^{a}	143 (106-181)^{b}	161 (124-198)^{a,b}
Fruits	160 (131-189)^{a}	187 (143-232)^{a,b}	204 (158-250)^{b}
Meat	106 (90-122)	106 (89-122)	97 (83-111)
Fish	22 (16-27)	26 (19-33)	27 (18-35)
Poultry	36 (25-47)	30 (21-40)	35 (23-47)
Eggs	24 (18-30)	22 (16-28)	19 (13-26)
Potatoes	74 (57-91)	29 (18-40)^{a}	31 (19-44)^{a}
Dietary fibre	***23 (21-26)*** ^{a}	***21 (19-23)*** ^{a}	***33 (31-36)*** ^{b}
Wholegrain	***68 (56-79)*** ^{a}	***13 (10-16)*** ^{b}	***179 (165-192)*** ^{c}
Water	2007 (1789-2225)^{a}	1795 (1569-2021)^{b}	2029 (1804-2255)^{a,b}

[1] Dietary intake (g/day) was based on the average of 4 days dietary registration by all subjects (n=50)

Differences between diets were assessed by a one-way ANOVA with Tukey's Multiple Comparison test. Different superscripts mean statistically different within a row ($P<0.05$).

Table S6 Associations between serum inflammatory markers and plasma alkylresorcinols

	Serum CRP		Serum IL-6	
Plasma alkylresorcinols	**Effect size**	**P-value**	**Effect size**	**P-value**
C17:0	-0.11	0.18	-0.18	0.0003
C19:0	-0.11	0.18	-0.11	0.027
C20:0	0.00	0.97	-0.01	0.84
C21:0	-0.12	0.12	-0.07	0.13
C22:0	-0.05	0.13	-0.02	0.35
C23:0	-0.12	0.11	-0.08	0.10
C24:0	-0.04	0.33	0.00	0.91
C25:0	-0.11	0.13	-0.08	0.06
C26:0	0.01	0.75	0.02	0.50
Total (C17:0-C26:0)	-0.13	0.11	-0.09	0.059
C17:0-to-C21:0 ratio	0.03	0.76	-0.17	0.024

Calculated using linear mixed model adjusting for age and gender (n=50) on log-transformed plasma alkylresorcinol data with added pseudocounts where the minimum value for each homolog was substituted instead of a zero value.

Table S7 Changes in metagenomic species (MGS)

MGS	Taxonomical annotation	Prevalence	Prevalence (WG->C)	Prevalence (C->WG)	Median fold change Wholegrain	Median fold change Control	Linear mixed model effect size	P-value	FDR-corrected P
MGS:igc654	Clostridiales	28	14	14	1.76	0.66	2.05	0.0004	0.16
MGS:igc102	Erysipelatoclostridium ramosum	25	14	11	0.81	0.77	-2.66	0.0008	0.16
MGS:igc460	Clostridiales	20	10	10	1.02	0.99	-2.48	0.001	0.16
MGS:igc633	Clostridiales	41	22	19	1.22	0.65	1.41	0.001	0.16
MGS:igc139	Ruminococcus	46	25	21	0.54	1.67	-1.64	0.002	0.18
MGS:igc291	Faecalibacterium prausnitzii	48	27	21	1.21	0.75	0.93	0.002	0.22
MGS:igc359	Clostridiales	43	24	19	1.17	1.04	1.77	0.004	0.30
MGS:igc309	Ruminococcus lactaris	40	23	17	1.01	0.53	1.82	0.005	0.31
MGS:igc734	Streptococcus thermophilus	48	27	21	0.59	0.87	-1.56	0.006	0.33
MGS:igc584	Holdemanella biformis	22	9	13	0.80	1.37	-1.49	0.007	0.38
MGS:igc517	Faecalibacterium prausnitzii	48	27	21	1.34	0.83	0.98	0.010	0.38
MGS:igc171	Faecalibacterium prausnitzii	48	27	21	1.20	0.99	0.59	0.011	0.38
MGS:igc213	Coprococcus	42	23	19	1.07	0.59	1.44	0.011	0.38
MGS:igc9	Bacteroides thetaiotaomicron	42	23	19	0.94	1.37	-0.70	0.011	0.38
MGS:igc263	Prevotella copri	34	19	15	1.06	0.87	1.52	0.011	0.38
MGS:igc292	Faecalibacterium prausnitzii	47	26	21	1.24	0.77	1.09	0.012	0.38
MGS:igc157	Clostridiales	27	12	15	0.76	1.55	-1.24	0.012	0.38
MGS:igc762	Clostridiales	35	18	17	0.69	1.05	-1.09	0.016	0.43
MGS:igc1140	Bacteria	12	8	4	0.97	1.14	5.17	0.017	0.43
MGS:igc784	Clostridiales bacterium 1_7_47FAA	23	9	14	0.65	1.37	-2.20	0.017	0.43
MGS:igc613	Clostridiales	13	8	5	1.54	0.72	2.81	0.018	0.43
MGS:igc89	Subdoligranulum sp. 4_3_54A2FAA	48	27	21	0.86	1.30	-0.69	0.020	0.43
MGS:igc886	Erysipelotrichaceae	19	11	8	1.16	0.61	2.61	0.021	0.43
MGS:igc389	Clostridiales	18	10	8	0.99	0.50	2.43	0.022	0.43
MGS:igc763	Clostridiales	25	11	14	0.64	1.16	-1.94	0.022	0.43
MGS:igc745	Streptococcus salivarius	48	27	21	0.88	1.33	-0.50	0.023	0.43
MGS:igc1203	Bacteria	42	23	19	0.99	0.47	0.93	0.023	0.43
MGS:igc318	Bacteria	27	15	12	0.59	1.17	-2.15	0.024	0.43
MGS:igc1259	Eukaryota	14	9	5	0.12	0.50	-3.44	0.024	0.43
MGS:igc818	Clostridiales	24	15	9	0.79	1.12	-1.67	0.024	0.43
MGS:igc938	Firmicutes	40	22	18	1.04	0.78	1.19	0.025	0.43
MGS:igc644	Clostridiales	32	20	12	1.06	0.56	1.63	0.029	0.46
MGS:igc100	Bacteroides	17	8	9	0.99	1.29	-1.84	0.029	0.46
MGS:igc732	butyrate-producing bacterium SS3/4	47	26	21	1.44	0.75	0.77	0.030	0.46
MGS:igc24	Bacteroides	39	22	17	0.79	1.24	-0.89	0.030	0.46
MGS:igc691	Lachnospiraceae	47	27	20	1.25	0.99	0.89	0.032	0.47
MGS:igc1200	Blautia	31	15	16	0.57	0.92	-1.52	0.034	0.48
MGS:igc347	Bacteroidales	14	8	6	0.84	0.53	-2.28	0.036	0.48
MGS:igc1207	Clostridiales	11	6	5	0.01	0.21	-4.90	0.036	0.48
MGS:igc54	[Clostridium] citroniae	41	21	20	0.96	0.87	-1.37	0.039	0.48
MGS:igc351	Clostridiales	31	16	15	0.95	0.98	1.62	0.039	0.48
MGS:igc640	Intestinimonas sp. GD2	31	16	15	0.67	0.78	-1.96	0.039	0.48
MGS:igc199	Clostridiales	10	4	6	6.84	2.82	-3.34	0.041	0.48
MGS:igc301	Tyzzerella nexilis	13	7	6	0.01	0.21	-3.47	0.045	0.48
MGS:igc801	Bacteria	16	7	9	1.32	1.04	1.82	0.046	0.48
MGS:igc758	Bifidobacterium dentium	19	12	7	0.38	1.12	-2.27	0.047	0.48
MGS:igc511	Dorea formicigenerans	48	27	21	1.00	0.99	0.53	0.048	0.48
MGS:igc281	Bacteria	11	6	5	0.43	1.51	-2.44	0.048	0.48
MGS:igc169	Anaerostipes hadrus	48	27	21	1.23	1.23	0.63	0.048	0.48
MGS:igc749	Coprococcus eutactus	18	10	8	1.25	0.04	2.26	0.048	0.48
MGS:igc832	Senegalimassilia anaerobia	23	11	12	0.82	1.04	-1.15	0.049	0.48

