

SUPPLEMENTARY DATA

Supplementary Table 1. Baseline characteristics of the participants as randomized to treatment group.

	Colesevelam	Placebo	P-value
Age (Years)	62.6 ± 1.3	60.2 ± 1.5	0.22
HbA_{1c} (%)	6.7 ± 0.1	6.8 ± 0.1	0.88
Weight (kg)	92 ± 3	93 ± 3	0.78
Fasting Glucose (mmol/l)	7.0 ± 0.3	7.4 ± 0.4	0.54
BMI (kg/m²)	30.8 ± 1.0	30.4 ± 0.9	0.78
Total Cholesterol (mmol/l)	4.35 ± 0.19	4.33 ± 0.14	0.93
Triglycerides (mmol/l)	1.67 ± 0.15	1.88 ± 0.27	0.68
HDL (mmol/l)	1.18 ± 0.06	1.27 ± 0.08	0.33
LDL (mmol/l)	2.50 ± 0.17	2.31 ± 0.13	0.38

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Supplementary Table 2. Tabulated Lipid Values (Means \pm SEMs).

	Colesevelam		Placebo	
	Baseline	Treatment	Baseline	Treatment
Total Cholesterol (mmol/l)	4.35 \pm 0.19	3.60 \pm 0.16	4.33 \pm 0.14	4.00 \pm 0.14
Triglycerides (mmol/l)	1.67 \pm 0.15	2.19 \pm 0.19	1.88 \pm 0.27	1.55 \pm 0.18
HDL (mmol/l)	1.18 \pm 0.06	1.08 \pm 0.10	1.27 \pm 0.08	1.20 \pm 0.07
LDL (mmol/l)	2.50 \pm 0.17	1.59 \pm 0.14	2.31 \pm 0.13	2.09 \pm 0.12

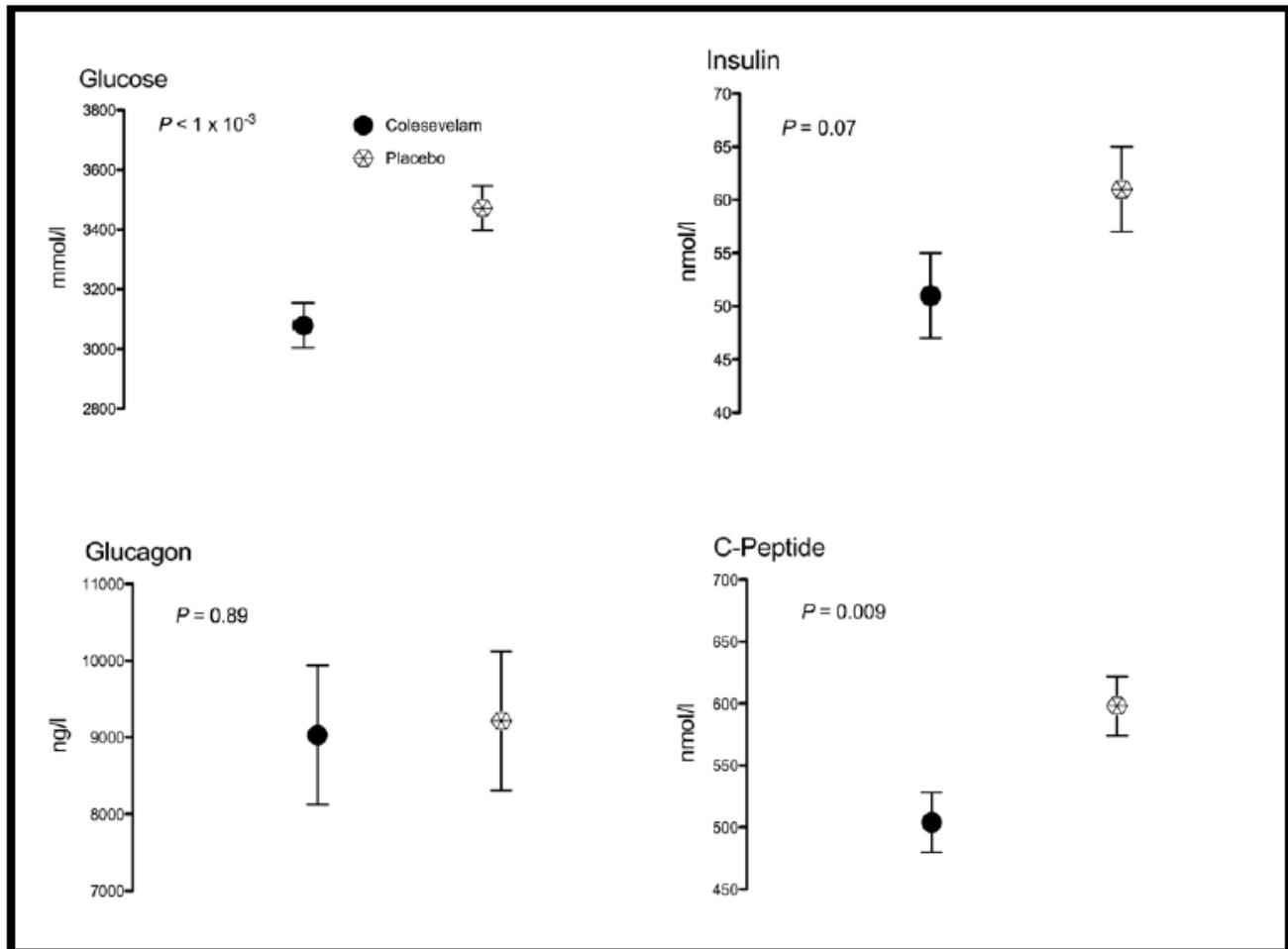
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Supplementary Table 3. AUC and AAB values for parameters measured. *AAB Meal Ra not calculated since baseline value was 0 and AUC reported in the text. ° Paired t-test. α LS Mean ANCOVA

