

Supplementary Table S1: Equations for the linear mixed models

Model	Equation
obesity-stratified	T2D ~ (cAge × sex) + (cAge ² × sex) + cAge + sex + cAge ² + gt + lnBMI + k lnFG ~ (cAge × sex) + (cAge ² × sex) + cAge + sex + cAge ² + gt + lnBMI + k
genotype-stratified	T2D ~ (cAge × sex) + (cAge ² × sex) + cAge + sex + cAge ² + lnBMI + k lnFG ~ (cAge × sex) + (cAge ² × sex) + cAge + sex + cAge ² + lnBMI + k

T2D = type 2 diabetes, k = kinship random effect, gt = additive rs373863828 genotype, cAge = centered and scaled age

Supplementary Table S2: Effect of (a) lnBMI and (b) rs37386388 on type 2 diabetes and fasting glucose in each cohort, stratified by obesity status

a. Predictor: lnBMI												
1990–95 Samoan cohort lnBMI				2002–03 Samoan cohort lnBMI			2010 Samoan cohort lnBMI			2006–2013 Aotearoa New Zealand cohort lnBMI		
Dependent variable: type 2 diabetes												
Stratum *	n	OR _(95% CI)	p	n	OR _(95% CI)	p	n	OR _(95% CI)	p	n	OR _(95% CI)	p
without obesity	409	0.56 (0.003, 98.36)	0.824	397	29.29 $(4.83 \times 10^{-7}, 1.78 \times 10^9)$	0.712	922	35.84 (2.95, 435.56)	0.005	588	3.08 (0.26, 36.67)	0.374
with obesity	604	18.06 (2.00, 163.37)	0.010	686	5.15 (1.17, 22.78)	0.031	1,939	2.80 (1.14, 6.87)	0.024	1,536	6.39 (3.05, 13.41)	9.14×10^{-7}
Dependent variable: lnFG												
Stratum *	n	β _(s.e.)	p	n	β _(s.e.)	p	n	β _(s.e.)	p	n	β _(s.e.)	p
without obesity	409	-0.021 (0.109)	0.847	358	0.309 (0.109)	0.005	849	0.281 (0.077)	2.62×10^{-4}	†	†	†
with obesity	604	0.181 (0.082)	0.028	574	0.172 (0.065)	0.008	1,738	0.149 (0.050)	0.003	†	†	†
b. Predictor: rs37386388												
1990–95 Samoan cohort rs37386388				2002–03 Samoan cohort rs37386388			2010 Samoan cohort rs37386388			2006–2013 Aotearoa New Zealand cohort rs37386388		
Dependent variable: type 2 diabetes												
Stratum *	n	OR _(95% CI)	p	n	OR _(95% CI)	p	n	OR _(95% CI)	p	n	OR _(95% CI)	p
without obesity	409	0.39 (0.11, 1.33)	0.132	397	0.46 (0.01, 42.15)	0.733	922	0.60 (0.40, 0.90)	0.014	588	0.63 (0.37, 1.06)	0.084
with obesity	604	0.74 (0.44, 1.24)	0.248	686	0.86 (0.59, 1.25)	0.428	1,939	0.60 (0.49, 0.74)	2.96×10^{-6}	1,536	0.68 (0.55, 0.85)	6.44×10^{-4}

Dependent variable: lnFG												
Stratum*	1990–95 Samoan cohort rs37386388			2002–03 Samoan cohort rs37386388			2010 Samoan cohort rs37386388			2006–2013 Aotearoa New Zealand cohort rs37386388		
	n	β (s.e.)	<i>p</i>	n	β (s.e.)	<i>p</i>	n	β (s.e.)	<i>p</i>	n	β (s.e.)	<i>p</i>
without obesity	409	-0.033 (0.017)	0.062	358	-0.059 (0.020)	0.004	849	-0.029 (0.012)	0.017	†	†	†
with obesity	604	-0.027 (0.016)	0.082	574	-0.006 (0.017)	0.720	1,738	-0.037 (0.010)	3.31 × 10⁻⁴	†	†	†

*without obesity: BMI ≤ 30 kg/m²; with obesity: BMI > 30 kg/m²

†Fasting glucose was not measured in the Aotearoa New Zealand cohort

Supplementary Table S3: Effect of lnBMI on type 2 diabetes and fasting glucose in each cohort, stratified by genotype