Calculated using linear mixed model adjusted for age and gender followed by correction for multiple testing by the Benjamini-Hochberg approach (n=48)

Table S8 Changes in prokaryotic KEGG orthologies

KEGG	Definition	Prevalence	Prevalence (WG->C)	Prevalence (C->WG)	Median fold change Wholegrain	Median fold change Control	Linear mixed model effect size	P-value	FDR-corrected P
K15915	undecaprenyl phosphate N,N'-diacetylbacillosamine 1-phosphate transferase [EC:2.7.8.36]	13	7	6	0.00	0.50	-1.35	1.79E-07	0.0004
K10188	lactose/L-arabinose transport system substrate-binding protein	37	17	20	1.36	0.70	1.31	2.62E-06	0.003
K18691	membrane-bound lytic murein transglycosylase F	18	10	8	0.00	0.50	-1.55	8.13E-05	0.05
K09802	uncharacterized protein	42	24	18	0.67	0.74	-0.98	0.0002	0.11
K12527	putative selenate reductase [EC:1.97.1.9]	38	21	17	1.00	0.00	0.85	0.001	0.39
K03342	para-aminobenzoate synthetase / 4-amino-4-deoxychorismate lyase [EC:2.6.1.85 4.1.3.38]	30	16	14	0.40	1.00	-1.55	0.001	0.39
K17680	twinkle protein [EC:3.6.4.12]	47	26	21	1.11	0.50	0.71	0.001	0.39
K19174	DNA phosphorothioation-dependent restriction protein DptG	28	17	11	0.00	1.00	-1.34	0.002	0.39
K02786	PTS system, lactose-specific IIA component [EC:2.7.1.207]	45	26	19	1.54	0.48	1.00	0.002	0.41
K10001	glutamate/aspartate transport system substrate-binding protein	31	15	16	0.00	0.00	-1.20	0.002	0.41
K05539	tRNA-dihydrouridine synthase A [EC:1.-.-.-]	38	21	17	0.75	1.19	-0.83	0.003	0.41
K14055	universal stress protein E	12	7	5	0.00	1.10	-1.51	0.003	0.41
K08987	putative membrane protein	41	21	20	0.09	1.24	-1.09	0.003	0.41
K09963	uncharacterized protein	39	23	16	0.18	0.83	-0.92	0.003	0.41
K02055	putative spermidine/putrescine transport system substrate-binding protein	13	7	6	4.00	0.00	2.02	0.003	0.41
K01941	urea carboxylase [EC:6.3.4.6]	16	8	8	0.50	0.00	0.68	0.003	0.41
K01277	dipeptidyl-peptidase III [EC:3.4.14.4]	47	26	21	1.19	0.79	0.78	0.004	0.41
K09712	uncharacterized protein	31	17	14	0.00	1.00	-1.21	0.004	0.43
K13631	AraC family transcriptional regulator, mar-sox-rob regulon activator	30	15	15	0.00	0.46	-0.88	0.004	0.43
K01902	succinyl-CoA synthetase alpha subunit [EC:6.2.1.5]	38	22	16	0.53	0.97	-0.76	0.004	0.43
K11905	type VI secretion system protein	33	17	16	0.00	0.18	-1.22	0.005	0.43
K02532	MFS transporter, OHS family, lactose permease	23	11	12	0.00	1.00	-1.10	0.005	0.46
K03338	5-dehydro-2-deoxygluconokinase [EC:2.7.1.92]	40	22	18	0.34	1.16	-0.97	0.006	0.50
K07164	uncharacterized protein	42	23	19	0.52	0.84	-0.85	0.006	0.53
K08963	methylthioribose-1-phosphate isomerase [EC:5.3.1.23]	48	27	21	1.18	0.83	0.62	0.007	0.53
K05346	deoxyribonucleoside regulator	32	16	16	0.00	0.00	-1.16	0.007	0.53
K03833	selenocysteine-specific elongation factor	48	27	21	0.87	1.21	-0.68	0.007	0.53
K08320	(d)CTP diphosphatase [EC:3.6.1.65]	11	7	4	0.00	1.50	-1.59	0.008	0.53
K09973	uncharacterized protein	37	21	16	0.50	0.67	-0.77	0.008	0.53
K08316	16S rRNA (guanine966-N2)-methyltransferase [EC:2.1.1.171]	48	27	21	0.31	0.54	-0.87	0.008	0.53
K06928	nucleoside-triphosphatase [EC:3.6.1.15]	11	6	5	1.00	0.00	0.69	0.008	0.53
K01476	arginase [EC:3.5.3.1]	20	11	9	1.00	0.50	1.10	0.009	0.54
K07704	two-component system, LytT family, sensor histidine kinase LytS [EC:2.7.13.3]	40	23	17	1.00	0.39	0.73	0.009	0.54
K01224	arabinogalactan endo-1,4-beta-galactosidase [EC:3.2.1.89]	48	27	21	0.80	1.19	-0.60	0.010	0.54
K01846	methylaspartate mutase sigma subunit [EC:5.4.99.1]	16	10	6	0.00	1.00	-1.32	0.010	0.54
K06143	inner membrane protein	25	15	10	0.00	0.25	-1.27	0.011	0.54
K02775	PTS system, galactitol-specific IIC component	45	24	21	0.45	0.74	-0.70	0.011	0.54
K07141	molybdenum cofactor cytidylyltransferase [EC:2.7.7.76]	48	27	21	1.21	0.87	0.35	0.011	0.54
K00658	2-oxoglutarate dehydrogenase E2 component (dihydrolipoamide succinyltransferase) [EC:2.3.1.61]	13	7	6	0.50	1.00	-1.37	0.011	0.54
K09691	lipopolysaccharide transport system ATP-binding protein	38	20	18	0.67	0.90	-0.88	0.011	0.54
K01447	N-acetylmuramoyl-L-alanine amidase [EC:3.5.1.28]	48	27	21	0.95	1.15	-0.43	0.012	0.54
K10543	D-xylose transport system substrate-binding protein	14	5	9	0.00	NA	-1.06	0.012	0.54
K07342	protein transport protein SEC61 subunit gamma and related proteins	47	26	21	0.47	0.39	0.71	0.012	0.54
K02380	FdhE protein	37	20	17	1.35	0.00	0.70	0.012	0.54
K14060	putative DNA-invertase from lambdoid prophage Rac	40	22	18	0.24	0.50	-0.88	0.013	0.54
K10009	cystine transport system permease protein	38	20	18	0.05	0.37	-1.23	0.013	0.54
K01483	ureidoglycolate lyase [EC:4.3.2.3]	37	20	17	0.33	0.46	-1.00	0.013	0.54