Parameter Measured*	Colesevelam		Placebo		Colesevelam	Placebo	P-Value ^α
	Baseline	Treatment	Baseline	Treatment	LS_Mean	LS_Mean	
AUC Glucose (mmol per 6hr)	3286 ± 142	3028 ± 130	3394 ± 140	3523 ± 168	3078±75	3472±75	0.0007
P-Value [°]	0.003		0.10				
AAB Glucose (mmol per 6hr)	748 ± 86	667 ± 88	742 ± 97	809 ± 94	664±56	812±56	0.07
P-Value [°]	0.13		0.31				
AAB ₂₄₀ Glucose (mmol per 4hr)	912 ± 80	827 ± 84	876 ± 84	954 ± 70	813±43	968±43	0.01
P-Value [°]	0.09		0.09				
AUC Insulin (nmol per 6hr)	67.3 ± 7.9	63.9 ± 6.1	72.7 ± 8.3	81.9 ± 11.6	66.6±4.2	79.1±4.2	0.04
P-Value [°]	0.33		0.23				
AAB Insulin (nmol per 6hr)	49.9 ± 5.9	47.8 ± 4.8	54.8 ± 6.8	63.5 ± 10.4	50.6±3.8	60.7±3.8	0.07
P-Value [°]	0.31		0.18				
AUC C-Peptide (nmol per 6hr)	920 ± 54	876 ± 50	929 ± 71	995 ± 80	880±32	991±32	0.018
P-Value [°]	0.14		0.07				
AAB C-Peptide (nmol per 6hr)	531 ± 37	504 ± 32	532 ± 50	599 ± 60	504±24	598±24	0.009
P-Value [°]	0.18		0.03				
AUC Glucagon (ng/l per 6hr)	39052 ± 2830	40464 ± 2837	38464 ± 2259	38954 ± 2130	40206±1121	39212±1121	0.54
P-Value [°]	0.24		0.67				
AAB Glucagon (ng/l per 6hr)	9556 ± 1207	9362 ± 1237	8451 ± 1065	8880 ± 1000	9029±906	9213±906	0.89
P-Value [°]	0.84		0.69				
AUC GLP-1 (nmol per 3hr)	5.20 ± 0.44	5.08 ± 0.33	5.82 ± 0.63	5.18 ± 0.42	5.25±0.23	5.01±0.23	0.46
P-Value [°]	0.86		0.23				
AAB GLP-1 (nmol per 3hr)	1.90 ± 0.28	1.18 ± 0.35	2.47 ± 0.55	1.71 ± 0.44	1.35±0.31	1.55±0.31	0.66
P-Value [°]	0.04		0.06				
AUC EGP (μmol per 6hr)	3041 ± 110	2986 ± 72	3192 ± 119	3051 ± 143	3002±113	3034±113	0.84
P-Value [°]	0.59		0.43				
AUB EGP (μmol per 6hr)	-3225 ± 136	-3150 ± 151	-3189 ± 218	-3398 ± 180	-3139±128	-3408±128	0.15
P-Value [°]	0.47		0.26				
AUC Rd (μmol per 6hr)	8642 ± 414	8155 ± 314	8784 ± 403	8761 ± 382	8201±228	8714±228	0.12
P-Value [°]	0.35		0.93				
AAB Rd (μmol per 6hr)	2418 ± 311	2046 ± 232	2390 ± 412	2369 ± 399	2037±227	2378±227	0.30
P-Value [°]	0.44		0.93				

