

## Supplemental Tables

Supplemental Table S1: Comparison of GEE model fitness for variable selection using quasi-likelihood information criteria.

Model	QIC	Delta
<b>log(ISI)</b>		
M7	-1610.5	0.0
M8	-1608.9	1.6
M9	-1607.9	2.6
M5	-1604.1	6.4
M6	-1602.4	8.1
M4	-1599.2	11.3
M3	-1575.6	34.8
M1	-1229.7	380.8
M0	-1228.2	382.3
M2	-1219.2	391.3
<b>log(ISSI-2)</b>		
M8	-2476.2	0.0
M9	-2474.3	1.9
M6	-2471.3	4.9
M7	-2467.4	8.9
M4	-2458.8	17.4
M5	-2456.5	19.7
M3	-2450.5	25.7
M2	-2226.5	249.7
M0	-2171.0	305.2
M1	-2168.5	307.8

Given the number of possible combinations of outcome and predictor variables, only ISI and ISSI-2 with total TGFA (nmol/mL) were used to compare various GEE models and to select a final model. Baseline age was used as including both the original age and the time variable would result in collinearity. Column names: QIC is the quasi-likelihood information criteria (smaller values, eg. larger negative values, indicate a better fit compared to other models), Delta is the QIC minus the lowest QIC (models with delta <10 are considered equivalent). Models were:

- M0: log(ISSI-2) or log(ISI) = total TGFA (nmol/mL) + years from baseline
- M1: M0 + fatty acid by time interaction
- M2: M0 + sex + ethnicity + baseline age
- M3: M2 + WC
- M4: M3 + ALT
- M5: M4 + physical activity (MET)
- M6: M5 + total NEFA
- M7: M6 + alcohol intake
- M8: M7 + family history of diabetes
- M9: M8 + smoking status

Supplemental Table S2: Concentration (nmol/mL) and relative percent (mol%) values of TGFA in PROMISE participants at the baseline visit (2004-2006).

<b>TGFA</b>	<b>Concentrations (nmol/mL)</b>	<b>Proportion (mol%)</b>
18:3 n-3	45.2 (31.1)	1.5 (0.6)
20:5 n-3	9.9 (8.1)	0.4 (0.4)
22:5 n-3	8.3 (5.7)	0.3 (0.2)
22:6 n-3	16.7 (14.5)	0.6 (0.6)
18:2 n-6	548.6 (298.7)	18.0 (4.2)
18:3 n-6	15.1 (9.9)	0.5 (0.2)
20:2 n-6	10.2 (4.7)	0.4 (0.1)
20:3 n-6	10.2 (6.0)	0.3 (0.1)
20:4 n-6	38.2 (19.1)	1.3 (0.5)
22:4 n-6	4.6 (2.9)	0.1 (0.1)
14:1 n-7	5.1 (6.1)	0.1 (0.1)
16:1 n-7	126.1 (98.8)	3.8 (1.3)
18:1 n-7	71.6 (34.8)	2.4 (0.4)
18:1 n-9	1168.5 (592.2)	37.8 (3.7)
20:1 n-9	8.5 (5.2)	0.3 (0.2)
22:1 n-9	1.0 (0.6)	0.0 (0.0)
24:1 n-9	2.2 (4.0)	0.1 (0.1)
14:0	62.4 (59.0)	1.8 (1.0)
16:0	868.0 (556.2)	26.6 (4.4)
18:0	113.6 (63.4)	3.7 (0.8)
20:0	1.9 (1.3)	0.1 (0.0)
22:0	1.5 (1.2)	0.1 (0.0)
Total	3137.5 (1686.6)	

Supplemental Table S3: Raw estimates and confidence interval values for *time*-adjusted GEE models of the association of the TGFA (mol% and nmol/mL) and total clinically-measured TG with insulin sensitivity and beta-cell function outcomes using the 6 year longitudinal data from the PROMISE cohort. Estimates represent a percent difference in the outcome per SD increase in the FA. P-values were adjusted for the BH false discovery rate, with an asterisk (\*) denoting a significant ( $p < 0.05$ ) association.