K02839	peptide chain release factor	35	19	16	0.38	0.50	-0.83	0.014	0.54
K13920	propanediol dehydratase small subunit [EC:4.2.1.28]	28	13	15	0.00	0.00	-0.91	0.014	0.54
K03649	TDG/mug DNA glycosylase family protein [EC:3.2.2.-]	12	9	3	1.50	0.40	1.35	0.014	0.54
K07459	putative ATP-dependent endonuclease of the OLD family	48	27	21	1.17	0.87	0.55	0.014	0.54
K02387	flagellar basal-body rod protein FlgB	48	27	21	0.67	1.40	-0.69	0.015	0.54
K10530	lactate oxidase [EC:1.13.12.-]	30	19	11	0.00	0.50	-0.97	0.015	0.54
K05516	curved DNA-binding protein	45	26	19	0.81	1.18	-0.56	0.015	0.54
K10984	PTS system, galactosamine-specific IIB component [EC:2.7.1.-]	10	5	5	0.00	0.82	-1.00	0.016	0.54
K02652	type IV pilus assembly protein PilB	40	24	16	0.30	0.60	-0.71	0.017	0.54
K00350	Na+-transporting NADH:ubiquinone oxidoreductase subunit E [EC:1.6.5.8]	48	27	21	0.78	0.94	-0.53	0.017	0.54
K11051	multidrug/hemolysin transport system permease protein	46	26	20	1.00	0.62	0.63	0.018	0.54
K10241	cellobiose transport system permease protein	14	7	7	0.00	0.00	-1.22	0.018	0.54
K06306	spore germination protein	48	27	21	1.50	1.00	0.74	0.019	0.54
K10824	nickel transport system ATP-binding protein [EC:3.6.3.24]	15	10	5	1.00	1.00	-1.03	0.019	0.54
K13018	UDP-2-acetamido-3-amino-2,3-dideoxy-glucuronate N-acetyltransferase [EC:2.3.1.201]	47	26	21	0.21	1.35	-0.84	0.019	0.54
K01708	galactarate dehydratase [EC:4.2.1.42]	14	7	7	0.22	0.77	-1.29	0.019	0.54
K13931	malonate decarboxylase delta subunit	37	22	15	0.25	0.19	-0.95	0.020	0.54
K14564	nucleolar protein 56	27	15	12	0.00	0.23	-0.94	0.020	0.54
K03491	lichenan operon transcriptional antiterminator	48	27	21	0.84	1.07	-0.47	0.020	0.54
K05020	glycine betaine transporter	16	10	6	1.52	1.07	1.35	0.020	0.54
K00526	ribonucleoside-diphosphate reductase beta chain [EC:1.17.4.1]	43	23	20	0.50	1.02	-0.66	0.020	0.54
K13683	putative colanic acid biosynthesis glycosyltransferase [EC:2.4.-.-]	12	3	9	0.17	1.00	1.63	0.020	0.54
K03212	23S rRNA (uracil747-C5)-methyltransferase [EC:2.1.1.189]	11	5	6	0.23	1.03	-1.22	0.021	0.54
K09773	[pyruvate, water dikinase]-phosphate phosphotransferase / [pyruvate, water dikinase] kinase [EC:2.7.4.28 2.7.11.33]	14	7	7	0.00	0.14	-1.26	0.021	0.54
K02806	PTS system, nitrogen regulatory IIA component [EC:2.7.1.-]	45	24	21	0.59	1.20	-0.73	0.021	0.54
K00364	GMP reductase [EC:1.7.1.7]	47	26	21	1.00	1.22	-0.70	0.021	0.54
K05952	uncharacterized protein	22	14	8	0.00	0.16	-1.08	0.022	0.54
K18979	epoxyqueuosine reductase [EC:1.17.99.6]	48	27	21	1.00	1.05	-0.65	0.022	0.54
K00112	glycerol-3-phosphate dehydrogenase subunit B [EC:1.1.5.3]	35	17	18	0.50	0.95	-0.76	0.022	0.54
K17235	arabinosaccharide transport system permease protein	29	15	14	0.00	0.00	-0.79	0.023	0.54
K08218	MFS transporter, PAT family, beta-lactamase induction signal transducer AmpG	48	27	21	0.88	1.31	-0.44	0.023	0.54
K03549	KUP system potassium uptake protein	29	17	12	0.00	0.33	-0.98	0.023	0.54
K02855	AraC family transcriptional regulator, L-rhamnose operon regulatory protein RhaS	48	27	21	0.92	0.69	0.82	0.023	0.54
K00603	glutamate formiminotransferase [EC:2.1.2.5]	39	20	19	0.78	1.00	-0.82	0.023	0.54
K10120	fructooligosaccharide transport system substrate-binding protein	26	14	12	0.00	0.50	-1.15	0.023	0.54
K03824	putative acetyltransferase [EC:2.3.1.-]	22	12	10	0.63	0.94	-0.82	0.023	0.54
K12507	acyl-CoA synthetase [EC:6.2.1.-]	20	13	7	0.35	0.48	-1.13	0.023	0.54
K02744	PTS system, N-acetylgalactosamine-specific IIA component [EC:2.7.1.-]	48	27	21	0.77	1.19	-0.46	0.023	0.54
K02803,K028	PTS system, N-acetylglucosamine-specific IIB component [EC:2.7.1.193], PTS system, N-acetylglucosamine-specific IIC comp	48	27	21	1.36	0.90	0.54	0.023	0.54
K10008	glutamate transport system ATP-binding protein [EC:3.6.3.-]	33	18	15	0.10	0.66	-0.69	0.025	0.55
K06015	N-acyl-D-amino-acid deacylase [EC:3.5.1.81]	44	25	19	0.62	0.89	-0.75	0.025	0.55
K12990	rhamnosyltransferase [EC:2.4.1.-]	36	20	16	0.83	0.38	1.01	0.026	0.55
K04103	indolepyruvate decarboxylase [EC:4.1.1.74]	10	6	4	1.00	23.50	-0.86	0.026	0.55
K03636	molybdopterin synthase sulfur carrier subunit	46	25	21	1.00	1.48	-0.57	0.027	0.55
K07588	LAO/AO transport system kinase [EC:2.7.-.-]	32	16	16	0.49	0.68	-0.97	0.027	0.55
K00091	dihydroflavonol-4-reductase [EC:1.1.1.219]	31	16	15	1.00	0.50	0.70	0.027	0.55
K03475	PTS system, ascorbate-specific IIC component	37	21	16	0.50	0.89	-1.01	0.027	0.55
K19114	CRISPR-associated protein Csh1	34	19	15	0.67	0.78	-0.96	0.028	0.55
K05795	tellurium resistance protein TerD	47	26	21	1.17	0.84	0.55	0.028	0.55

