SUPPLEMENTARY DATA

Longitudinal metabolic and gut bacterial profiling of pregnant women with previous bariatric surgery

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Figure S1: Summary of sampling by individual. Each point represents a sampling event for an individual and is coloured based on which samples were collected and analysed. The size of the point represents the BMI category of the individual at that time point. *T1 11-14 weeks gestation; T2 20-24 weeks gestation; T3 28-30 weeks gestation; T4 30-33 weeks gestation; T5 35-37 weeks gestation; T6 delivery*

Table S1: Samples analysed. Number of samples analysed for each biospecimen type at each time point**.**

| | Group | Maternal | | | | | | | Infant |
		T1	T2	T3	T4	T5	T6	Total	T6
Serum	NBS	54	47	47	43	38	27	256	30
	RES	6	10	12	8	10	7	53	10
	MAL	12	15	15	15	17	11	85	14
Urine	NBS	63	61	58	52	51	41	326	18
	RES	6	11	11	12	12	12	64	6
	MAL	16	16	17	18	18	16	101	4
Faeces	NBS	9	11	-	21	-	-	41	-
	MAL	10	7	-	10	-	-	27	-

NBS no bariatric surgery; RES restrictive; MAL malabsorptive; T1 11-14 weeks gestation; T2 20-24 weeks gestation; T3 28-30 weeks gestation; T4 30-33 weeks gestation; T5 35-37 weeks gestation; T6 delivery

Table S2: Clinical characteristics and pregnancy outcomes of the study participants

Variable	No bariatric surgery (n = 70)	Post-bariatric surgery (n = 41)	Restrictive (n = 16)	Malabsorptive (n = 25)
Maternal age, years	29.72 ± 5.26	33.46 ± 4.58*	32.56 ± 4.32*	34.04 ± 4.8*
Parity, n (%)				
Nulliparous	43 (61.4)	20 (48.8)	9 (56.3)	11 (44.0)
Parous	27 (38.6)	21 (51.2)	7 (43.8)	14 (56.0)
Racial group, n (%)				
White	54 (77.1)	31 (75.6)	12 (75)	19 (76.0)
Other	16 (22.9)	10 (24.4)	4 (25)	6 (24.0)
Conception, n (%)				
Spontaneous	67 (95.7)	38 (92.7)	16 (100.0)	22 (88.0)
Assisted reproductive techniques	3 (4.3)	3 (7.3)	0 (0)	3 (12.0)
Smoking, n (%)				
No	67 (95.7)	36 (87.8)	15 (93.8)	21 (84.0)
Yes	3 (4.3)	5 (12.2)	1 (6.3)	4 (16.0)
Time between surgery and conception, months	-	58.34 ± 31.24	49.12 ± 30.54	64.24 ± 30.83ⱡ
BMI prior to surgery, kg/m^2	-	47.19 ± 7.95	41.95 ± 6.47	50.54 ± 7.01ⱡ
Booking BMI, kg/m^2	34.12 ± 5.68	32.94 ± 5.10	32.96 ± 7.29	32.93 ± 4.10
Gestational age at delivery, weeks	39.44 ± 1.34	38.67 ± 2.266*	38.95 ± 2.31	38.49 ± 2.26*
Mode of delivery, n (%)				
Vaginal	38 (54.3)	21 (51.2)	6 (37.5)	15 (60.0)
Caesarean section	32 (45.7)	20 (48.8)	10 (62.5)	10 (40.0)
Birth weight, g	3520.92 ± 603.86	3062.53 ± 588.32*	3096.75 ± 519.07*	3040.64 ± 638.12*
Birth weight percentile	59.48 ± 33.30	39.01 ± 27.35*	39.29 ± 26.25*	38.83 ± 28.57*

*Data are expressed as mean ± standard deviation or as otherwise stated. *P <0.05 comparison to no bariatric surgery group; ⱡP <0.05 comparison between restrictive and malabsorptive groups*

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Table S3: Summary of OPLS-DA model statistics. OPLS-DA model statistics for two-group comparisons are reported for each time point after excluding extreme outliers identified from PCA models.

Time point	Biofluid	Samples	Outliers Excluded	Class	R^2X	R^2Y	Q^2	*P* value
11-14 weeks (T1)	Urine	NBS n = 63	NBS n = 3	NBS vs RES	0.119	0.776	-0.117	NS
		RES n = 6	RES n = 1	RES vs MAL	0.171	0.935	-0.025	NS
		MAL n = 16	MAL n = 2	**NBS vs MAL**	**0.088**	**0.830**	**0.159**	**0.015388**
	Serum	NBS n = 54	NBS n = 0	NBS vs RES	0.022	0.817	-0.274	NS
		RES n = 6	RES n = 0	RES vs MAL	0.058	0.929	-0.044	NS
		MAL n = 12	MAL n = 0	NBS vs MAL	0.037	0.749	-0.156	NS
20-24 weeks (T2)	Urine	NBS n = 61	NBS n = 1	NBS vs RES	0.096	0.810	0.094	NS
		RES n = 11	RES n = 1	RES vs MAL	0.140	0.941	0.297	NS
		MAL n = 16	MAL n = 0	**NBS vs MAL**	**0.095**	**0.843**	**0.324**	**1.17E-05**
	Serum	NBS n = 47	NBS n = 0	NBS vs RES	0.027	0.830	-0.067	NS
		RES n = 10	RES n = 0	RES vs MAL	0.051	0.900	0.056	NS
		MAL n = 15	MAL n = 0	NBS vs MAL	0.031	0.825	0.114	NS
28-30 weeks (T3)	Urine	NBS n = 58	NBS n = 0	NBS vs RES	0.111	0.826	0.046	NS
		RES n = 11	RES n = 1	RES vs MAL	0.187	0.893	0.343	NS
		MAL n = 17	MAL n = 3	**NBS vs MAL**	**0.100**	**0.843**	**0.407**	**3.71E-07**
	Serum	NBS n = 47	NBS n = 0	NBS vs RES	0.033	0.748	-0.218	NS
		RES n = 12	RES n = 0	RES vs MAL	0.049	0.948	0.216	NS
		MAL n = 15	MAL n = 0	NBS vs MAL	0.040	0.744	0.091	NS
30-33 weeks (T4)	Urine	NBS n = 52	NBS n = 2	NBS vs RES	0.121	0.790	0.052	NS
		RES n = 12	RES n = 1	RES vs MAL	0.131	0.921	0.086	NS
		MAL n = 18	MAL n = 1	**NBS vs MAL**	**0.119**	**0.812**	**0.344**	**2.42E-05**
	Serum	NBS n = 43	NBS n = 0	NBS vs RES	0.034	0.742	-0.098	NS
		RES n = 8	RES n = 0	RES vs MAL	0.075	0.881	0.214	NS
		MAL n = 15	MAL n = 0	**NBS vs MAL**	**0.042**	**0.775**	**0.178**	**0.027**
35-37 weeks (T5)	Urine	NBS n = 51	NBS n = 2	NBS vs RES	0.117	0.802	0.023	NS
		RES n = 12	RES n = 0	RES vs MAL	0.135	0.935	0.001	NS
		MAL n = 18	MAL n = 0	**NBS vs MAL**	**0.109**	**0.852**	**0.483**	**2.11E-08**
	Serum	NBS n = 38	NBS n = 0	NBS vs RES	0.026	0.908	-0.377	NS
		RES n = 10	RES n = 0	RES vs MAL	0.054	0.916	0.224	NS
		MAL n = 17	MAL n = 0	**NBS vs MAL**	**0.048**	**0.847**	**0.245**	**0.006**
Delivery (T6)	Urine	NBS n = 41	NBS n = 2	NBS vs RES	0.087	0.844	0.055	NS
		RES n = 12	RES n = 0	RES vs MAL	0.164	0.907	0.110	NS
		MAL n = 16	MAL n = 4	NBS vs MAL	0.134	0.767	0.067	NS
	Serum	NBS n = 27	NBS n = 0	NBS vs RES	0.035	0.895	-0.116	NS
		RES n = 7	RES n = 0	RES vs MAL	0.068	0.903	-0.103	NS
		MAL n = 11	MAL n = 0	NBS vs MAL	0.055	0.789	0.028	NS
	Cord Blood	NBS n = 30	NBS n = 0	NBS vs RES	0.030	0.886	-0.022	NS
		RES n =10	RES n =0	RES vs MAL	0.043	0.925	-0.025	NS
		MAL n = 14	MAL n = 0	NBS vs MAL	0.037	0.885	0.031	NS
	Newborn urine	NBS n = 18	NBS n = 0	Univariate analysis only				
		RES n = 6	RES n = 0					
		MAL n = 4	MAL n = 0					