<b>Fatty acid</b>	<b>log(HOMA2-%S)</b>	<b>log(ISI)</b>	<b>log(IGI/IR)</b>	<b>log(ISSI-2)</b>
<b>Totals</b>				
Clinical TAG	-23.4 (-28.9, -17.6)*	-24.1 (-29.6, -18.1)*	-18.2 (-25.3, -10.3)*	-10.7 (-15.3, -6.0)*
Total	-22.2 (-27.5, -16.5)*	-22.9 (-28.4, -17.0)*	-16.4 (-23.3, -9.0)*	-9.8 (-14.1, -5.3)*
<b>nmol/mL</b>				
14:0	-19.1 (-23.7, -14.2)*	-19.6 (-24.2, -14.6)*	-11.3 (-17.3, -4.9)*	-6.9 (-10.5, -3.2)*
16:0	-23.0 (-28.3, -17.4)*	-23.8 (-29.2, -18.0)*	-17.2 (-24.0, -9.8)*	-10.2 (-14.5, -5.7)*
18:0	-20.8 (-26.3, -15.0)*	-21.3 (-27.1, -15.1)*	-15.7 (-22.5, -8.3)*	-9.3 (-13.5, -4.9)*
20:0	-12.6 (-16.6, -8.4)*	-12.1 (-16.7, -7.2)*	-7.7 (-13.3, -1.8)*	-5.3 (-8.3, -2.2)*
22:0	-12.1 (-16.4, -7.5)*	-12.7 (-17.5, -7.8)*	-2.2 (-8.2, 4.1)	-1.8 (-4.8, 1.2)
18:1 n-9	-21.4 (-26.0, -16.6)*	-22.0 (-26.8, -16.9)*	-16.7 (-23.1, -9.8)*	-9.8 (-13.7, -5.7)*
20:1 n-9	-14.9 (-19.0, -10.5)*	-14.2 (-18.9, -9.3)*	-13.2 (-19.7, -6.1)*	-7.2 (-10.9, -3.4)*
22:1 n-9	-14.0 (-19.6, -8.0)*	-12.3 (-18.5, -5.5)*	-12.0 (-16.6, -7.0)*	-6.3 (-9.0, -3.4)*
24:1 n-9	-4.3 (-8.5, 0.1)	-6.4 (-10.9, -1.6)*	3.5 (-2.5, 9.9)	1.8 (-1.3, 4.9)
14:1 n-7	-14.9 (-19.5, -10.1)*	-15.2 (-19.9, -10.3)*	-9.4 (-15.1, -3.3)*	-5.5 (-8.7, -2.2)*
16:1 n-7	-19.2 (-24.3, -13.7)*	-19.9 (-25.2, -14.3)*	-15.0 (-21.9, -7.5)*	-8.6 (-12.8, -4.2)*
18:1 n-7	-22.2 (-26.0, -18.1)*	-23.0 (-27.1, -18.6)*	-17.0 (-22.7, -11.0)*	-9.9 (-13.2, -6.4)*
18:2 n-6	-18.7 (-23.4, -13.7)*	-19.1 (-23.9, -14.0)*	-12.1 (-18.2, -5.6)*	-7.5 (-11.3, -3.5)*
18:3 n-6	-12.8 (-17.6, -7.7)*	-12.5 (-17.6, -7.1)*	-8.3 (-14.2, -2.0)*	-5.0 (-8.5, -1.3)*
20:2 n-6	-15.4 (-20.4, -10.1)*	-15.8 (-20.9, -10.3)*	-12.5 (-19.1, -5.3)*	-6.8 (-10.9, -2.5)*
20:3 n-6	-17.5 (-22.7, -12.0)*	-18.1 (-23.3, -12.6)*	-12.3 (-18.6, -5.4)*	-7.4 (-11.4, -3.3)*
20:4 n-6	-17.0 (-24.3, -9.0)*	-17.8 (-25.3, -9.6)*	-12.8 (-21.1, -3.6)*	-7.5 (-12.8, -1.8)*
22:4 n-6	-17.7 (-25.2, -9.5)*	-18.2 (-25.9, -9.9)*	-9.5 (-17.0, -1.3)*	-5.6 (-10.3, -0.7)*
18:3 n-3	-15.6 (-19.5, -11.6)*	-16.6 (-20.7, -12.3)*	-10.3 (-15.4, -4.8)*	-6.3 (-9.2, -3.4)*
20:5 n-3	-5.1 (-8.9, -1.1)*	-7.8 (-11.7, -3.8)*	-3.5 (-8.5, 1.7)	-3.1 (-5.8, -0.2)*
22:5 n-3	-7.2 (-11.3, -2.8)*	-7.2 (-11.6, -2.6)*	-10.1 (-15.2, -4.7)*	-6.3 (-9.0, -3.5)*
22:6 n-3	-6.8 (-10.6, -2.8)*	-9.6 (-13.6, -5.5)*	-4.5 (-9.2, 0.4)	-3.6 (-6.1, -0.9)*
<b>mol%</b>				
14:0	-14.2 (-18.0, -10.2)*	-14.1 (-18.2, -9.8)*	-5.4 (-11.3, 1.0)	-3.9 (-7.0, -0.7)*
16:0	-20.1 (-23.7, -16.3)*	-20.7 (-24.5, -16.6)*	-14.4 (-19.8, -8.6)*	-8.6 (-11.6, -5.6)*
18:0	3.9 (-0.7, 8.8)	3.9 (-0.9, 9.1)	2.0 (-4.8, 9.4)	0.9 (-2.5, 4.4)
20:0	9.8 (2.8, 17.4)*	10.6 (3.1, 18.5)*	8.8 (1.6, 16.4)*	3.8 (0.1, 7.7)
22:0	4.4 (-0.5, 9.5)	4.5 (-0.1, 9.4)	11.6 (5.7, 17.9)*	5.7 (3.0, 8.5)*
18:1 n-9	14.6 (9.1, 20.3)*	15.3 (9.1, 21.9)*	5.4 (-0.8, 12.1)	4.4 (1.2, 7.6)*
20:1 n-9	7.4 (1.9, 13.1)*	9.1 (3.8, 14.8)*	2.8 (-4.3, 10.4)	2.3 (-1.6, 6.3)
22:1 n-9	10.0 (4.4, 15.8)*	12.2 (6.3, 18.3)*	6.1 (-1.0, 13.7)	4.0 (0.4, 7.7)*
24:1 n-9	3.4 (-1.2, 8.3)	1.6 (-3.1, 6.6)	10.6 (4.1, 17.5)*	4.9 (1.7, 8.2)*
14:1 n-7	-10.2 (-14.4, -5.7)*	-9.9 (-14.4, -5.2)*	-4.4 (-10.3, 1.8)	-2.8 (-5.9, 0.4)
16:1 n-7	-10.8 (-15.2, -6.2)*	-11.0 (-15.6, -6.2)*	-9.1 (-14.9, -2.9)*	-5.2 (-8.2, -2.0)*
18:1 n-7	7.0 (1.5, 12.7)*	7.2 (1.6, 13.1)*	5.0 (-1.5, 11.9)	3.7 (0.4, 7.0)*
18:2 n-6	12.8 (6.9, 19.0)*	13.7 (7.5, 20.3)*	11.4 (4.6, 18.7)*	5.9 (2.5, 9.4)*
18:3 n-6	8.9 (4.2, 13.8)*	11.1 (6.2, 16.2)*	9.1 (2.7, 16.0)*	4.9 (1.8, 8.1)*
20:2 n-6	21.6 (16.3, 27.1)*	22.6 (16.9, 28.6)*	11.3 (4.5, 18.7)*	7.7 (4.4, 11.2)*