K06421	small acid-soluble spore protein D (minor alpha/beta-type SASP)	14	8	6	0.00	0.00	1.24	0.028	0.55
K10039	putative glutamine transport system substrate-binding protein	36	20	16	0.00	1.00	-0.96	0.028	0.55
K03811	nicotinamide mononucleotide transporter	48	27	21	0.71	1.01	-0.63	0.028	0.55
K09764	uncharacterized protein	48	27	21	1.22	0.94	0.47	0.028	0.55
K15876	cytochrome c nitrite reductase small subunit	16	7	9	2.00	0.00	0.90	0.028	0.55
K07812	trimethylamine-N-oxide reductase (cytochrome c) [EC:1.7.2.3]	11	6	5	0.00	0.00	-0.91	0.028	0.55
K07705	two-component system, LytT family, response regulator LytT	14	5	9	0.00	0.00	-1.12	0.029	0.55
K06861	lipopolysaccharide export system ATP-binding protein [EC:3.6.3.-]	40	22	18	1.00	0.52	0.65	0.029	0.56
K01966	propionyl-CoA carboxylase beta chain [EC:6.4.1.3]	43	24	19	0.50	1.00	-0.73	0.029	0.56
K13498	indole-3-glycerol phosphate synthase / phosphoribosylanthranilate isomerase [EC:4.1.1.48 5.3.1.24]	46	26	20	0.75	1.22	-0.62	0.030	0.56
K07250	4-aminobutyrate aminotransferase / (S)-3-amino-2-methylpropionate transaminase [EC:2.6.1.19 2.6.1.22]	46	25	21	0.21	0.85	-0.75	0.031	0.56
K05792	tellurite resistance protein TerA	27	16	11	0.00	0.00	-0.85	0.031	0.56
K08138	MFS transporter, SP family, xylose:H+ symportor	48	27	21	1.30	0.92	0.46	0.031	0.56
K01278	dipeptidyl-peptidase 4 [EC:3.4.14.5]	35	20	15	1.00	0.29	0.89	0.031	0.56
K14260	alanine-synthesizing transaminase [EC:2.6.1.66 2.6.1.2]	42	24	18	0.48	0.33	0.61	0.031	0.56
K02530	DeoR family transcriptional regulator, lactose phosphotransferase system repressor	39	23	16	0.66	0.33	0.82	0.032	0.56
K07058	membrane protein	48	27	21	1.00	1.20	-0.46	0.032	0.56
K12940	aminobenzoyl-glutamate utilization protein A	26	17	9	0.00	0.87	-1.16	0.032	0.56
K01739	cystathionine gamma-synthase [EC:2.5.1.48]	11	6	5	0.00	0.33	-1.00	0.033	0.56
K07115	23S rRNA (adenine2030-N6)-methyltransferase [EC:2.1.1.266]	16	11	5	1.30	1.35	1.28	0.033	0.56
K08227	MFS transporter, LPLT family, lysophospholipid transporter	35	19	16	0.67	0.84	-0.75	0.033	0.56
K09760	DNA recombination protein RmuC	48	27	21	1.01	0.89	0.44	0.033	0.56
K01281	X-Pro dipeptidyl-peptidase [EC:3.4.14.11]	40	21	19	0.40	0.31	-0.81	0.034	0.56
K07794	putative tricarboxylic transport membrane protein	23	11	12	0.20	0.00	-0.96	0.035	0.57
K06418	small acid-soluble spore protein A (major alpha-type SASP)	19	9	10	0.50	0.00	1.32	0.035	0.57
K01372	bleomycin hydrolase [EC:3.4.22.40]	47	26	21	1.10	0.73	0.55	0.035	0.57
K01621	xylulose-5-phosphate/fructose-6-phosphate phosphoketolase [EC:4.1.2.9 4.1.2.22]	44	23	21	0.86	1.06	-0.64	0.035	0.57
K02972	stationary-phase-induced ribosome-associated protein	43	24	19	0.98	1.00	-0.49	0.037	0.58
K00897	kanamycin kinase [EC:2.7.1.95]	27	15	12	0.00	0.31	-0.89	0.037	0.58
K06189	magnesium and cobalt transporter	24	14	10	0.00	0.29	-1.09	0.037	0.58
K00121	S-(hydroxymethyl)glutathione dehydrogenase / alcohol dehydrogenase [EC:1.1.1.284 1.1.1.1]	39	22	17	0.49	0.95	-0.70	0.038	0.59
K03299	gluconate:H+ symporter, GntP family	48	27	21	1.13	1.42	-0.40	0.038	0.59
K00899	5-methylthioribose kinase [EC:2.7.1.100]	46	26	20	1.67	0.75	0.51	0.038	0.59
K04072	acetaldehyde dehydrogenase / alcohol dehydrogenase [EC:1.2.1.10 1.1.1.1]	47	27	20	0.94	1.00	-0.36	0.038	0.59
K04565	superoxide dismutase, Cu-Zn family [EC:1.15.1.1]	46	25	21	0.50	1.11	-0.62	0.039	0.59
K00098	L-idonate 5-dehydrogenase [EC:1.1.1.264]	45	26	19	0.50	1.00	-0.56	0.039	0.59
K09801	uncharacterized protein	25	12	13	0.00	0.95	-1.05	0.040	0.59
K03462	nicotinamide phosphoribosyltransferase [EC:2.4.2.12]	28	16	12	0.00	0.36	-0.85	0.040	0.59
K17837	metallo-beta-lactamase class B [EC:3.5.2.6]	39	21	18	0.61	0.12	0.60	0.041	0.59
K06221	2,5-diketo-D-gluconate reductase A [EC:1.1.1.346]	47	27	20	0.71	0.95	-0.44	0.041	0.59
K14083	trimethylamine---corrinoid protein Co-methyltransferase [EC:2.1.1.250]	31	17	14	0.33	0.88	-0.65	0.042	0.59
K18816	aminoglycoside 6'-N-acetyltransferase I [EC:2.3.1.82]	41	23	18	0.19	0.82	-0.62	0.042	0.59
K01354	oligopeptidase B [EC:3.4.21.83]	29	18	11	0.03	0.31	-0.99	0.042	0.59
K06423	small acid-soluble spore protein F (minor alpha/beta-type SASP)	48	27	21	0.96	0.79	0.30	0.042	0.59
K01205	alpha-N-acetylglucosaminidase [EC:3.2.1.50]	48	27	21	0.66	0.67	0.60	0.042	0.59
K00786		37	19	18	0.14	1.00	-0.83	0.042	0.59
K00428	cytochrome c peroxidase [EC:1.11.1.5]	39	22	17	0.18	0.86	-0.69	0.043	0.60
K13922	propionaldehyde dehydrogenase [EC:1.2.1.87]	41	23	18	0.47	0.80	-0.67	0.043	0.60
K11618	two-component system, NarL family, response regulator LiaR	23	11	12	0.00	0.50	-0.99	0.044	0.60
K02020	molybdate transport system substrate-binding protein	47	26	21	0.96	0.96	-0.41	0.044	0.60
K11927	ATP-dependent RNA helicase RhlE [EC:3.6.4.13]	45	26	19	1.06	0.54	0.64	0.044	0.60
K03228	type III secretion protein T	20	6	14	0.50	0.00	-0.95	0.044	0.60
K08224	MFS transporter, YNFM family, putative membrane transport protein	12	6	6	0.00	0.00	-1.48	0.046	0.60
K12995	rhamnosyl/mannosyltransferase [EC:2.4.1.-]	48	27	21	0.92	1.21	-0.49	0.046	0.60
K03576	LysR family transcriptional regulator, regulator for metE and metH	47	27	20	1.00	0.65	0.56	0.046	0.60
K18284	adenosylhomocysteine/aminodeoxyfutalosine nucleosidase [EC:3.2.2.9 3.2.2.30]	14	7	7	1.00	0.00	0.83	0.046	0.60
K09780	uncharacterized protein	21	11	10	0.50	0.00	0.68	0.047	0.60
K07712	two-component system, NtrC family, nitrogen regulation response regulator GlnG	40	21	19	0.76	0.75	-0.77	0.048	0.60
K03214	RNA methyltransferase, TrmH family [EC:2.1.1.-]	23	13	10	0.00	0.00	-1.11	0.048	0.60
K01247	DNA-3-methyladenine glycosylase II [EC:3.2.2.21]	48	27	21	0.75	1.02	-0.51	0.048	0.60
K11144	primosomal protein DnaI	29	15	14	0.00	0.67	-0.84	0.049	0.60
K02103	GntR family transcriptional regulator, arabinose operon transcriptional repressor	45	26	19	0.55	1.15	-0.55	0.049	0.60
K00756	pyrimidine-nucleoside phosphorylase [EC:2.4.2.2]	48	27	21	0.91	1.57	-0.42	0.049	0.60
K01661	naphthoate synthase [EC:4.1.3.36]	45	27	18	0.89	1.00	-0.47	0.049	0.60
K07347	outer membrane usher protein	29	15	14	0.00	0.60	-0.84	0.050	0.60
K09936	bacterial/archaeal transporter family-2 protein	48	27	21	0.87	1.25	-0.37	0.050	0.60
K11214	sedoheptulokinase [EC:2.7.1.14]	24	12	12	0.00	0.00	-0.61	0.050	0.60