NBS no bariatric surgery; RES restrictive; MAL malabsorptive; NS not significant (P<0.05)
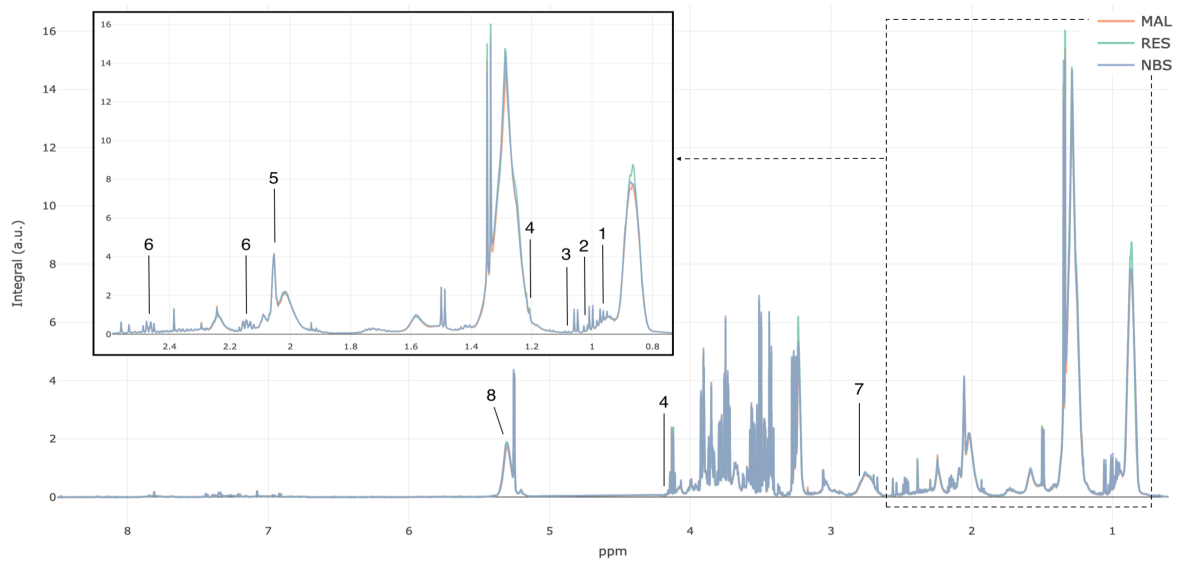
Figure S2: Overlayed median ¹H NMR serum spectra. A median spectrum is plotted for each study group. Annotated peaks and peak groups are those that were considered discriminatory in OPLS-DA models comparing malabsorptive (MAL) and no bariatric surgery (NBS) patients. The representative spectrum for restrictive (RES) patients is also plotted. 1 leucine; 2 isoleucine; 3 isobutyrate; 4 D-β-hydroxybutyrate ; 5 N-acetyl glycoprotein (GlycA) ; 6 glutamine ; 7 lipids (C=CCH$_2$C=C) ; 8 unsaturated lipids (CH=CH)

Table S4: Metabolite identification

Metabolite	¹H NMR Chemical Shifts*	Confirmed by	Biofluid
Leucine	0.96 (2xd), 1.71 (m), 3.73 (t)	STOCSY/STORM, J-res	Serum
Isoleucine	0.94 (t), 1.01 (d)	STOCSY/STORM, J-res	Serum
Isobutyrate	1.09 (d)	STOCSY/STORM, J-res, HSQC	Serum
N–acetyl glycoprotein	2.05 (s)	STOCSY/STORM, J-res, HSQC	Serum
Glutamine	2.14 (m), 2.46 (m), 3.77 (t)	STOCSY/STORM, J-res, HSQC	Serum
D-β-hydroxybutyrate	1.22 (d), 2.37 (m), 4.17 (m)	STOCSY/STORM, J-res	Serum
Valine	0.99 (d), 1.04 (d)	STOCSY/STORM, J-res	Urine
α-ketoisovalerate	1.11 (d)	STOCSY/STORM, J-res	Urine
Methylmalonate	1.24 (d)	STOCSY/STORM, J-res	Urine
Creatinine	3.05 (s), 4.06 (s)	STOCSY/STORM, J-res	Urine
p-cresol sulfate	2.35 (s), 7.21 (d), 7.28 (d)	STOCSY/STORM, J-res, HSQC	Urine
p-hydroxyphenylacetate	3.45 (s), 6.86 (d), 7.17 (d)	STOCSY/STORM, J-res, HSQC, spike in	Urine
Phenylacetylglutamine	1.92 (m), 2.11 (m), 2.27 (m), 3.67 (m), 4.19 (m), 7.36 (t), 7.43 (t)	STOCSY/STORM, J-res, HSQC	Urine
Unknown	7.34 (d), 7.48 (t)	STOCSY/STORM, J-res, HSQC	Urine
Indoxyl sulfate	7.5 (d), 7.7 (d)	STOCSY/STORM, J-res, HSQC, spike in	Urine