20:3 n-6	4.3 (-0.1, 9.0)	4.1 (-0.6, 9.0)	2.9 (-2.2, 8.2)	1.3 (-1.3, 4.0)
20:4 n-6	10.1 (5.0, 15.4)*	9.3 (3.4, 15.6)*	4.8 (-1.4, 11.4)	3.0 (-0.1, 6.1)
22:4 n-6	1.8 (-2.8, 6.7)	2.2 (-2.4, 7.0)	7.9 (1.3, 14.9)*	4.3 (1.3, 7.4)*
18:3 n-3	5.5 (0.4, 10.9)*	5.4 (-0.3, 11.4)	5.5 (-1.8, 13.2)	2.4 (-1.2, 6.1)
20:5 n-3	8.2 (1.7, 15.1)*	4.9 (-1.8, 12.0)	7.3 (1.6, 13.3)*	2.8 (-0.1, 5.8)
22:5 n-3	12.9 (7.3, 18.8)*	12.6 (6.3, 19.2)*	4.2 (-2.0, 10.9)	2.2 (-1.0, 5.5)
22:6 n-3	5.4 (0.1, 11.0)	2.3 (-3.0, 7.8)	5.3 (0.2, 10.7)	1.9 (-0.8, 4.7)

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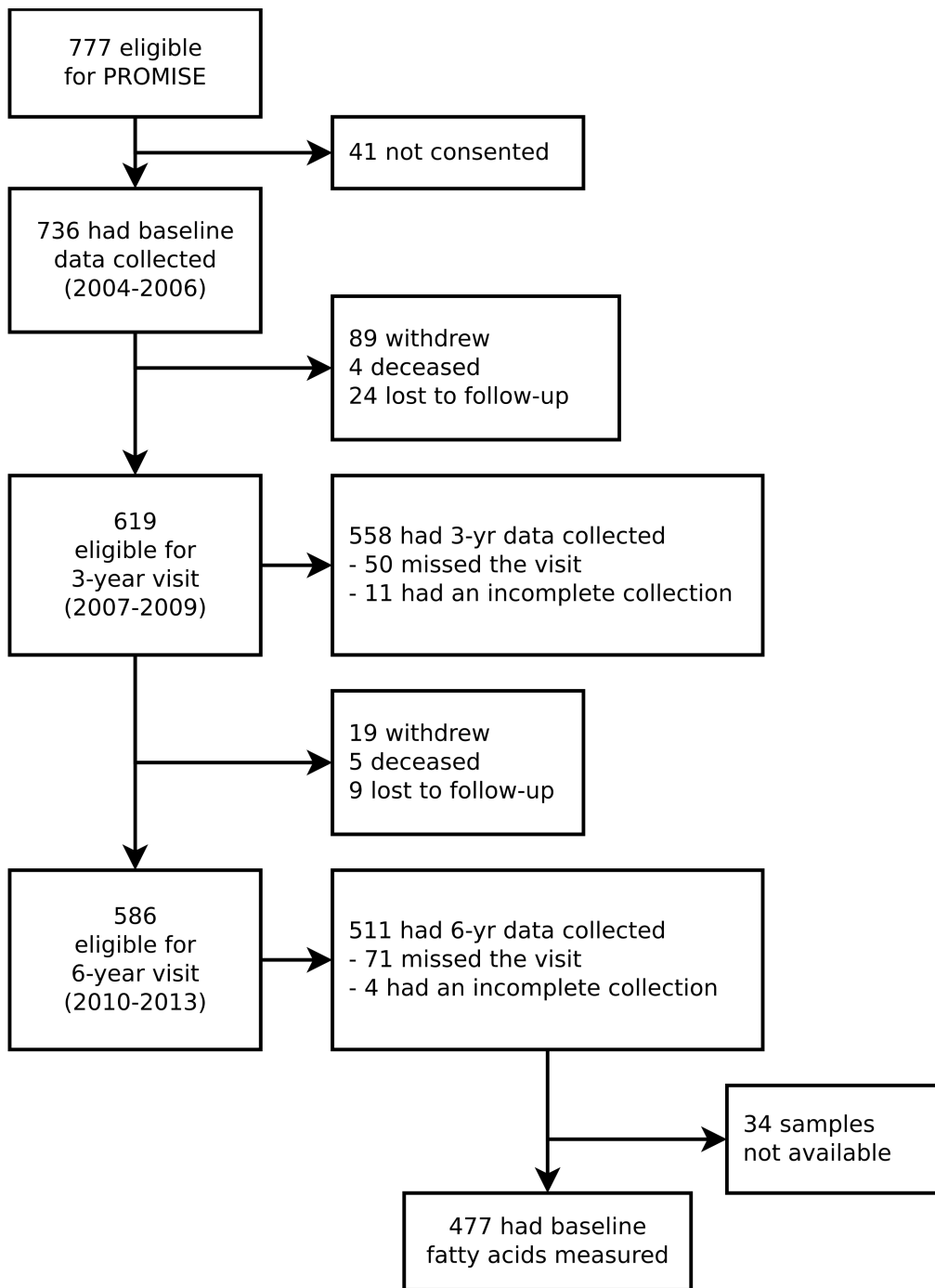
Supplemental Table S4: Raw estimates and confidence interval values for *fully*-adjusted GEE models of the association of the TGFA (mol% and nmol/mL) and total clinically-measured TG with insulin sensitivity and beta-cell function outcomes using the 6 year longitudinal data from the PROMISE cohort. Variables controlled for were follow-up time, WC, baseline age, ethnicity, sex, ALT, physical activity, and total NEFA. Estimates represent a percent difference in the outcome per SD increase in the FA. P-values were adjusted for the BH false discovery rate, with an asterisk (\*) denoting a significant (p<0.05) association.