Calculated using linear mixed model adjusted for age and gender followed by correction for multiple testing by the Benjamini-Hochberg approach (n=48)

Table S9 Changes in prokaryotic families of carbohydrate active enzymes (CAZy)

CAZy	Known Activities	Prevalence	Prevalence (WG->C)	Prevalence (C->WG)	Median fold change Wholegrain	Median fold change Control	Linear mixed model effect size	P-value	FDR-corrected P
GH6	endoglucanase (EC 3.2.1.4); cellobiohydrolase (EC 3.2.1.91)	44	25	19	0.98	1.08	-0.67	0.019	0.28
GH22	lysozyme type C (EC 3.2.1.17); lysozyme type i (EC 3.2.1.17); α-lactalbumin	48	27	21	1.08	1.01	0.42	0.022	0.28
GH79	β-glucuronidase (EC 3.2.1.31); hyaluronoglucuronidase (EC 3.2.1.36); heparanase (EC 3.2.1.166	48	27	21	1.05	0.72	0.38	0.025	0.28
GH111	keratan sulfate hydrolase (endo-β-N-acetylglucosaminidase) (EC 3.2.1.-)	48	27	21	1.05	1.08	0.24	0.030	0.28
GT25	lipopolysaccharide β-1,4-galactosyltransferase (EC 2.4.1.-); β-1,3-glucosyltransferase (EC 2.4.1.	48	27	21	0.94	1.13	-0.30	0.036	0.28
GT22	Dol-P-Man: Man6GlcNAc2-PP-Dol α-1,2-mannosyltransferase (EC 2.4.1.259); Dol-P-Man: Man8	48	27	21	0.96	1.12	-0.43	0.041	0.28
GT23	N-acetyl-β-D-glucosaminide α-1,6-L-fucosyltransferase (EC 2.4.1.68); chitin-oligosaccharide α-1	48	27	21	0.93	1.18	-0.38	0.044	0.28
GH44	endoglucanase (EC 3.2.1.4); xyloglucanase (EC 3.2.1.151)	48	27	21	1.29	0.91	0.51	0.045	0.28
GT82	UDP-GalNAc: β-1,4-N-acetylgalactosaminyltransferase (EC 2.4.1.-)	48	27	21	0.99	0.85	0.30	0.047	0.28
GH75	chitosanase (EC 3.2.1.132)	48	27	21	1.09	0.90	0.30	0.047	0.28

Calculated using linear mixed model adjusted for age and gender followed by correction for multiple testing by the Benjamini-Hochberg approach (n=48)

Table S10A Changes in gut microbiota at phylum level assessed by 16S rRNA gene sequencing

Phylum	P-value	FDR-corrected P	Linear mixed model effect size
p__Verrucomicrobia	0.22	0.82	0.67
p__Lentisphaerae	0.29	0.82	0.40
p__Proteobacteria	0.43	0.82	-0.21
p__Fusobacteria	0.44	0.82	0.21
p__Actinobacteria	0.64	0.82	-0.09
p__Cyanobacteria	0.66	0.82	0.15
p__Firmicutes	0.68	0.82	-0.01
p__Euryarchaeota	0.71	0.82	0.20
p__Bacteroidetes	0.74	0.82	0.09
p__Tenericutes	0.75	0.82	0.14
p__TM7	0.96	0.96	-0.01

Calculated using linear mixed model adjusted for age and gender followed by correction for multiple testing by the Benjamini-Hochberg approach (n=48)

Table S10B Changes in gut microbiota at class level assessed by 16S rRNA gene sequencing

Class	P-value	FDR-corrected P	Linear mixed model effect size
c__Sphingobacteriia	0.01	0.28	0.61

Calculated using linear mixed model adjusted for age and gender followed by correction for multiple testing by the Benjamini-Hochberg approach (n=48)

Table S10C Changes in gut microbiota at order level assessed by 16S rRNA gene sequencing

Order	P-value	FDR-corrected P	Linear mixed model effect size
o__Sphingobacteriales	0.01	0.44	0.61

Calculated using linear mixed model adjusted for age and gender followed by correction for multiple testing by the Benjamini-Hochberg approach (n=48)

Table S10D Changes in gut microbiota at family level assessed by 16S rRNA gene sequencing

Family	P-value	FDR-corrected P	Linear mixed model effect size
f__Sphingobacteriaceae	0.013	0.47	0.61
f__Corynebacteriaceae	0.017	0.47	-0.71

Calculated using linear mixed model adjusted for age and gender followed by correction for multiple testing by the Benjamini-Hochberg approach (n=48)

Table S10E Changes in gut microbiota at genus level assessed by 16S rRNA gene sequencing