*s=singlet, d=doublet, t=triplet, m=multiplet
STOCSY: Statistical Total Correlation Spectroscopy; STORM: Subset Optimisation by Reference Matching; HSQC: Hetero-nuclear Single Quantum Coherence (2D NMR)
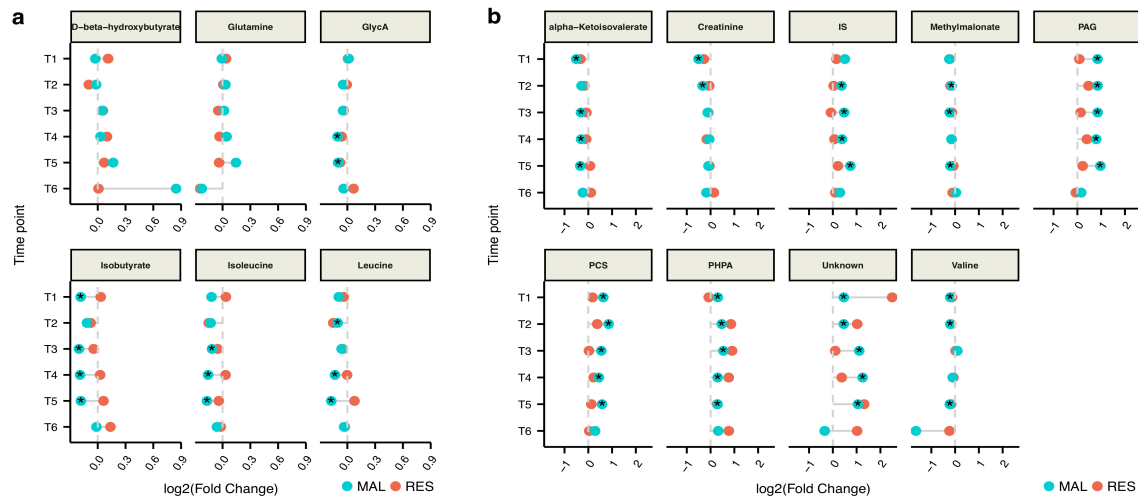
Figure S3: Maternal metabolic changes depend on type of bariatric surgery. For each discriminatory metabolite identified in (a) serum or (b) urine samples, changes in relative concentrations for malabsorptive (MAL) and restrictive (RES) groups are plotted at each time point. The no bariatric surgery (NBS) group was used as the reference group in fold change calculations. *T1 11-14 weeks gestation; T2 20-24 weeks gestation; T3 28-30 weeks gestation; T4 30-33 weeks gestation; T5 35-37 weeks gestation; T6 delivery; GlycA N-acetyl glycoprotein; IS indoxyl sulfate; PAG phenylacetylglutamine; PCS p-cresol sulfate; PHPA p-hydroxyphenylacetate; *P_{adj} <0.05 (Mann-Whitney U)*

Table S5: Maternal metabolic changes depend on type of bariatric surgery. For each discriminatory metabolite identified by OPLS-DA (malabsorptive versus no bariatric surgery), changes in relative concentrations are detailed at each time point with no bariatric surgery as the reference group. Calculations in the restrictive group are shown for comparison.

Metabolite	Biofluid	Time point	Restrictive			Malabsorptive		
			$\log_2$FC	*P*	*P$_{adj}$*	$\log_2$FC	*P*	*P$_{adj}$*
Isoleucine	Serum	T1	0.036	NS	NS	-0.119	NS	NS
		T2	-0.149	3.15E-02	NS	-0.128	3.54E-02	NS
		T3	-0.053	NS	NS	-0.114	2.14E-02	4.18E-02
		T4	0.033	NS	NS	-0.156	1.11E-02	2.56E-02
		T5	-0.041	NS	NS	-0.168	4.62E-03	1.49E-02
		T6	-0.02	NS	NS	-0.061	NS	NS
Leucine	Serum	T1	-0.04	NS	NS	-0.093	NS	NS
		T2	-0.152	7.02E-03	NS	-0.105	2.65E-02	4.97E-02
		T3	-0.049	NS	NS	-0.062	NS	NS
		T4	-0.003	NS	NS	-0.133	2.39E-03	8.97E-03
		T5	0.077	NS	NS	-0.174	1.26E-04	1.14E-03
		T6	-0.028	NS	NS	-0.035	NS	NS
Isobutyrate	Serum	T1	0.032	NS	NS	-0.184	1.45E-03	5.69E-03
		T2	-0.077	NS	NS	-0.116	NS	NS
		T3	-0.044	NS	NS	-0.203	3.61E-04	1.86E-03
		T4	0.026	NS	NS	-0.191	2.54E-04	1.76E-03
		T5	0.062	NS	NS	-0.182	3.70E-04	1.86E-03
		T6	0.137	NS	NS	-0.014	NS	NS
Glutamine	Serum	T1	0.038	NS	NS	-0.008	NS	NS
		T2	0.009	NS	NS	0.031	NS	NS
		T3	-0.046	NS	NS	0.016	NS	NS
		T4	-0.032	NS	NS	0.044	NS	NS
		T5	-0.037	NS	NS	0.145	4.81E-02	NS
		T6	-0.242	NS	NS	-0.224	NS	NS
D-β-hydroxybutyrate	Serum	T1	0.112	NS	NS	-0.026	NS	NS
		T2	-0.096	NS	NS	-0.018	NS	NS
		T3	0.056	NS	NS	0.047	NS	NS
		T4	0.1	NS	NS	0.03	NS	NS
		T5	0.07	NS	NS	0.167	NS	NS
		T6	0.008	NS	NS	0.847	NS	NS
GlycA	Serum	T1	0.007	NS	NS	0.014	NS	NS
		T2	-0.007	NS	NS	-0.046	NS	NS
		T3	-0.039	NS	NS	-0.046	NS	NS
		T4	-0.062	NS	NS	-0.105	1.57E-02	3.37E-02
		T5	-0.079	NS	NS	-0.099	2.02E-02	4.04E-02
		T6	0.067	NS	NS	-0.04	NS	NS
PAG	Urine	T1	0.082	NS	NS	0.85	1.02E-04	1.02E-03
		T2	0.469	NS	NS	0.854	2.99E-05	4.38E-04
		T3	0.137	NS	NS	0.853	4.73E-05	5.32E-04
		T4	0.397	NS	NS	0.794	3.39E-05	4.38E-04
		T5	0.222	NS	NS	0.97	1.27E-06	1.14E-04
		T6	-0.064	NS	NS	0.162	NS	NS
		T1	0.178	NS	NS	0.631	1.42E-03	5.69E-03
		T2	0.375	NS	NS	0.856	2.40E-04	1.76E-03