<b>Fatty acid</b>	<b>log(HOMA2-%S)</b>	<b>log(ISI)</b>	<b>log(IGI/IR)</b>	<b>log(ISSI-2)</b>
<b>Totals</b>				
Clinical TAG	-13.8 (-18.1, -9.3)*	-14.8 (-19.3, -10.1)*	-9.3 (-15.3, -2.9)*	-4.9 (-8.3, -1.4)*
Total TAG	-13.1 (-17.3, -8.7)*	-14.3 (-18.7, -9.6)*	-7.9 (-13.5, -1.9)*	-4.3 (-7.5, -1.1)*
<b>nmol/mL</b>				
14:0	-11.2 (-14.8, -7.4)*	-12.3 (-16.2, -8.3)*	-4.8 (-9.9, 0.6)	-2.8 (-5.5, 0.0)
16:0	-13.5 (-17.6, -9.1)*	-14.8 (-19.2, -10.2)*	-8.4 (-14.1, -2.4)*	-4.6 (-7.7, -1.3)*
18:0	-12.1 (-16.2, -7.7)*	-13.1 (-17.7, -8.3)*	-8.3 (-14.0, -2.2)*	-4.6 (-7.7, -1.4)*
20:0	-6.3 (-9.7, -2.7)*	-6.6 (-10.7, -2.2)*	-4.0 (-9.4, 1.7)	-3.0 (-5.7, -0.2)
22:0	-7.8 (-11.6, -3.9)*	-8.0 (-12.3, -3.6)*	-1.2 (-6.7, 4.6)	-1.3 (-3.8, 1.4)
18:1 n-9	-12.4 (-16.3, -8.4)*	-13.6 (-17.8, -9.2)*	-7.9 (-13.4, -2.1)*	-4.2 (-7.2, -1.1)*
20:1 n-9	-7.3 (-10.5, -3.9)*	-7.3 (-11.0, -3.5)*	-6.3 (-11.8, -0.4)	-2.9 (-5.7, 0.1)
22:1 n-9	-6.3 (-10.1, -2.3)*	-5.0 (-9.6, -0.2)	-4.9 (-9.7, 0.1)	-1.8 (-4.1, 0.7)
24:1 n-9	-3.2 (-6.2, -0.1)	-4.5 (-7.9, -0.9)*	1.0 (-4.0, 6.2)	0.5 (-1.9, 3.0)
14:1 n-7	-8.1 (-11.5, -4.6)*	-9.1 (-12.8, -5.4)*	-3.7 (-8.7, 1.6)	-1.9 (-4.4, 0.7)
16:1 n-7	-10.1 (-13.9, -6.1)*	-11.2 (-15.3, -7.0)*	-6.1 (-11.7, -0.1)	-2.9 (-5.8, 0.1)
18:1 n-7	-12.2 (-16.0, -8.1)*	-13.2 (-17.6, -8.6)*	-6.3 (-12.0, -0.2)	-3.0 (-6.0, 0.0)
18:2 n-6	-11.6 (-15.5, -7.6)*	-12.3 (-16.3, -8.0)*	-6.0 (-11.4, -0.4)	-3.8 (-6.7, -0.7)*
18:3 n-6	-7.7 (-11.4, -3.8)*	-8.2 (-12.4, -3.8)*	-4.8 (-9.8, 0.5)	-2.7 (-5.5, 0.2)
20:2 n-6	-7.6 (-11.4, -3.6)*	-8.3 (-12.4, -4.0)*	-4.6 (-9.7, 0.7)	-2.0 (-4.8, 0.9)
20:3 n-6	-9.1 (-12.8, -5.3)*	-10.2 (-14.1, -6.2)*	-4.4 (-9.3, 0.7)	-2.6 (-5.3, 0.2)
20:4 n-6	-8.8 (-13.5, -3.9)*	-10.1 (-15.1, -4.8)*	-5.6 (-11.2, 0.3)	-3.0 (-6.3, 0.5)
22:4 n-6	-9.2 (-13.9, -4.2)*	-10.0 (-14.8, -4.9)*	-3.3 (-8.3, 2.1)	-1.7 (-4.5, 1.3)
18:3 n-3	-10.1 (-13.3, -6.9)*	-11.1 (-14.5, -7.5)*	-6.0 (-10.9, -0.9)*	-3.7 (-6.1, -1.2)*
20:5 n-3	-2.6 (-5.8, 0.6)	-5.4 (-8.8, -1.9)*	-0.4 (-4.8, 4.2)	-1.3 (-3.5, 1.0)
22:5 n-3	-2.3 (-5.8, 1.5)	-3.2 (-7.2, 1.1)	-1.7 (-6.9, 3.8)	-1.7 (-4.3, 0.8)
22:6 n-3	-4.2 (-7.6, -0.6)*	-6.8 (-10.4, -3.1)*	-0.3 (-4.4, 4.1)	-1.3 (-3.5, 0.8)
<b>mol%</b>				
14:0	-9.6 (-12.7, -6.4)*	-10.2 (-13.7, -6.6)*	-2.7 (-8.1, 3.0)	-2.1 (-4.7, 0.7)
16:0	-11.9 (-15.0, -8.6)*	-12.8 (-16.4, -9.2)*	-7.1 (-12.2, -1.8)*	-3.9 (-6.5, -1.3)*
18:0	2.5 (-1.1, 6.3)	2.1 (-1.8, 6.1)	-1.6 (-7.5, 4.8)	-1.2 (-4.0, 1.7)
20:0	6.6 (2.1, 11.2)*	6.8 (1.9, 12.0)*	3.2 (-2.6, 9.3)	0.9 (-2.2, 4.0)
22:0	1.3 (-2.0, 4.7)	2.0 (-1.5, 5.5)	4.3 (-1.9, 10.8)	1.6 (-1.0, 4.3)
18:1 n-9	8.8 (4.7, 13.1)*	9.3 (4.4, 14.4)*	3.9 (-1.7, 9.8)	3.2 (0.5, 6.0)*
20:1 n-9	5.9 (1.9, 10.1)*	6.9 (2.1, 12.0)*	2.2 (-4.4, 9.2)	1.9 (-1.9, 5.9)
22:1 n-9	6.9 (3.0, 10.9)*	8.7 (4.3, 13.3)*	3.9 (-2.1, 10.4)	2.7 (-0.2, 5.7)
24:1 n-9	0.8 (-2.8, 4.5)	0.3 (-3.7, 4.4)	3.9 (-2.1, 10.2)	1.2 (-1.6, 4.1)
14:1 n-7	-6.6 (-9.9, -3.2)*	-7.1 (-10.7, -3.3)*	-1.6 (-6.8, 4.0)	-0.9 (-3.5, 1.8)
16:1 n-7	-6.1 (-9.5, -2.6)*	-6.4 (-10.2, -2.5)*	-2.2 (-8.0, 4.0)	-0.9 (-3.7, 2.0)
18:1 n-7	7.2 (3.1, 11.4)*	8.1 (3.5, 12.8)*	9.0 (2.9, 15.4)*	5.7 (2.9, 8.6)*
18:2 n-6	5.8 (1.5, 10.3)*	7.5 (2.7, 12.6)*	3.2 (-2.4, 9.0)	1.1 (-1.5, 3.8)