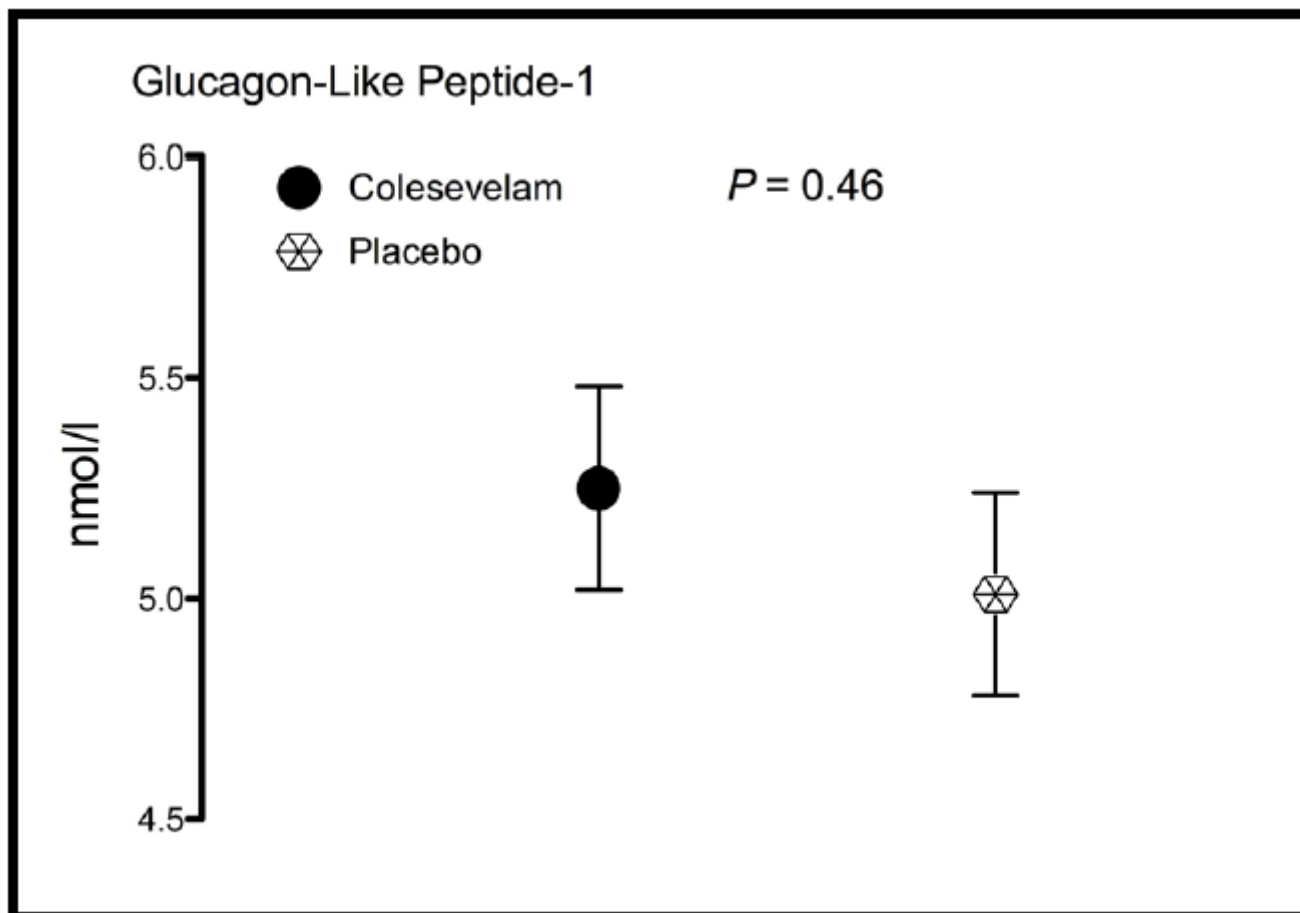
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Supplementary Figure 1. LS Means for integrated glucose (AUC), Insulin (AAB), Glucagon (AAB) and C-Peptide (AAB) responses after 12 weeks of treatment with colesevelam or Placebo. Note that SE are based on pooled residual variation.