PCS	Urine	T3	0.028	NS	NS	0.547	1.49E-02	3.26E-02
		T4	0.228	NS	NS	0.444	1.01E-02	2.39E-02
		T5	0.13	NS	NS	0.581	3.69E-03	1.28E-02
		T6	0.04	NS	NS	0.286	NS	NS
IS	Urine	T1	0.151	NS	NS	0.505	4.10E-02	NS
		T2	0.035	NS	NS	0.365	8.85E-03	2.28E-02
		T3	-0.081	NS	NS	0.478	8.02E-03	2.12E-02
		T4	0.069	NS	NS	0.388	6.51E-03	1.77E-02
		T5	0.212	NS	NS	0.739	1.83E-05	4.38E-04
		T6	0.105	NS	NS	0.297	NS	NS
PHPA	Urine	T1	-0.077	NS	NS	0.305	7.77E-04	3.50E-03
		T2	0.854	4.51E-02	NS	0.47	1.34E-03	5.69E-03
		T3	0.905	2.53E-02	NS	0.539	3.41E-05	4.38E-04
		T4	0.764	4.42E-03	NS	0.3	9.69E-03	2.39E-02
		T5	0.279	3.34E-02	NS	0.296	4.98E-03	1.55E-02
		T6	0.767	NS	NS	0.321	4.20E-02	NS
Unknown	Urine	T1	2.495	8.54E-03	NS	0.463	3.60E-04	1.86E-03
		T2	1.025	4.19E-02	NS	0.459	6.08E-03	1.73E-02
		T3	0.1	NS	NS	1.111	6.15E-03	1.73E-02
		T4	0.375	3.36E-02	NS	1.252	2.68E-05	4.38E-04
		T5	1.319	1.89E-03	NS	1.055	3.71E-04	1.86E-03
		T6	1.021	4.69E-02	NS	-0.343	NS	NS
Creatinine	Urine	T1	-0.282	NS	NS	-0.505	3.10E-05	4.38E-04
		T2	-0.057	NS	NS	-0.333	2.53E-03	9.12E-03
		T3	-0.096	NS	NS	-0.119	NS	NS
		T4	-0.159	NS	NS	-0.055	NS	NS
		T5	-0.045	NS	NS	-0.086	NS	NS
		T6	0.141	NS	NS	-0.173	NS	NS
α-ketoisovalerate	Urine	T1	-0.327	NS	NS	-0.504	2.24E-04	1.76E-03
		T2	-0.161	NS	NS	-0.284	NS	NS
		T3	-0.078	NS	NS	-0.307	1.77E-02	3.63E-02
		T4	-0.087	NS	NS	-0.301	2.27E-02	4.36E-02
		T5	0.073	NS	NS	-0.335	1.77E-02	3.63E-02
		T6	0.106	NS	NS	-0.23	NS	NS
Methylmalonate	Urine	T1	-0.224	NS	NS	-0.242	3.87E-02	NS
		T2	-0.191	NS	NS	-0.143	1.27E-02	2.86E-02
		T3	-0.133	NS	NS	-0.23	3.83E-03	1.28E-02
		T4	-0.148	NS	NS	-0.153	NS	NS
		T5	-0.073	NS	NS	-0.198	1.00E-02	2.39E-02
		T6	-0.102	NS	NS	0.038	NS	NS
Valine	Urine	T1	-0.13	NS	NS	-0.204	5.31E-03	1.59E-02
		T2	-0.175	8.95E-03	NS	-0.204	3.72E-04	1.86E-03
		T3	0.021	2.32E-02	NS	0.097	NS	NS
		T4	-0.071	NS	NS	-0.1	3.67E-02	NS
		T5	-0.169	9.34E-03	NS	-0.224	4.80E-04	2.28E-03
		T6	-0.237	NS	NS	-1.649	NS	NS