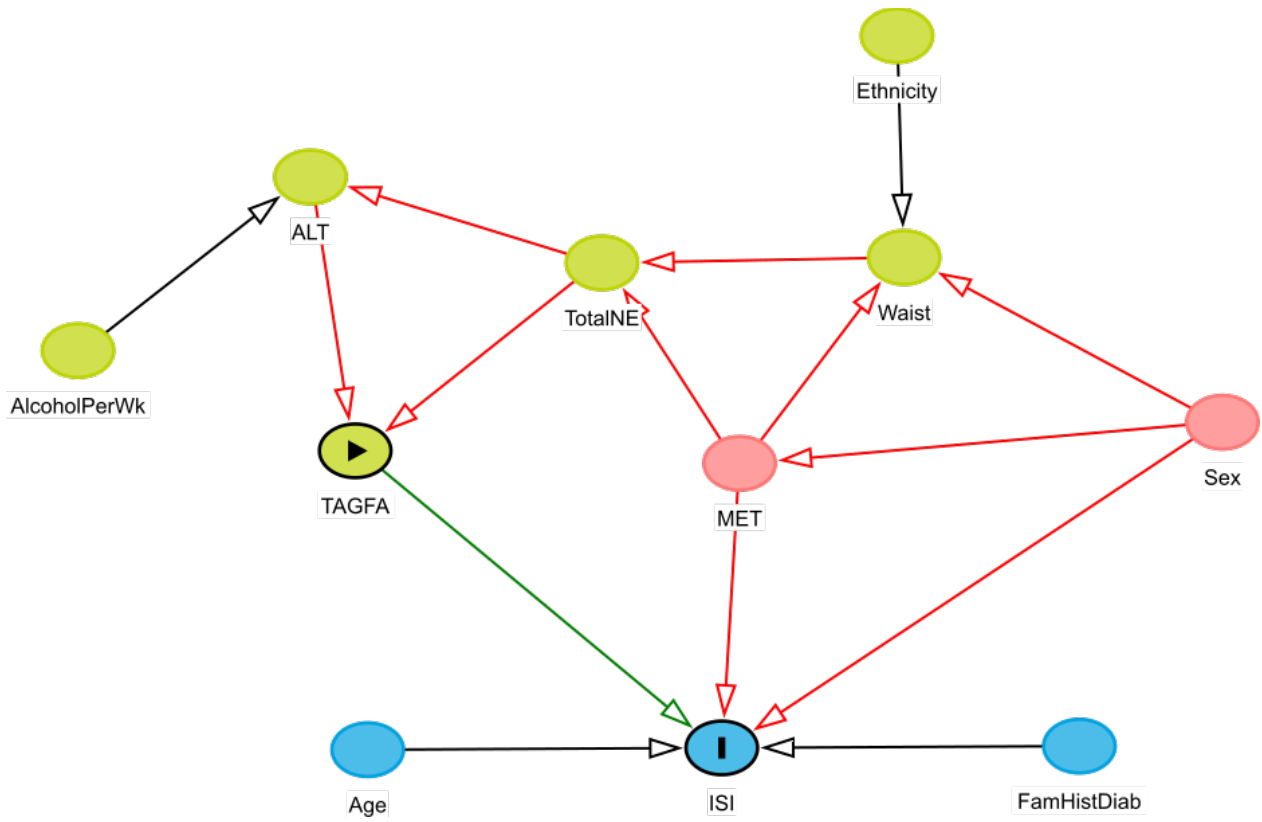
18:3 n-6	3.4 (-0.7, 7.6)	4.7 (0.2, 9.5)	2.1 (-3.6, 8.1)	1.1 (-1.7, 3.9)
20:2 n-6	14.4 (10.4, 18.6)*	15.9 (11.2, 20.7)*	6.9 (0.9, 13.1)*	5.0 (2.1, 7.9)*
20:3 n-6	4.3 (0.7, 8.0)*	4.2 (0.2, 8.3)	2.6 (-2.0, 7.4)	1.1 (-1.2, 3.5)
20:4 n-6	6.5 (2.5, 10.7)*	5.9 (1.1, 11.1)*	1.3 (-3.9, 6.8)	1.0 (-1.5, 3.6)
22:4 n-6	2.4 (-1.1, 6.0)	2.9 (-0.8, 6.8)	4.2 (-1.7, 10.4)	2.4 (-0.2, 5.0)
18:3 n-3	1.0 (-2.7, 4.7)	1.5 (-2.7, 5.8)	0.3 (-5.4, 6.3)	-0.6 (-3.3, 2.1)
20:5 n-3	4.2 (-0.1, 8.6)	1.3 (-3.4, 6.3)	3.8 (-0.5, 8.2)	0.8 (-1.4, 3.0)
22:5 n-3	8.7 (4.7, 12.8)*	7.9 (3.1, 13.0)*	4.3 (-0.7, 9.5)	1.7 (-0.8, 4.4)
22:6 n-3	2.4 (-1.1, 6.0)	-0.2 (-4.0, 3.8)	3.3 (-0.7, 7.5)	0.6 (-1.6, 2.7)