1990–95 Samoan cohort lnBMI				2002–03 Samoan cohort lnBMI			2010 Samoan cohort lnBMI			2006–2013 Aotearoa New Zealand cohort lnBMI		
Dependent variable: type 2 diabetes												
Stratum	n	OR _(95% CI)	p	n	OR _(95% CI)	p	n	OR _(95% CI)	p	n	OR _(95% CI)	p
GG	574	4.37 (0.50, 38.42)	0.184	643	3.73 (1.06, 13.10)	0.040	1,513	4.81 (2.18, 10.62)	1.01 × 10⁻⁴	1,381	9.19 (4.79, 17.61)	2.43 × 10⁻¹¹
GA	370	19.01 (1.43, 252.20)	0.026	392	29.55 (0.01, 1.47 × 10 ⁵)	0.436	1,116	8.58 (0.07, 1.0 × 10 ³)	0.375	669	5.91 (2.18, 16.00)	4.73 × 10⁻⁴
AA	69	*	*	48	†	†	232	1.77 (0.19, 16.93)	0.619	74	‡	‡
Dependent variable: lnFG												
Stratum	n	β _(s.e.)	p	n	β _(s.e.)	p	n	β _(s.e.)	p	n	β _(s.e.)	p
GG	574	0.140 (0.061)	0.021	537	0.223 (0.049)	4.58 × 10⁻⁶	1,331	0.296 (0.037)	5.73 × 10⁻¹⁶	§	§	§
GA	370	0.148 (0.071)	0.038	353	0.263 (0.068)	1.17 × 10⁻⁴	1,036	0.219 (0.046)	2.08 × 10⁻⁶	§	§	§
AA	69	0.064 (0.121)	0.597	42	0.383 (0.126)	0.002	220	0.103 (0.088)	0.243	§	§	§

*Too few type 2 diabetes cases (n = 2) to run analysis.

†Too few type 2 diabetes cases (n = 6) to run analysis.

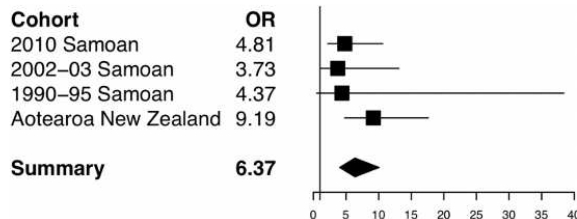
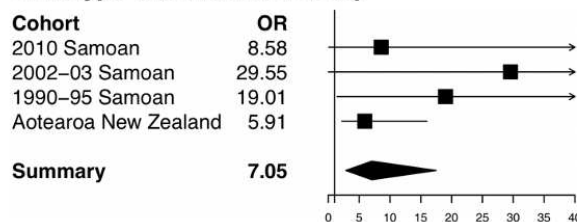
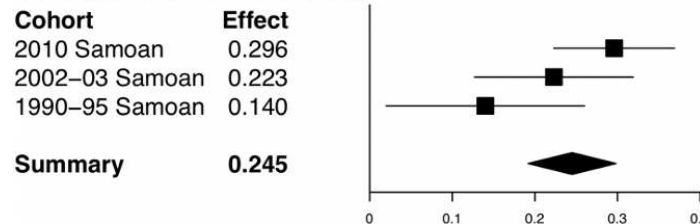
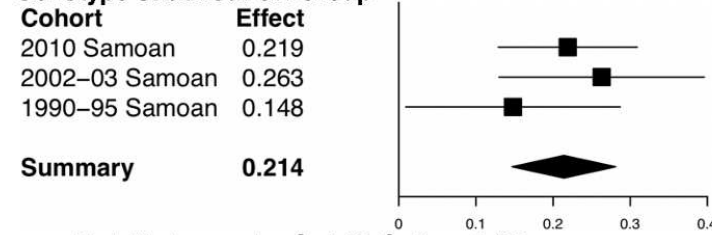
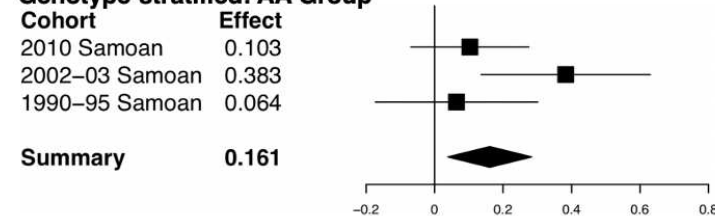
‡Too few type 2 diabetes cases (n = 16) to run analysis.

§Fasting glucose was not measured in the Aotearoa New Zealand cohort

Supplementary Table S4: Effect of lnBMI and rs373863828 on type 2 diabetes and fasting glucose in the meta-analysis, stratified by obesity status using the Polynesian obesity cutoff (32 kg/m²).