Genus	P-value	FDR-corrected P	Linear mixed model effect size
g__Corynebacterium	0.017	0.75	-0.71
g__Pedobacter	0.020	0.75	0.63
g__Ruminococcus	0.026	0.75	-0.49
g__Eggerthella	0.041	0.85	-0.54

Calculated using linear mixed model adjusted for age and gender followed by correction for multiple testing by the Benjamini-Hochberg approach (n=48)

Table S10F Changes in gut microbiota at OTU level assessed by 16S rRNA gene sequencing

OTU ID	Taxonomy	P-value	FDR-corrected P	Linear mixed model effect size
OTU_879	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Clostridiaceae; g__; s__	0.0001	0.09	-1.09
OTU_74	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.001	0.35	-0.97
OTU_2727	k__Bacteria; p__Proteobacteria; c__Betaproteobacteria; o__Burkholderiales; f__Alcaligenaceae; g__Sutterella; s__	0.002	0.35	1.15
OTU_1362	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.002	0.35	0.62
OTU_2209	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Lachnospiraceae; g__; s__	0.003	0.35	0.69
OTU_1325	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Lachnospiraceae; g__Blautia; s__	0.003	0.35	0.83
OTU_421	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.003	0.35	-0.67
OTU_78	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__Oscillospira; s__	0.003	0.35	1.13
OTU_614	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__Oscillospira; s__	0.003	0.35	0.87
OTU_1114	k__Bacteria; p__Bacteroidetes; c__Sphingobacteriia; o__Sphingobacteriales; f__Sphingobacteriaceae; g__Pedobacter; s__	0.004	0.38	0.74
OTU_925	k__Bacteria; p__Actinobacteria; c__Actinobacteria; o__Bifidobacteriales; f__Bifidobacteriaceae; g__Bifidobacterium; s__longum	0.005	0.41	0.66
OTU_1048	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.006	0.41	0.62
OTU_742	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.006	0.41	0.72
OTU_923	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Lachnospiraceae; g__Coprococcus; s__	0.007	0.41	-0.59
OTU_477	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__Oscillospira; s__	0.007	0.41	-0.81
OTU_439	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.008	0.46	-0.73
OTU_592	k__Bacteria; p__Verrucomicrobia; c__Verrucomicrobiae; o__Verrucomicrobiales; f__Verrucomicrobiaceae; g__Akkermansia; s__muciniphila	0.008	0.46	0.83
OTU_448	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__; g__; s__	0.011	0.52	0.49
OTU_850	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.011	0.52	-0.58
OTU_2648	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Lachnospiraceae; g__; s__	0.014	0.64	0.71
OTU_142	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Lachnospiraceae; g__; s__	0.016	0.64	0.65
OTU_1409	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Lachnospiraceae; g__Coprococcus; s__	0.017	0.64	0.50
OTU_956	k__Bacteria; p__Actinobacteria; c__Actinobacteria; o__Bifidobacteriales; f__Bifidobacteriaceae; g__Bifidobacterium; s__	0.018	0.64	-0.70
OTU_226	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.018	0.64	0.72
OTU_1207	k__Bacteria; p__Verrucomicrobia; c__Verrucomicrobiae; o__Verrucomicrobiales; f__Verrucomicrobiaceae; g__Akkermansia; s__muciniphila	0.018	0.64	0.82
OTU_34	k__Bacteria; p__Firmicutes; c__Bacilli; o__Lactobacillales; f__Streptococcaceae; g__Streptococcus; s__	0.018	0.64	-0.81
OTU_551	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__; g__; s__	0.019	0.64	0.92
OTU_401	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.020	0.64	-0.62
OTU_42	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Clostridiaceae; g__; s__	0.021	0.65	-0.83
OTU_205	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__Ruminococcus; s__	0.022	0.65	-0.81
OTU_945	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.022	0.65	-0.52
OTU_224	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__; g__; s__	0.024	0.65	0.75
OTU_670	k__Bacteria; p__Bacteroidetes; c__Sphingobacteriia; o__Sphingobacteriales; f__Sphingobacteriaceae; g__Sphingobacterium; s__	0.024	0.65	0.54
OTU_1892	k__Bacteria; p__Verrucomicrobia; c__Verrucomicrobiae; o__Verrucomicrobiales; f__Verrucomicrobiaceae; g__Akkermansia; s__muciniphila	0.026	0.65	0.72
OTU_2488	k__Bacteria; p__Firmicutes; c__Erysipelotrichi; o__Erysipelotrichales; f__Erysipelotrichaceae; g__; s__	0.026	0.65	0.42
OTU_632	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Lachnospiraceae; g__Coprococcus; s__	0.027	0.65	-0.86
OTU_1907	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.027	0.65	-0.44
OTU_312	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Clostridiaceae; g__; s__	0.028	0.65	-0.77
OTU_157	k__Bacteria; p__Firmicutes; c__Erysipelotrichi; o__Erysipelotrichales; f__Erysipelotrichaceae; g__; s__	0.029	0.65	-0.82
OTU_423	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Lachnospiraceae; g__; s__	0.030	0.65	-0.89
OTU_201	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__; g__; s__	0.030	0.65	1.01
OTU_986	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__Oscillospira; s__	0.031	0.65	-0.42
OTU_2394	k__Bacteria; p__Firmicutes; c__Erysipelotrichi; o__Erysipelotrichales; f__Erysipelotrichaceae; g__; s__	0.032	0.65	0.47
OTU_2116	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Lachnospiraceae; g__; s__	0.032	0.65	0.41
OTU_2088	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.032	0.65	-0.47
OTU_446	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__; g__; s__	0.033	0.65	-0.61
OTU_1	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Lachnospiraceae; g__; s__	0.034	0.66	0.44
OTU_2753	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.036	0.68	0.54
OTU_2661	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__; g__; s__	0.037	0.69	0.51
OTU_378	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.039	0.69	-0.54
OTU_462	k__Bacteria; p__Firmicutes; c__Erysipelotrichi; o__Erysipelotrichales; f__Erysipelotrichaceae; g__; s__	0.039	0.69	1.45
OTU_2224	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__Ruminococcus	0.039	0.69	-0.92
OTU_38	k__Bacteria; p__Bacteroidetes; c__Bacteroidia; o__Bacteroidales; f__Bacteroidaceae; g__Bacteroides; s__fragilis	0.040	0.69	-0.78
OTU_27	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Lachnospiraceae; g__Coprococcus; s__eutactus	0.042	0.70	0.98
OTU_1291	k__Bacteria; p__Proteobacteria; c__Gammaproteobacteria; o__Pseudomonadales; f__Moraxellaceae; g__Acinetobacter; s__johnsonii	0.042	0.70	0.87
OTU_400	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__Anaerotruncus; s__	0.044	0.72	-0.64
OTU_267	k__Bacteria; p__Proteobacteria; c__Betaproteobacteria; o__Burkholderiales; f__Alcaligenaceae; g__Sutterella; s__	0.046	0.72	1.54
OTU_2559	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Lachnospiraceae; g__Coprococcus; s__	0.046	0.72	0.44
OTU_1967	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.047	0.72	-0.57
OTU_488	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Christensenellaceae; g__; s__	0.048	0.72	-0.57
OTU_540	k__Bacteria; p__Proteobacteria; c__Gammaproteobacteria; o__Pseudomonadales; f__Moraxellaceae; g__Enhydrobacter; s__	0.049	0.72	0.86
OTU_517	k__Bacteria; p__Firmicutes; c__Clostridia; o__Clostridiales; f__Ruminococcaceae; g__; s__	0.049	0.72	-0.46

Calculated using linear mixed model adjusted for age and gender followed by correction for multiple testing by the Benjamini-Hochberg approach (n=48)

Table S11 Associations between metagenomic species and wholegrain intake, fibre intake, serum IL-6 concentrations and serum CRP concentrations.