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**Supplemental Figures**

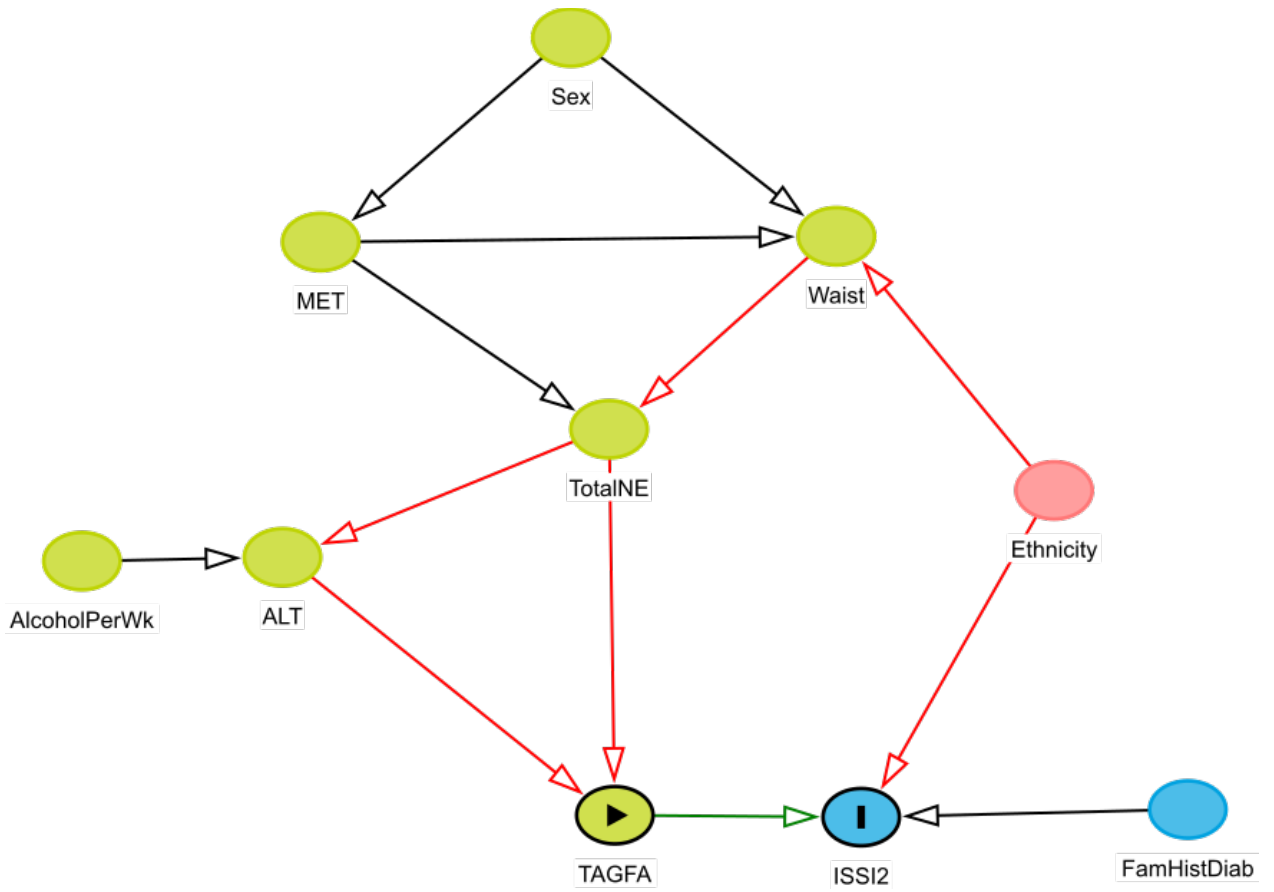


Supplemental Figure S1: CONSORT diagram of PROMISE participants over the 3 visits.