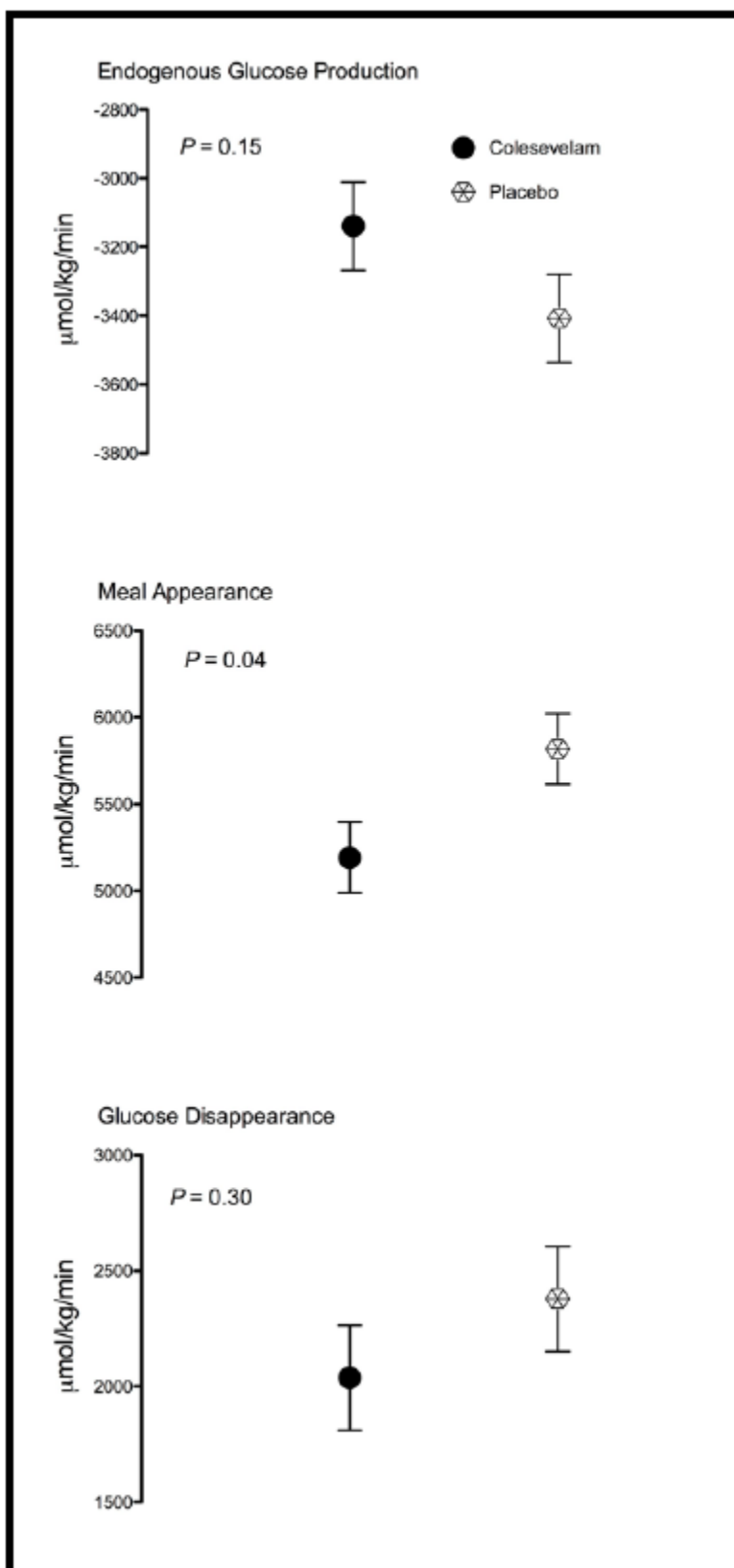
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Supplementary Figure 2. LS Mean for integrated (AUC) GLP-1 responses after 12 weeks of treatment with colesevelam or Placebo.