GlycA N-acetyl glycoprotein; PAG phenylacetylglutamine; PCS p-cresol sulfate; IS indoxyl sulfate; PHPA p-hydroxyphenylacetate; T1 11-14 weeks gestation; T2 20-24 weeks gestation; T3 28-30 weeks gestation; T4 30-33 weeks gestation; T5 35-37 weeks gestation; T6 delivery; FC fold change; NS not significant (P<0.05)
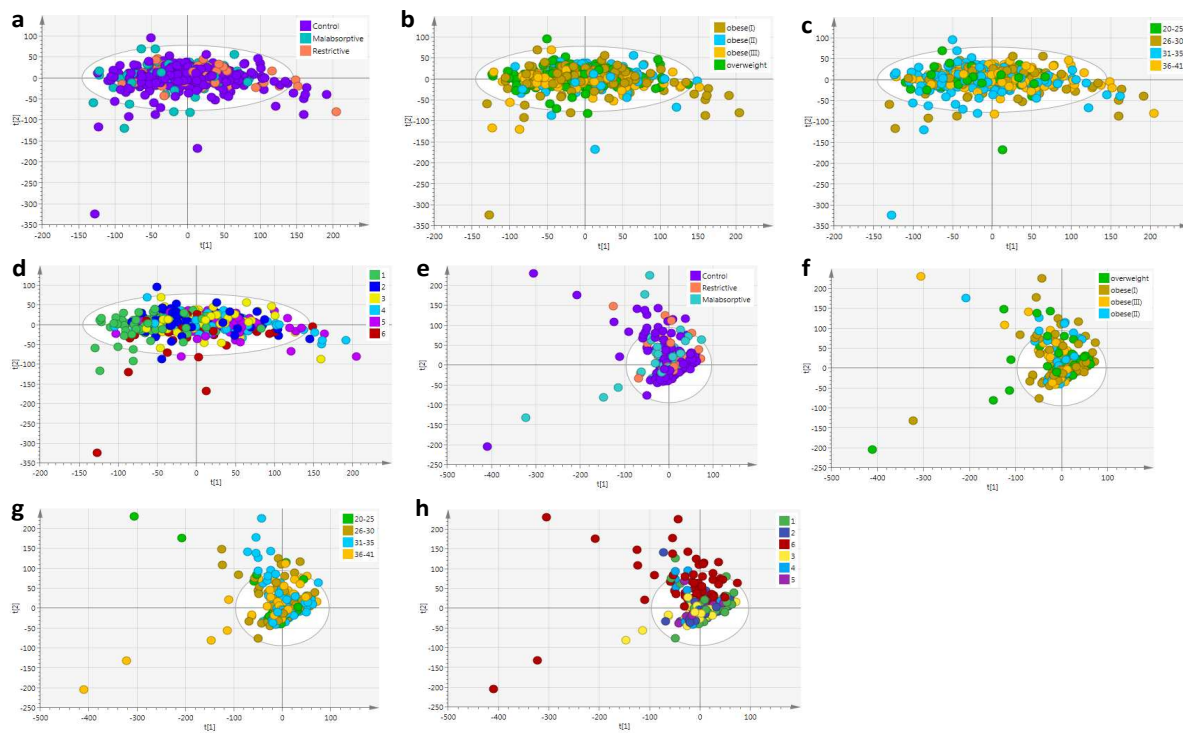
Figure S4: Principal component analysis (PCA) of ¹H NMR spectral data. Unsupervised PCA models were calculated with all samples analysed to assess overall variation in metabolic profiles. Serum metabolic profiles did not vary according to a) study group, b) BMI, or c) age but variation due to d) time point was observed between first trimester (T1) samples and those taken during later pregnancy (T2-T5) or at delivery (T6). Urinary metabolic profiles did not display overt signatures according to e) study group, f) BMI, or g) age but variation but due to h) time point was evident between samples taken during pregnancy (T1-T5) and those taken at delivery (T6). *T1 11-14 weeks gestation; T2 20-24 weeks gestation; T3 28-30 weeks gestation; T4 30-33 weeks gestation; T5 35-37 weeks gestation; T6 delivery*
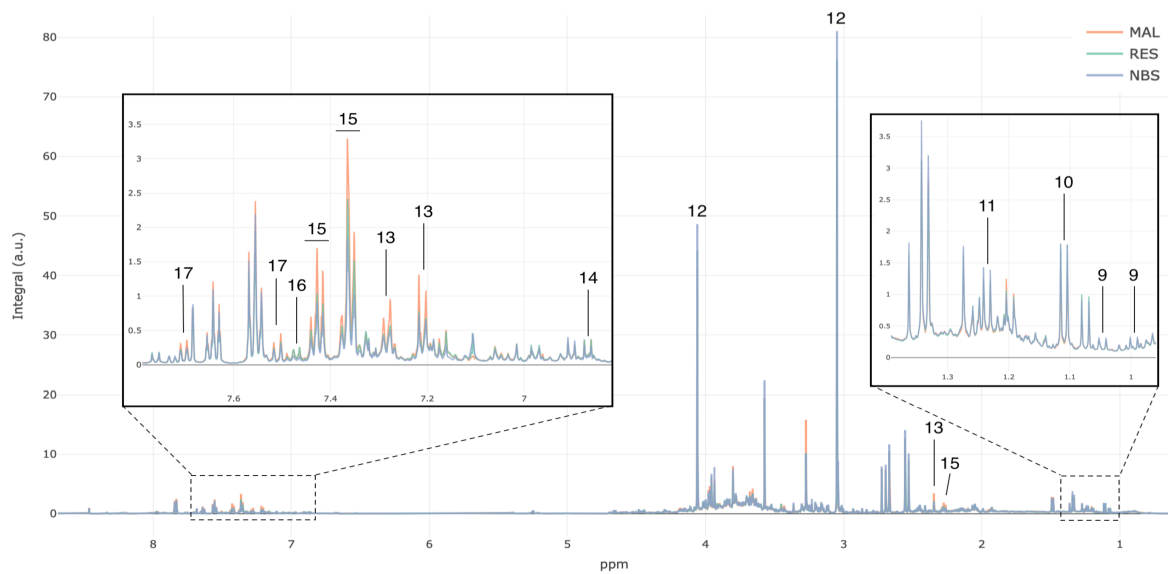
Figure S5: Overlayed median ¹H NMR urine spectra. A median spectrum is plotted for each study group with annotated peaks and peak groups. Annotated metabolites were considered discriminatory in OPLS-DA models comparing malabsorptive (MAL) and no bariatric surgery (NBS) patients. The representative spectrum for restrictive (RES) patients is also plotted. 9 valine; 10 α-ketoisovalerate; 11 methylmalonate; 12 creatinine; 13 *p*-cresol sulfate; 14 *p*-hydroxyphenylacetate; 15 phenylacetylglutamine; 16 unknown; 17 indoxyl sulfate
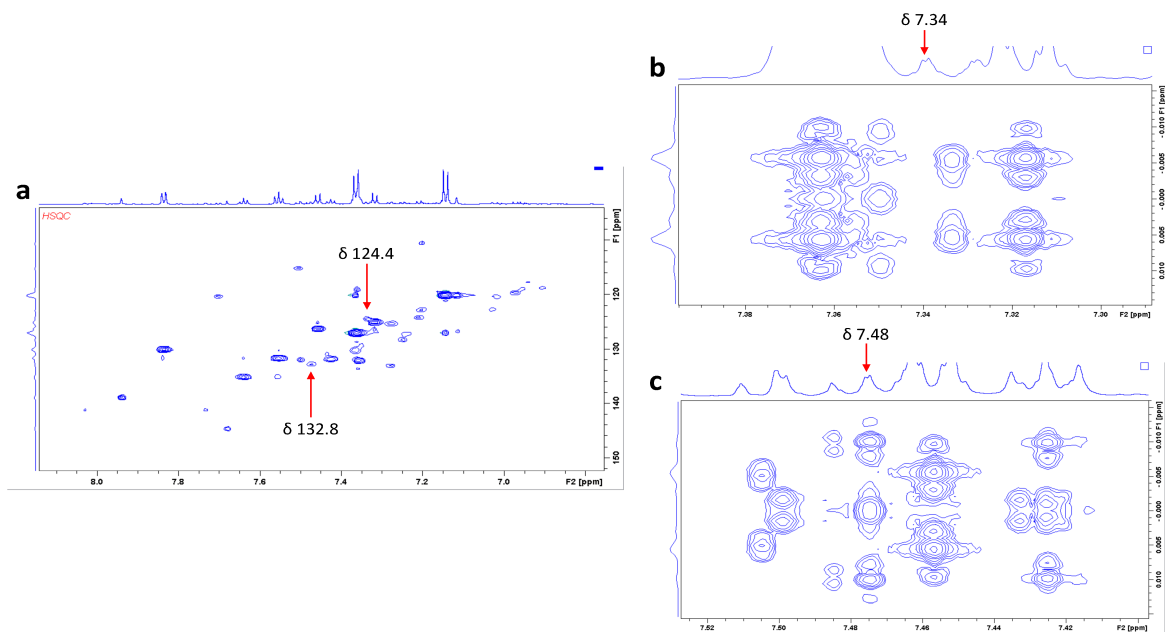