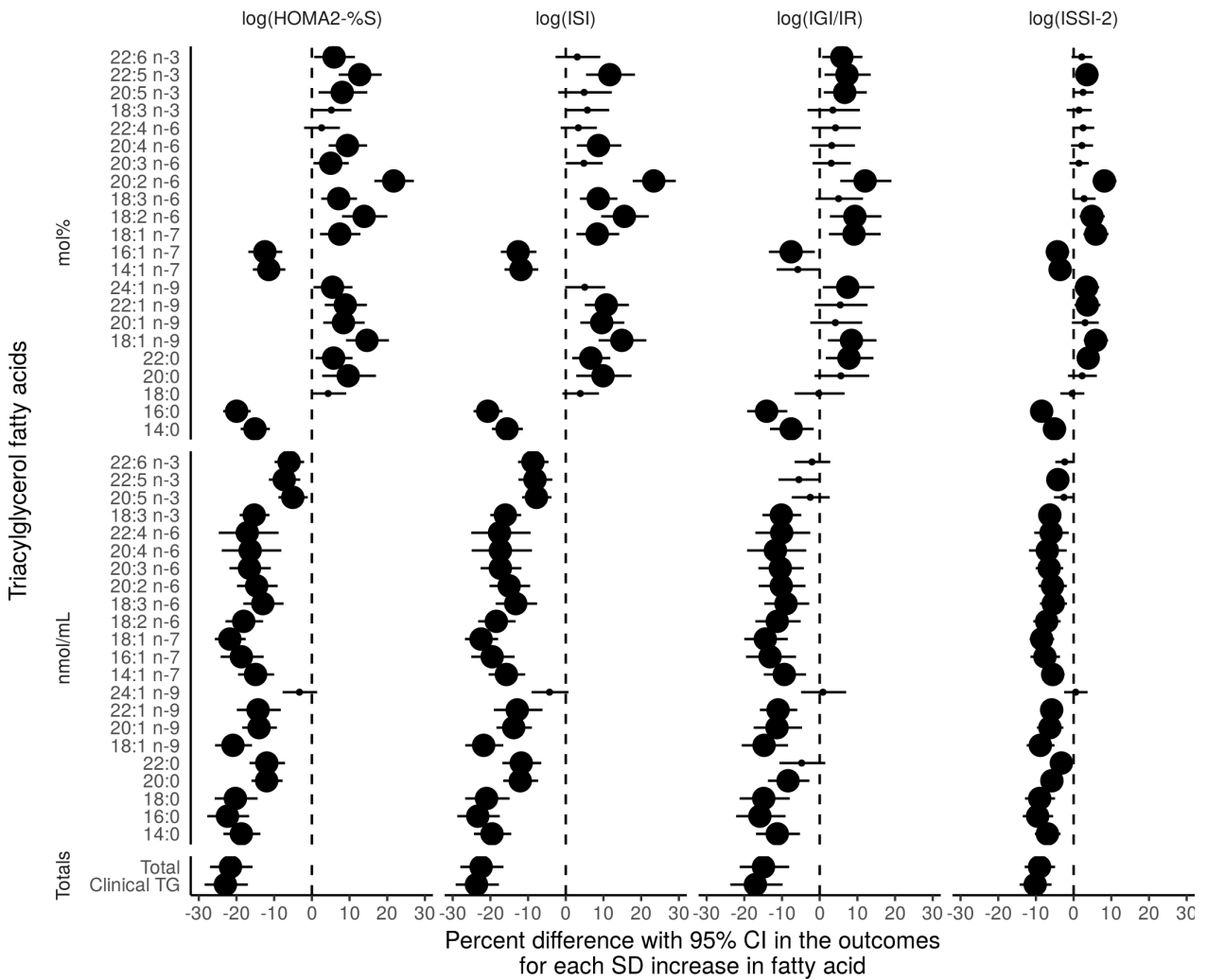


Supplemental Figure S2: Directed acyclic graphic output from the DAGitty online software for insulin sensitivity.