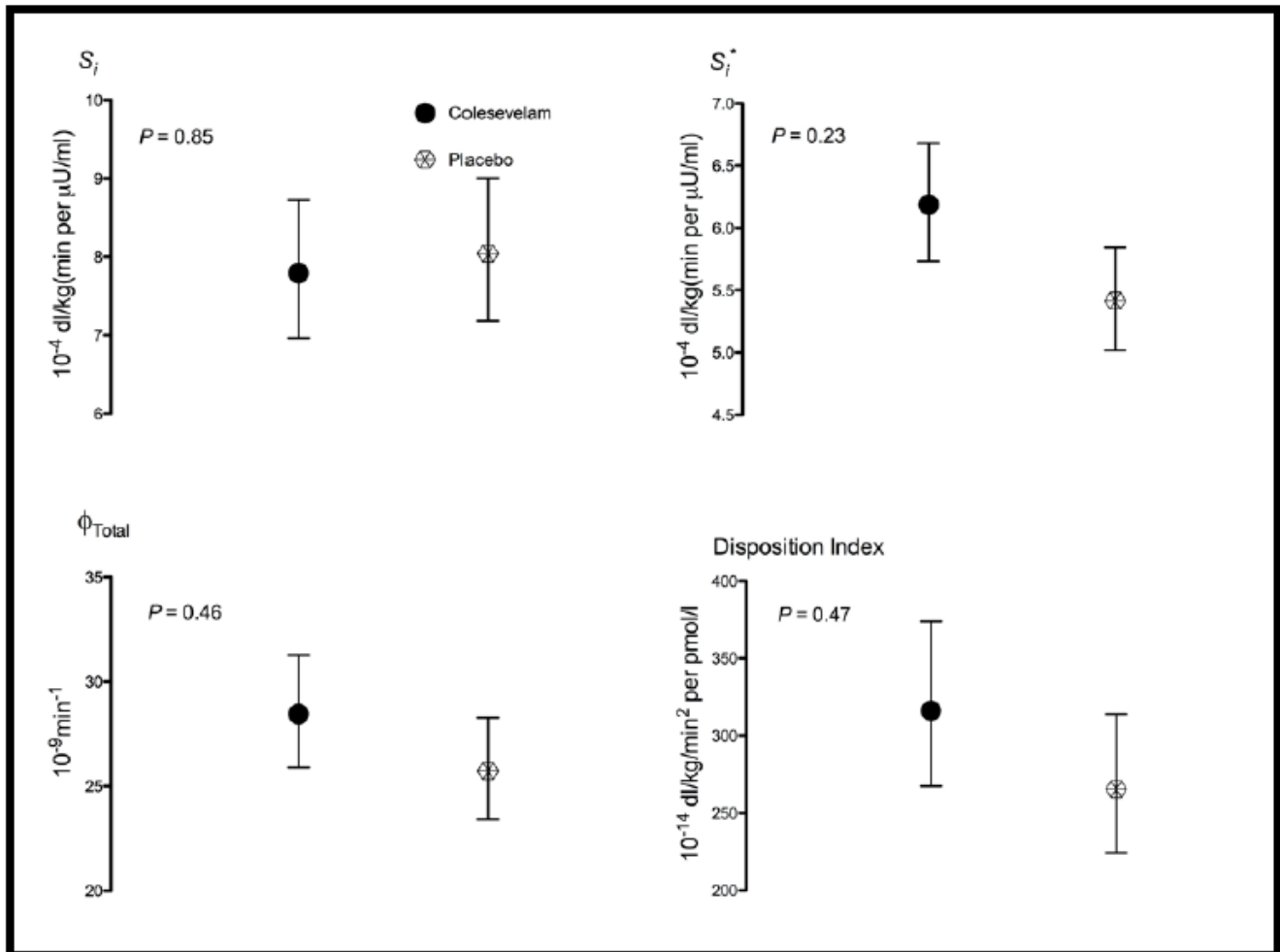
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Supplementary Figure 3. LS Means for integrated EGP (AAB), Meal Ra (AUC) and Rd (AAB) after 12 weeks of treatment with colesevelam or Placebo. Note that SE are based on pooled residual variation.



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Supplementary Figure 4. LS Means for indices of insulin secretion and action after 12 weeks of treatment with colesevelam or Placebo.



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Supplementary Figure 5. Lipid profiles at baseline and after 12 weeks of treatment with colesevlam or placebo. * $p < 0.05$ from within-group baseline value (paired, 2-tailed t-test). α $p < 0.05$ for post-treatment values in each group (unpaired, 2-tailed t-test).