		Association to wholegrain intake		Association to fibre intake		Association to serum IL-6		Association to serum CRP	
MGS	**Taxonomical annotation**	**Effect size**	**FDR P-value**	**Effect size**	**FDR P-value**	**Effect size**	**FDR P-value**	**Effect size**	**FDR P-value**
MGS:igc654	Clostridiales	0.20	5.84E-04	0.72	1.59E-02	-0.03	9.35E-01	0.04	9.29E-01
MGS:igc102	Erysipelatoclostridium ramosum	-0.20	1.82E-03	-0.30	3.23E-01	0.44	3.86E-02	0.10	9.15E-01
MGS:igc460	Clostridiales	-0.11	7.23E-02	-0.31	2.96E-01	-0.03	9.35E-01	0.06	9.29E-01
MGS:igc633	Clostridiales	0.11	1.41E-01	0.47	2.14E-01	-0.15	8.40E-01	0.03	9.72E-01
MGS:igc139	Ruminococcus	-0.21	2.64E-02	-0.78	8.04E-02	0.08	8.89E-01	0.09	9.29E-01
MGS:igc291	Faecalibacterium prausnitzii	0.17	1.71E-03	0.53	3.45E-02	-0.13	8.40E-01	-0.01	9.72E-01
MGS:igc359	Clostridiales	0.15	1.37E-01	1.05	3.45E-02	-0.40	5.02E-01	-0.27	7.29E-01
MGS:igc309	Ruminococcus lactaris	0.25	8.29E-03	0.26	5.91E-01	-0.22	8.40E-01	-0.11	9.29E-01
MGS:igc734	Streptococcus thermophilus	-0.21	5.40E-02	-0.10	7.84E-01	-0.19	8.40E-01	0.18	7.29E-01
MGS:igc584	Holdemanella biformis	-0.11	1.15E-02	-0.25	2.75E-01	0.05	8.89E-01	0.01	9.72E-01
MGS:igc517	Faecalibacterium prausnitzii	0.14	4.66E-02	0.34	2.94E-01	-0.04	9.22E-01	0.03	9.72E-01
MGS:igc171	Faecalibacterium prausnitzii	0.10	8.71E-02	0.44	1.11E-01	0.01	9.76E-01	0.04	9.29E-01
MGS:igc213	Coprococcus	0.20	3.81E-02	0.47	3.06E-01	-0.34	5.02E-01	-0.17	8.74E-01
MGS:igc9	Bacteroides thetaiotaomicron	-0.16	1.71E-03	-0.51	3.45E-02	0.08	8.40E-01	0.00	9.98E-01
MGS:igc263	Prevotella copri	0.05	5.01E-01	0.45	2.14E-01	-0.13	8.40E-01	-0.08	9.29E-01
MGS:igc292	Faecalibacterium prausnitzii	0.19	3.09E-03	0.71	2.63E-02	-0.08	8.40E-01	-0.02	9.72E-01
MGS:igc157	Clostridiales	-0.10	6.16E-02	-0.24	3.34E-01	0.05	8.89E-01	0.02	9.72E-01
MGS:igc762	Clostridiales	-0.14	2.98E-02	-0.36	2.76E-01	0.22	5.58E-01	0.16	7.29E-01
MGS:igc1140	Bacteria	0.15	1.08E-01	0.69	1.34E-01	0.04	9.35E-01	-0.01	9.89E-01
MGS:igc784	Clostridiales bacterium 1_7_47FAA	-0.15	1.09E-02	-0.26	3.34E-01	0.10	8.40E-01	0.05	9.29E-01
MGS:igc613	Clostridiales	0.14	2.55E-03	0.54	2.63E-02	-0.07	8.40E-01	0.04	9.29E-01
MGS:igc89	Subdoligranulum sp. 4_3_54A2FAA	-0.21	5.84E-04	-0.69	2.63E-02	0.22	5.02E-01	0.08	9.15E-01
MGS:igc886	Erysipelotrichaceae	0.03	6.46E-01	0.09	7.42E-01	-0.47	2.24E-02	-0.14	7.29E-01
MGS:igc389	Clostridiales	0.12	3.81E-02	0.09	7.42E-01	-0.07	8.40E-01	-0.13	7.29E-01
MGS:igc763	Clostridiales	-0.06	3.68E-01	-0.29	3.16E-01	0.12	8.40E-01	-0.07	9.29E-01
MGS:igc745	Streptococcus salivarius	-0.05	4.09E-01	0.13	6.17E-01	-0.05	8.89E-01	0.08	9.15E-01
MGS:igc1203	Bacteria	0.22	5.92E-03	0.61	1.14E-01	-0.30	5.02E-01	-0.16	8.28E-01
MGS:igc318	Bacteria	-0.21	1.47E-02	-0.70	8.47E-02	-0.30	5.02E-01	-0.14	9.15E-01
MGS:igc1259	Eukaryota	-0.10	2.56E-01	-0.76	8.04E-02	-0.18	8.40E-01	-0.27	6.38E-01
MGS:igc818	Clostridiales	-0.05	3.68E-01	-0.30	2.90E-01	0.02	9.39E-01	-0.07	9.29E-01
MGS:igc938	Firmicutes	0.11	9.66E-02	0.30	3.34E-01	-0.01	9.76E-01	-0.01	9.72E-01
MGS:igc64	Clostridiales	-0.02	6.63E-01	-0.13	5.91E-01	0.00	9.76E-01	-0.03	9.29E-01
MGS:igc100	Bacteroides	-0.06	1.97E-01	-0.06	7.74E-01	-0.03	9.20E-01	-0.01	9.72E-01
MGS:igc732	butyrate-producing bacterium SS3/4	0.20	5.92E-03	0.51	1.28E-01	-0.22	5.58E-01	-0.09	9.15E-01
MGS:igc24	Bacteroides	-0.09	6.41E-02	-0.56	2.63E-02	0.13	8.40E-01	-0.01	9.72E-01
MGS:igc691	Lachnospiraceae	0.02	8.34E-01	0.29	4.38E-01	-0.44	1.25E-01	-0.34	1.57E-01
MGS:igc1200	Blautia	-0.11	9.64E-02	-0.41	2.42E-01	-0.03	9.35E-01	0.01	9.72E-01
MGS:igc347	Bacteroidales	-0.08	1.07E-01	-0.33	2.19E-01	-0.06	8.40E-01	0.04	9.29E-01
MGS:igc1207	Clostridiales	-0.19	5.41E-02	-0.99	3.45E-02	0.58	3.86E-02	0.21	7.29E-01
MGS:igc54	[Clostridium] citroniae	-0.13	7.92E-02	-0.09	7.74E-01	0.06	8.98E-01	-0.11	9.15E-01
MGS:igc351	Clostridiales	0.28	3.60E-03	0.55	2.53E-01	0.18	8.40E-01	0.08	9.29E-01
MGS:igc640	Intestinimonas sp. GD2	-0.02	7.95E-01	-0.02	9.54E-01	0.34	5.02E-01	-0.04	9.72E-01
MGS:igc199	Clostridiales	-0.01	8.79E-01	0.22	4.83E-01	0.11	8.40E-01	0.06	9.29E-01
MGS:igc301	Tyzzerella nexilis	-0.18	7.20E-02	-1.03	2.63E-02	0.71	1.01E-02	0.36	2.47E-01
MGS:igc801	Bacteria	0.06	3.05E-01	0.16	5.51E-01	-0.17	6.44E-01	-0.05	9.29E-01
MGS:igc758	Bifidobacterium dentium	-0.12	3.98E-02	-0.50	8.04E-02	0.09	8.40E-01	0.04	9.29E-01
MGS:igc511	Dorea formicigenerans	0.02	7.17E-01	0.11	6.17E-01	-0.21	4.48E-01	-0.09	8.28E-01
MGS:igc281	Bacteria	-0.05	2.81E-01	-0.12	6.17E-01	0.10	8.40E-01	-0.06	9.29E-01
MGS:igc169	Anaerostipes hadrus	0.02	7.32E-01	0.43	1.53E-01	-0.24	5.02E-01	-0.18	6.38E-01
MGS:igc749	Coprococcus eutactus	0.18	6.86E-03	0.56	8.47E-02	-0.11	8.40E-01	-0.13	8.28E-01
MGS:igc832	Senegalimassilia anaerobia	-0.04	4.01E-01	-0.08	7.42E-01	-0.04	8.40E-01	0.03	9.29E-01