Meta-analysis lnBMI				Meta-analysis rs373863828		
Dependent variable: type 2 diabetes						
Stratum*	n	OR (95% CI)	p	n	OR (95% CI)	p
without obesity	3,211 (393 cases)	6.27 (1.90, 20.75)	0.003	3,211	0.58 (0.45, 0.74)	9.70 × 10⁻⁶
with obesity	3,870 (866 cases)	4.41 (2.35, 8.25)	3.68 × 10⁻⁶	3,870	0.73 (0.63, 0.85)	2.82 × 10⁻⁵
Dependent variable: natural log transformed fasting glucose						
Stratum*	n	β (s.e.)	p	n	β (s.e.)	p
without obesity	2,180	0.191 (0.041)	4.11 × 10⁻⁶	2,180	-0.030 (0.008)	8.17 × 10⁻⁵
with obesity	2,352	0.093 (0.044)	0.036	2,352	-0.033 (0.009)	1.22 × 10⁻⁴

*without obesity: BMI ≤ 32 kg/m²; with obesity: BMI > 32 kg/m²

Supplementary Figure S1: Comparison of the cohort odds ratios and effect sizes in the obesity and genotype-stratified groups.**a. Dependent variable: type 2 diabetes (T2D)****InBMI → T2D****Genotype-stratified: GG Group**Test of heterogeneity: $\chi^2 = 2.51$; $I^2 = 0$; $p = 0.473$ **Genotype-stratified: GA Group**Test of heterogeneity: $\chi^2 = 0.8$; $I^2 = 0$; $p = 0.849$ **b. Dependent variable: lnFG****InBMI → lnFG****Genotype-stratified: GG Group**Test of heterogeneity: $\chi^2 = 5.06$; $I^2 = 60.5$; $p = 0.079$ **Genotype-stratified: GA Group**Test of heterogeneity: $\chi^2 = 1.40$; $I^2 = 0$; $p = 0.498$ **Genotype-stratified: AA Group**Test of heterogeneity: $\chi^2 = 4.18$; $I^2 = 52.2$; $p = 0.124$

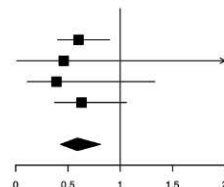
c. Dependent variable: type 2 diabetes (T2D)

rs37386388 → T2D

Obesity-stratified: without obesity

Cohort	OR
2010 Samoan	0.60
2002–03 Samoan	0.46
1990–95 Samoan	0.39
Aotearoa New Zealand	0.63

Summary 0.59

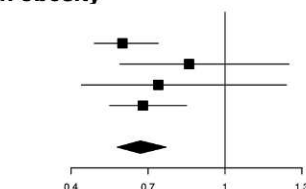


Test of heterogeneity: $\chi^2 = 0.52$; $I^2 = 0$; $p = 0.914$

Obesity-stratified: with obesity

Cohort	OR
2010 Samoan	0.60
2002–03 Samoan	0.86
1990–95 Samoan	0.74
Aotearoa New Zealand	0.68

Summary 0.67



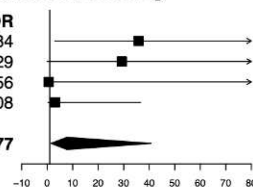
Test of heterogeneity: $\chi^2 = 2.78$; $I^2 = 0$; $p = 0.426$

lnBMI → T2D

Obesity-stratified: without obesity

Cohort	OR
2010 Samoan	35.84
2002–03 Samoan	29.29
1990–95 Samoan	0.56
Aotearoa New Zealand	3.08

Summary 7.77

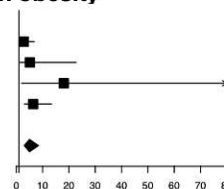


Test of heterogeneity: $\chi^2 = 3.00$; $I^2 = 0$; $p = 0.392$

Obesity-stratified: with obesity

Cohort	OR
2010 Samoan	2.80
2002–03 Samoan	5.15
1990–95 Samoan	18.06
Aotearoa New Zealand	6.39