Figure S6: Chemical shifts of unknown metabolite. a) Hetero-nuclear Single Quantum Coherence (HSQC) spectrum detailing ¹³C chemical shifts and b-c) J-resolved spectra detailing the proton-proton coupling of the ¹H chemical shifts.
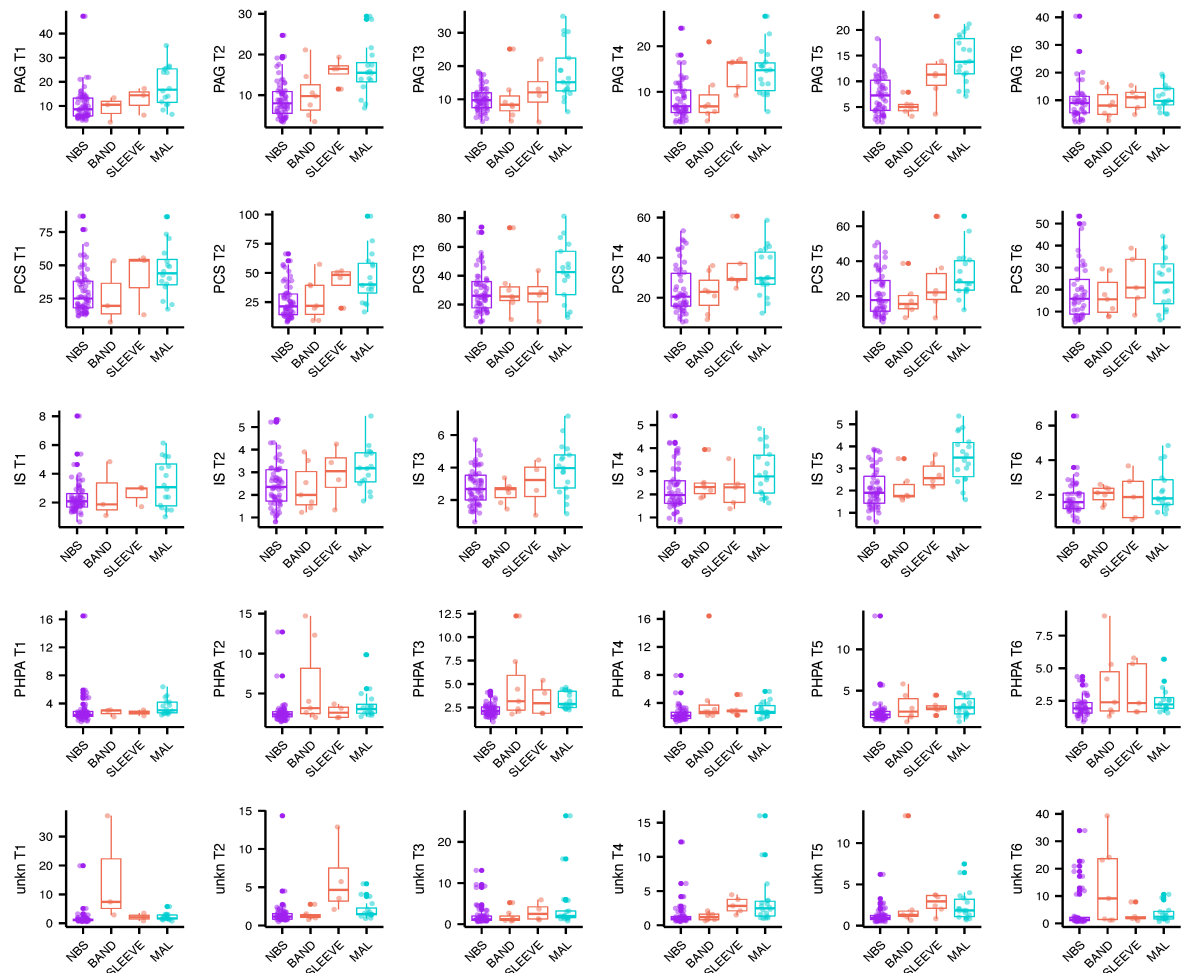
Figure S7: Relative concentrations of urinary host-microbial co-metabolites vary depending on bariatric surgery sub-type. Relative concentrations of each metabolite (by row) at each time point (by column) are represented in arbitrary units. Restrictive patients are separated by surgery sub-type (band or sleeve). *NBS no bariatric surgery; MAL malabsorptive; PAG phenylacetylglutamine; PCS p-cresol sulfate; IS indoxyl sulfate; PHPA p-hydroxyphenylacetate; unkn unknown ; T1 11-14 weeks gestation; T2 20-24 weeks gestation; T3 28-30 weeks gestation; T4 30-33 weeks gestation; T5 35-37 weeks gestation; T6 delivery*

Table S6: Differentially abundant taxa in malabsorptive group. For each taxonomic rank, differential abundance was assessed by calculating $\log_2$(FC) of taxa relative abundances at each time point and applying the Mann-Whitney U test. Taxa with $P_{adj} < 0.05$ are reported.

Rank	Time point	Taxon	Mean relative abundance malabsorptive	Mean relative abundance control	P value	$\log_2$(FC)	P_{adj}
Phylum	T1	*Proteobacteria*	0.13632	0.02701	0.0017	2.34	0.0237
Phylum	T4	*Bacteroidetes*	0.39265	0.52280	0.0016	-0.41	0.0237
Phylum	T4	*Proteobacteria*	0.16318	0.03249	5.45E-05	2.33	0.0020
Class	T1	*Gammaproteobacteria*	0.12379	0.01714	0.0022	2.85	0.0248
Class	T1	*Clostridia*	0.28025	0.40068	0.0048	-0.52	0.0357
Class	T1	*Bacilli*	0.05978	0.00789	0.0007	2.92	0.0144
Class	T2	*Bacilli*	0.03774	0.00694	0.0011	2.44	0.0202
Class	T4	*Bacteroidia*	0.39459	0.52538	0.0019	-0.41	0.0248
Class	T4	*Gammaproteobacteria*	0.13910	0.01069	2.61E-05	3.70	0.0020
Class	T4	*Bacilli*	0.07171	0.00987	5.45E-05	2.86	0.0020
Order	T1	*Enterobacteriales*	0.12097	0.01627	0.0048	2.89	0.0357
Order	T1	*Clostridiales*	0.28024	0.40059	0.0048	-0.52	0.0357
Order	T1	*Lactobacillales*	0.05906	0.00789	0.0007	2.90	0.0144
Order	T2	*Enterobacteriales*	0.11434	0.02743	0.0066	2.06	0.0425
Order	T2	*Lactobacillales*	0.03772	0.00689	0.0011	2.45	0.0202
Order	T4	*Bacteroidales*	0.39470	0.52539	0.0019	-0.41	0.0248
Order	T4	*Enterobacteriales*	0.12698	0.00888	4.54E-05	3.84	0.0020
Order	T4	*Lactobacillales*	0.07137	0.00982	5.45E-05	2.86	0.0020
Order	T4	*Pasteurellales*	0.01194	0.00181	0.0043	2.72	0.0357
Order	T4	*Actinomycetales*	0.00084	0.00025	0.0043	1.76	0.0357
Family	T1	*Enterobacteriaceae*	0.12514	0.01639	0.0048	2.93	0.0357
Family	T1	*Streptococcaceae*	0.05582	0.00795	0.0029	2.81	0.0285
Family	T1	*Micrococcaceae*	0.00028	8.76E-05	0.0042	1.66	0.0357
Family	T2	*Enterobacteriaceae*	0.11799	0.02810	0.0066	2.07	0.0425
Family	T2	*Enterococcaceae*	0.00290	1.30E-05	0.0003	7.80	0.0086
Family	T2	*Streptococcaceae*	0.03420	0.00689	0.0021	2.31	0.0248
Family	T2	*Micrococcaceae*	0.00027	4.95E-05	0.0028	2.45	0.0285
Family	T4	*Enterobacteriaceae*	0.12905	0.00927	4.54E-05	3.80	0.0020
Family	T4	*Enterococcaceae*	0.00179	2.78E-05	0.0003	6.01	0.0086
Family	T4	*Streptococcaceae*	0.07027	0.00983	5.45E-05	2.84	0.0020
Family	T4	*Pasteurellaceae*	0.01203	0.00183	0.0043	2.72	0.0357
Family	T4	*Carnobacteriaceae*	0.00032	6.41E-05	0.0013	2.30	0.0222
Family	T4	*Micrococcaceae*	0.00023	8.65E-05	0.0079	1.40	0.0497
Genus	T1	*Escherichia.Shigella*	0.11566	0.01274	0.0022	3.18	0.0248