Calculated using linear mixed model adjusted for age and gender followed by correction for multiple testing by the Benjamini-Hochberg approach (n=48)

Table S12 Effects of the wholegrain and refined grain diet on plasma short-chain fatty acids

Metabolite	Refined grain *Median (25th-75th percentile)*		Wholegrain *Median (25th-75th percentile)*		P-value[1]
	Baseline	**End**	**Baseline**	**End**	
Acetic acid (µmol/L)	71.4 (55.2-97.1)	73.3 (59.6-111.5)	76.4 (55.9-103.5)	81.5 (62.3-109.2)	0.96
Propionic acid (µmol/L)	3.90 (3.26-4.67)	3.67 (3.28-4.35)	3.76 (3.24-4.66)	3.77 (3.33-4.57)	0.47
Butyric acid[2] (µmol/L)	0.49 (0.40-0.78)	0.54 (0.40-0.71)	0.55 (0.37-0.70)	0.65 (0.42-0.92)	0.14
Isobutyric acid (µmol/L)	1.25 (0.72-1.41)	1.25 (0.74-1.37)	1.04 (0.73-1.39)	1.19 (0.77-1.37)	0.44
Isovaleric acid (µmol/L)	0.45 (0.35-0.55)	0.45 (0.35-0.54)	0.42 (0.32-0.55)	0.47 (0.34-0.58)	0.26
Valeric acid (µmol/L)	0.09 (0.06-0.12)	0.08 (0.06-0.11)	0.09 (0.07-0.11)	0.08 (0.07-0.11)	0.31
Caproic acid (µmol/L)	0.50 (0.40-0.56)	0.47 (0.39-0.54)	0.48 (0.42-0.56)	0.50 (0.39-0.54)	0.97

[1] Linear mixed model adjusting for age and gender (n=50).

[2] We noted that a comparison of the treatment groups at end of the periods indicated higher plasma concentrations of butyrate after the wholegrain intervention as compared to the refined grain intervention (Paired t-test; P=0.022).

Table S13 List of urinary metabolites differing between the whole-grain and refined grain interventions identified by UPLC-MS and GC-MS

Technique	Tentative structural assignment	ID level[a]	Adduct	Retention time	Experimental	MS/MS fragmentation	Authentic standard	Database	Mass error
				(min)	*m/z*	*m/z*	*m/z*	*m/z*	(mDa)
UPLC-MS	Pyrocatechol-O-glucuronide	1	$[M+NH_4]^+$	1.3	304.1025	199.1697, 141.0177, 111.1166	111.044 Pyrocatechol $[M+H]^+$	304.1027	0.2
UPLC-MS	2-aminophenol-sulphate	1	$[M-H]^-$	1.5	188.0021	129.0190, 108.0454 $[M-H-SO_3]^-$, 79.9584 $[SO_3]^-$		188.0012	0.9
			$[M+H]^+$	1.5	190.0167	110.0600 $[M+H-sulphate]^+$ (2-aminophenol)	110.06 2-aminophenol $[M+H]^+$	190.0169	0.2
UPLC-MS	Pyrocatechol-sulphate	1	$[M-H]^-$	1.6	188.9861	170.0438, 109.0300 $[M-H-sulphate]^-$	109.0299 Pyrocatechol $[M-H]^-$	188.9852	0.9
UPLC-MS	DHPPA-glucuronide	1	$[M-H]^-$	3.2	357.0816	310.1161, 181.0484 $[M-H-glucuronide]^-$, 175.0245, 137.0601, 113.0244 (glucuronide), 95.0143	181.0501 DHPPA $[M-H]^-$	357.0816	0.0
			$[M+NH_4]^+$	3.2	376.1237	183.0651 $[M+H-glucuronide]^+$, 165.0547 $[M+H-glucuronide-H_2O]^+$	183.065 DHPPA	376.1238	0.1
			$[M+Na]^+$	3.2	381.0791	Not obtained	[M+H]+	381.0792	0.1
GC-MS	3-methyladipic acid	2	MCF-derivative	13.24					

UPLC-MS, ultra-performance liquid chromatography mass spectrometry; GC-MS, gas chromatography mass spectrometry; DHPPA, 3-(3,5-dihydroxyphenyl)-1-propanoic acid.

[a] Identification levels by Sumner et al, 2007; Metabolomics doi:10.1007/s11306-007-0082-2

Table S14 Associations between serum inflammatory markers and urine metabolites

	Serum CRP		Serum IL-6	
Urine metabolites	**Effect size**	**P-value**	**Effect size**	**P-value**
DHPPA-glucuronide	-0.49	0.032	-0.44	0.002
2-aminophenol-sulphate	-0.41	0.018	-0.18	0.10
Pyrocatechol-glucuronide	-0.59	0.023	-0.14	0.41
Pyrocatechol-sulphate	-0.39	0.19	0.00	1.00
3-methyladipic acid	-0.31	0.10	-0.23	0.06

3,5-dihydroxyhydrocinnamic acid (DHPPA)-glucuronide

Calculated using linear mixed model adjusting for age and gender on log-transformed urine metabolome data (n=48).