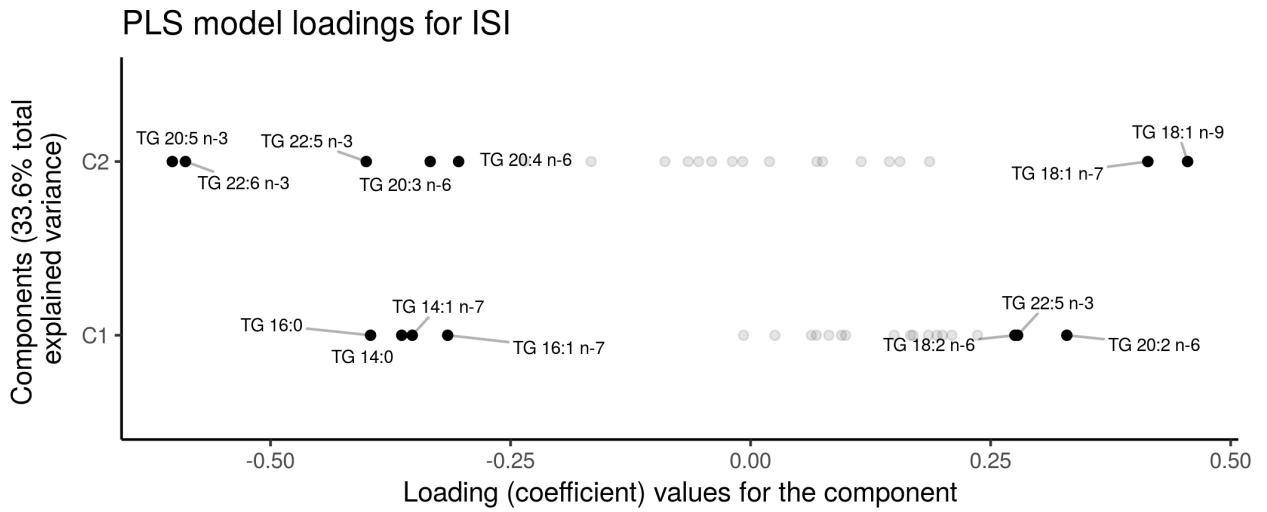
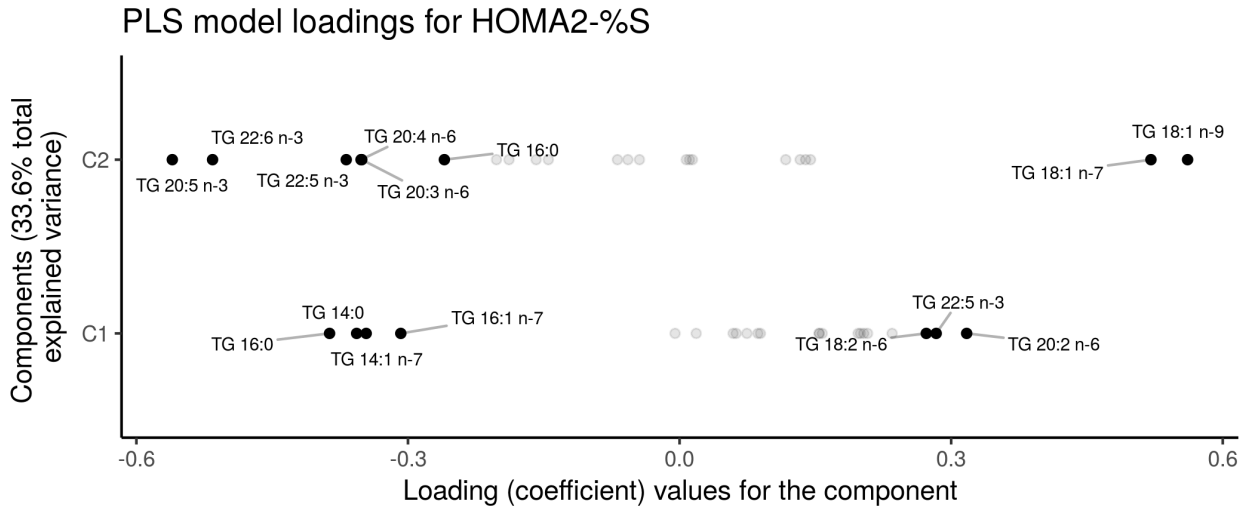




Supplemental Figure S3: Directed acyclic graph output from the DAGitty online software for beta-cell function.



Supplemental Figure S4: Fully-adjusted (without waist size) GEE models of the association of the TGFA (mol% and nmol/mL) and total clinically-measured TG with insulin sensitivity and beta-cell function outcomes using the 6 year longitudinal data from the PROMISE cohort. Variables controlled for were follow-up time, baseline age, ethnicity, sex, ALT, physical activity, and total NEFA. X-axis values represent a percent difference in the outcome per SD increase in the FA. P-values were adjusted for the BH false discovery rate, with the largest dot representing a significant ( $p < 0.05$ ) association.



Supplemental Figure S5: PLS loadings (or weights) for each of the TGFA. A larger loading indicates a higher contribution to the PLS component score.