Genus	T1	*Streptococcus*	0.06395	0.00895	0.0022	2.84	0.0248
Genus	T1	*Anaerostipes*	0.00281	0.01592	0.0037	-2.50	0.0350
Genus	T1	*Holdemanella*	0.02151	0.00238	0.0066	3.18	0.0425
Genus	T1	*Rothia*	0.00031	9.97E-05	0.0055	1.64	0.0380
Genus	T2	*Enterococcus*	0.00323	1.45E-05	0.0003	7.80	0.0086
Genus	T2	*Streptococcus*	0.03881	0.00794	0.0028	2.29	0.0285
Genus	T2	*Butyricimonas*	0.00191	0.00029	0.0050	2.70	0.0357
Genus	T2	*Rothia*	0.00030	5.59E-05	0.0028	2.43	0.0285
Genus	T4	*Escherichia.Shigella*	0.12798	0.00838	5.44E-05	3.93	0.0020
Genus	T4	*Enterococcus*	0.00202	3.12E-05	0.0003	6.02	0.0086
Genus	T4	*Streptococcus*	0.07909	0.01096	5.45E-05	2.85	0.0020
Genus	T4	*Anaerostipes*	0.00395	0.01148	0.0064	-1.54	0.0425
Genus	T4	*Haemophilus*	0.01321	0.00202	0.0049	2.71	0.0357
Genus	T4	*Veillonella*	0.00982	0.00120	0.0004	3.04	0.0097
Genus	T4	*Acidaminococcus*	0.00350	7.71E-05	0.0044	5.50	0.0357
Genus	T4	*Solobacterium*	0.00118	0.00029	0.0014	2.01	0.0223
Genus	T4	*Granulicatella*	0.00035	7.13E-05	0.0015	2.31	0.0233

FC fold change; T1 11-14 weeks gestation; T2 20-24 weeks gestation; T4 30-33 weeks gestation

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Table S7: Differentially abundant amplicon sequence variants. 16S rRNA gene amplicon sequences belonging to genera of interest that are significantly (P_{adj} <0.05) more abundant (DESeq2) in the malabsorptive group compared to no bariatric surgery controls.

Genus	log$_2$(FC)	P_{adj}	Species assignment	
			RDP	SILVA
Escherichia/ Shigella	4.96	0.0132	coli	coli/flexneri
	9.31	0.0005	-	coli
	7.15	2.40E-05	coli	coli/fergusonii
	3.95	0.0412	coli/dysenteriae	-
	5.71	0.0357	-	coli
	7.3	1.20E-05	coli	coli
	5.21	0.0293	coli/flexneri	coli/flexneri/sonnei
	3.3	0.0184	-	-
	22.69	6.80E-12	coli	coli
	6.27	3.60E-06	coli	coli/fergusonii
	3.31	0.0002	-	-
Streptococcus	5.26	0.0408	gordonii	gordonii/sanguinis
	7.52	1.10E-13	vestibularis	vestibularis
	3.68	6.70E-07	salivarius/ vestibularis	-
	4.09	0.0076	salivarius/ vestibularis	salivarius
	5.4	0.0376	salivarius	salivarius
	4.24	1.40E-05	-	infantis
	3.45	0.0313	mitis/sanguinis	-
	4.05	0.0001	mutans	mutans
	3.61	0.0297	parasanguinis	parasanguinis
	3.39	0.0201	mitis/parasanguinis	mitis
	2.78	0.0135	parasanguinis	parasanguinis
	3.34	0.0049	-	parasanguinis
Enterococcus	6.98	1.00E-12	faecalis/faecium	faecalis
Rothia	2.01	0.0316	mucilaginosa	-

FC fold change

Table S8: Relative concentrations of metabolites correlate with maternal insulin resistance and fetal/birth weight. Spearman's (ρ) correlations between metabolite relative concentrations at each time point and clinical or biochemical measures. Statistically significant (P_{adj} <0.05) correlations are detailed along with partial correlations.