Summary 5.01



Test of heterogeneity: $\chi^2 = 3.34$; $I^2 = 10.1$; $p = 0.343$

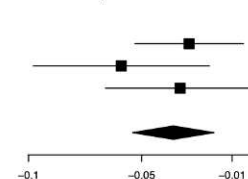
d. Dependent variable: lnFG

rs37386388 → lnFG

Obesity-stratified: without obesity

Cohort	Effect
2010 Samoan	-0.029
2002–03 Samoan	-0.059
1990–95 Samoan	-0.033

Summary -0.036

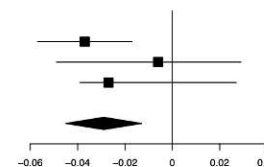


Test of heterogeneity: $\chi^2 = 1.69$; $I^2 = 0$; $p = 0.429$

Obesity-stratified: with obesity

Cohort	Effect
2010 Samoan	-0.037
2002–03 Samoan	-0.006
1990–95 Samoan	-0.027

Summary -0.029



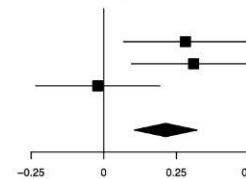
Test of heterogeneity: $\chi^2 = 2.48$; $I^2 = 19.4$; $p = 0.289$

lnBMI → lnFG

Obesity-stratified: without obesity

Cohort	Effect
2010 Samoan	0.281
2002–03 Samoan	0.309
1990–95 Samoan	-0.021

Summary 0.213

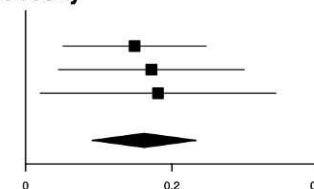


Test of heterogeneity: $\chi^2 = 6.16$; $I^2 = 67.6$; $p = 0.046$

Obesity-stratified: with obesity

Cohort	Effect
2010 Samoan	0.149
2002–03 Samoan	0.172
1990–95 Samoan	0.181

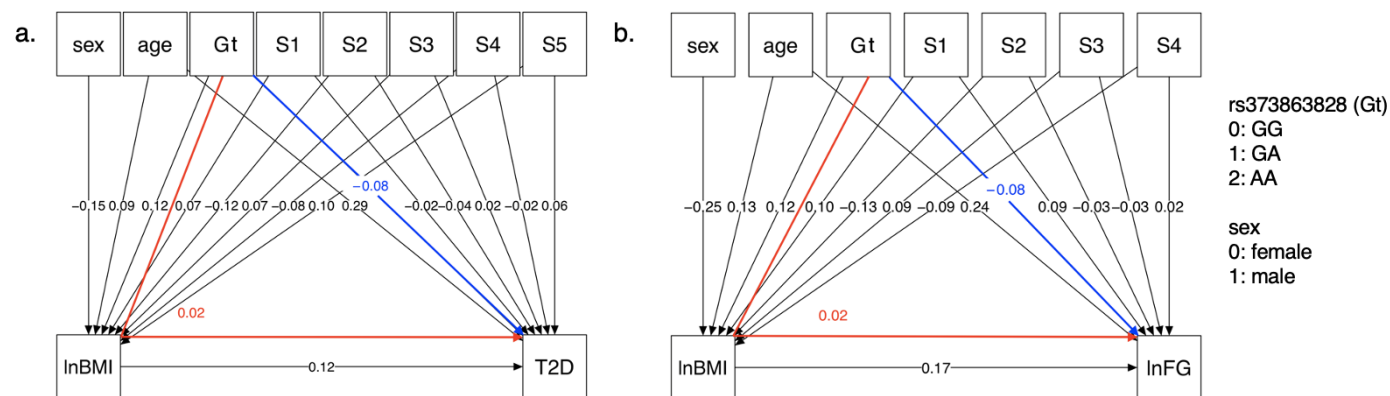
Summary 0.162



Test of heterogeneity: $\chi^2 = 0.15$; $I^2 = 0$; $p = 0.930$

Caption: Forest plots for a comparison of the cohort odds ratios (OR) and 95% confidence intervals in the (a) genotype-stratified and (c) obesity-stratified models with type 2 diabetes as the dependent variable and a comparison of the cohort effect sizes and 95% confidence intervals in the (b) genotype-stratified and (d) obesity-stratified models with lnFG as the dependent variable. In the genotype-stratified analyses (a), there were too few type 2 diabetes cases to run the analyses in the 2002-03 Samoan, 1990-95 Samoan, and Aotearoa New Zealand cohorts.

Supplementary Figure S2: Pooled analysis Path Analysis Model with Study Cohort Variables



Caption: When study cohort variables (S1 – S5) are included in the model, the rs373863828 genotype (Gt) has both direct (blue) and indirect (red) effects on (a) type 2 diabetes (T2D) and (b) lnFG as mediated by lnBMI. For (a), the RMSEA is < 0.001 (90% CI 0.000–0.020) indicating that the path model is a very good fit. For (b), the RMSEA is < 0.064 (90% CI 0.041–0.090) indicating that the path model is a mediocre fit.