Variable 1	Variable 2	ρ	P	P_{adj}	Partial ρ	P	P_{adj}
PAG_T1	Fasting Maternal Insulin (microU/ml)	-0.37	0.00063	0.00751	-0.28	0.01335	0.02114
PCS_T1	Fasting Maternal Insulin (microU/ml)	-0.36	0.00111	0.00974	-0.28	0.01229	0.02031
IS_T1	Fasting Maternal Insulin (microU/ml)	-0.31	0.00447	0.02349	-0.30	0.00753	0.01607
PAG_T2	Fasting Maternal Insulin (microU/ml)	-0.46	0.00001	0.00040	-0.32	0.00327	0.00879
PCS_T2	Fasting Maternal Insulin (microU/ml)	-0.35	0.00076	0.00796	-0.23	0.03351	0.03979
Ile_T2	Fasting Maternal Insulin (microU/ml)	0.4	0.00052	0.00727	0.38	0.00119	0.00664
Leu_T2	Fasting Maternal Insulin (microU/ml)	0.38	0.00116	0.00974	0.37	0.00184	0.00865
PAG_T3	Fasting Maternal Insulin (microU/ml)	-0.46	0.00001	0.00044	-0.33	0.00269	0.00865
PCS_T3	Fasting Maternal Insulin (microU/ml)	-0.42	0.00006	0.00155	-0.33	0.00252	0.00865
PAG_T4	Fasting Maternal Insulin (microU/ml)	-0.4	0.00021	0.00348	-0.36	0.00101	0.00664
PCS_T4	Fasting Maternal Insulin (microU/ml)	-0.4	0.00018	0.00328	-0.39	0.00041	0.00466
PAG_T5	Fasting Maternal Insulin (microU/ml)	-0.48	0.00001	0.00040	-0.39	0.00049	0.00466
PCS_T5	Fasting Maternal Insulin (microU/ml)	-0.41	0.00023	0.00353	-0.30	0.00858	0.01717
IS_T5	Fasting Maternal Insulin (microU/ml)	-0.41	0.00017	0.00328	-0.36	0.00122	0.00664
Leu_T5	Fasting Maternal Insulin (microU/ml)	0.36	0.00444	0.02349	0.34	0.00761	0.01607
PCS_T6	Fasting Maternal Insulin (microU/ml)	-0.32	0.00719	0.03551	-0.22	NS	NS
PAG_T1	Maternal HOMA-IR	-0.35	0.00148	0.01068	-0.25	0.02701	0.03311
PCS_T1	Maternal HOMA-IR	-0.35	0.00161	0.01079	-0.27	0.01638	0.02305
IS_T1	Maternal HOMA-IR	-0.29	0.00822	0.03943	-0.27	0.01488	0.02262
PAG_T2	Maternal HOMA-IR	-0.46	0.00001	0.00040	-0.32	0.00347	0.00879
PCS_T2	Maternal HOMA-IR	-0.33	0.00153	0.01068	-0.20	NS	NS
Ile_T2	Maternal HOMA-IR	0.38	0.00089	0.00828	0.35	0.00261	0.00865
Leu_T2	Maternal HOMA-IR	0.33	0.00418	0.02341	0.31	0.00994	0.01808
PAG_T3	Maternal HOMA-IR	-0.41	0.00010	0.00235	-0.26	0.01813	0.02461
PCS_T3	Maternal HOMA-IR	-0.35	0.00081	0.00796	-0.23	0.03463	0.03988

Ile_T3	Maternal HOMA-IR	0.3	0.00991	0.04500	0.20	NS	NS
PAG_T4	Maternal HOMA-IR	-0.37	0.00068	0.00766	-0.32	0.00340	0.00879
PCS_T4	Maternal HOMA-IR	-0.35	0.00148	0.01068	-0.31	0.00470	0.01115
PAG_T5	Maternal HOMA-IR	-0.44	0.00005	0.00155	-0.34	0.00273	0.00865
PCS_T5	Maternal HOMA-IR	-0.33	0.00298	0.01857	-0.21	NS	NS
IS_T5	Maternal HOMA-IR	-0.36	0.00138	0.01068	-0.29	0.01047	0.01808
Leu_T5	Maternal HOMA-IR	0.32	0.01084	0.04794	0.29	0.02488	0.03260
PAG_T2	EFW T2	-0.31	0.00321	0.01925	-0.26	0.01582	0.02305
PCS_T2	EFW T2	-0.29	0.00657	0.03344	-0.28	0.01014	0.01808
Ile_T2	EFW T2	0.3	0.00949	0.04428	0.20	NS	NS
IS_T5	EFW T5	-0.32	0.00402	0.02328	-0.26	0.02681	0.03311
PAG_T6	Birth weight	-0.36	0.00270	0.01743	-0.46	0.00020	0.00371
IS_T6	Birth weight	-0.4	0.00059	0.00751	-0.49	5.22E-05	0.00198351

PAG phenylacetylglutamine; PCS p-cresol sulfate; IS indoxyl sulfate; Ile isoleucine; Leu leucine; HOMA-IR Homeostatic Model Assessment of Insulin Resistance; EFW estimated fetal weight; T1 11-14 weeks gestation; T2 20-24 weeks gestation; T3 28-30 weeks gestation; T4 30-33 weeks gestation; T5 35-37 weeks gestation; T6 delivery
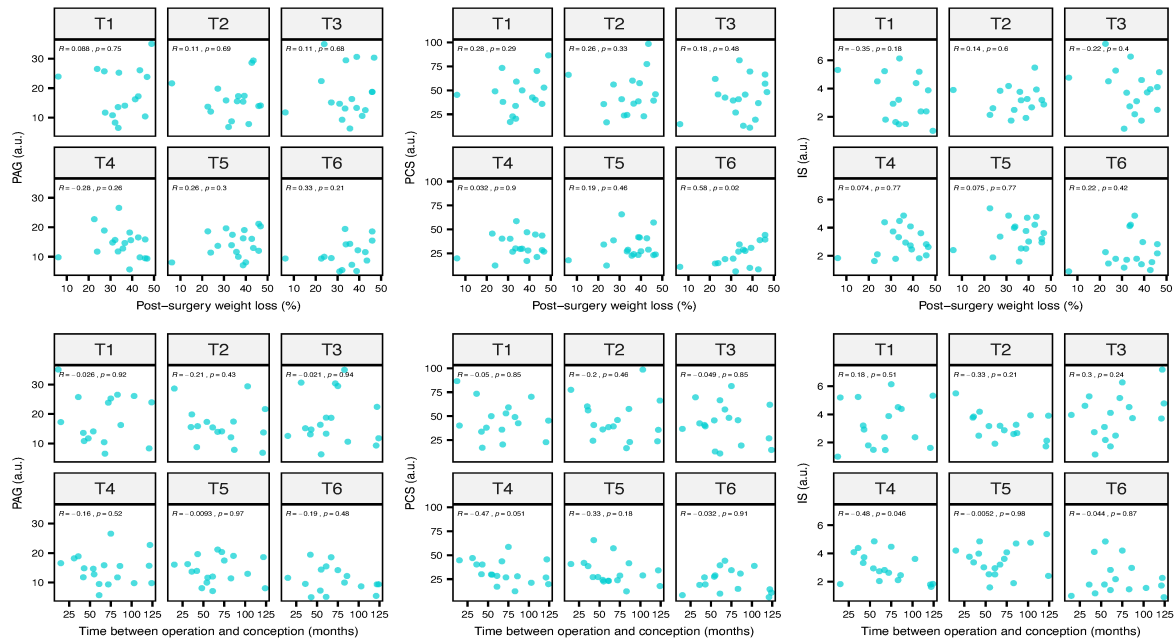

Figure S8: Key metabolites are not associated with percentage of weight lost or length of time since surgery in malabsorptive patients. Spearman correlations between metabolite relative concentrations at each time point and (a) percentage of weight lost from time of surgery to conception or (b) number of months between time of surgery and conception. Relative concentrations are reported in arbitrary units (a.u.). *PAG phenylacetylglutamine; PCS p-cresol sulfate; IS indoxyl sulfate.*