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The online supplemental material provides information on the absolute levels and interquartile ranges of all the metabolites tested for association with glycemia (Supplementary Table 1) and the consistency of the cross-sectional associations in the two cohorts as well as at the follow-up survey (Supplementary Figure 2). These data are relevant to assess the completeness and stability of the metabolite associations since only significant associations are presented in the main manuscript. In addition, we provide an overview of the study flow in order to clarify exclusion criteria, meta-analysis of cross-sectional associations and analysis of prospective data (Supplementary Figure 1). Finally, associations of the metabolites with insulin sensitivity and total insulin secretion indices are assessed to elucidate the differences of the metabolite associates with fasting and postload glucose (Supplementary Figure 3).

Supplementary Table 1. Baseline and follow-up metabolite concentrations and 6-year tracking of the metabolites

	Pieksämäki 1997 (n=864)	**Health 2000 Study (n=1,009)**	**Pieksämäki 2004 (n=618)**	***6.5-year tracking r (95% CI)***
Fasting glucose	5.7 [5.4-6.1]	5.6 [5.2-6.0]	5.7 [5.3-6.1]	0.55 (0.47-0.63)
2h glucose	5.4 [4.6-6.4]	6.2 [5.1-7.5]	5.6 [4.8-6.5]	0.43 (0.35-0.51)
Alanine	0.41 [0.37-0.45]	0.41 [0.37-0.46]	0.42 [0.38-0.46]	0.47 (0.39-0.55)
Glycine	0.29 [0.26-0.33]	0.28 [0.25-0.33]	0.32 [0.28-0.44]	0.57 (0.49-0.65)
Glutamine	0.59 [0.55-0.63]	0.51 [0.47-0.57]	0.54 [0.51-0.58]	0.53 (0.45-0.61)
Lactate	1.7 [1.4-2.0]	1.3 [1.1-1.5]	1.5 [1.3-1.8]	0.15 (0.07-0.23)
Pyruvate	0.075 [0.064-0.091]	0.077 [0.063-0.097]	0.070 [0.057-0.084]	0.39 (0.31-0.47)
Citrate	0.097 [0.087-0.11]	0.11 [0.095-0.12]	0.10 [0.088-0.12]	0.34 (0.26-0.42)
Sum of branched-chain amino acids	0.33 [0.30-0.38]	0.32 [0.28-0.37]	0.34 [0.30-0.39]	0.66 (0.58-0.74)
Leucine	0.083 [0.073-0.095]	0.081 [0.070-0.093]	0.085 [0.074-0.098]	0.66 (0.58-0.74)
Isoleucine	0.054 [0.045-0.064]	0.052 [0.044-0.063]	0.056 [0.047-0.068]	0.66 (0.58-0.74)
Valine	0.20 [0.18-0.22]	0.19 [0.17-0.22]	0.20 [0.18-0.23]	0.56 (0.48-0.64)
Phenylalanine	0.074 [0.068-0.081]	0.074 [0.067-0.084]	0.075 [0.068-0.083]	0.42 (0.34-0.50)
Tyrosine	0.055 [0.048-0.063]	0.054 [0.046-0.062]	0.058 [0.050-0.065]	0.52 (0.44-0.60)
Histidine	0.067 [0.062-0.073]	0.061 [0.055-0.068]	0.067 [0.062-0.072]	0.33 (0.25-0.40)
Acetate	0.043 [0.037-0.051]	0.052 [0.043-0.063]	0.043 [0.037-0.051]	0.27 (0.19-0.35)
Acetoacetate	0.035 [0.026-0.049]	0.035 [0.026-0.049]	0.037 [0.028-0.054]	0.30 (0.22-0.38)
Creatinine	0.059 [0.053-0.067]	0.061 [0.053-0.071]	0.063 [0.056-0.071]	0.74 (0.66-0.82)
Urea	0.053 [0.039-0.068]	0.059 [0.042-0.076]	0.046 [0.027-0.063]	0.10 (0.02-0.18)
α1-acid glycoprotein	1.4 [1.3-1.5]	1.3 [1.2-1.5]	1.3 [1.2-1.4]	0.60 (0.52-0.68)
Total fatty acids	10 [9.3-12]	12 [11-15]	11 [9.8-12]	0.51 (0.43-0.59)
Monounsat. fatty acids	3.0 [2.5-3.6]	3.5 [2.9-4.3]	3.1 [2.6-3.7]	0.55 (0.47-0.63)
Docosahexaenoic acids	0.19 [0.15-0.24]	0.23 [0.18-0.31]	0.22 [0.17-0.27]	0.57 (0.49-0.65)
Linoleic acids	3.1 [2.8-3.5]	3.2 [2.8-3.7]	3.2 [2.8-3.5]	0.47 (0.39-0.55)
Polyunsaturated fatty acids other than linoleic acid	2.1 [1.8-2.4]	2.5 [2.1-3.0]	2.3 [2.0-2.7]	0.58 (0.50-0.66)
ω-3 fatty acids	0.37 [0.30-0.46]	0.53 [0.43-0.67]	0.40 [0.32-0.52]	0.43 (0.35-0.51)
ω-6 fatty acids	3.6 [3.3-4.0]	4.0 [3.6-4.7]	3.8 [3.4-4.2]	0.47 (0.39-0.55)
ω-7, ω-9 and saturated fatty acids	6.5 [5.6-7.6]	7.5 [6.5-9.2]	6.7 [5.9-7.7]	0.51 (0.43-0.59)
ω-3/total fatty acids [%]	3.4 [2.9-4.1]	4.3 [3.6-5.1]	3.7 [2.9-4.6]	0.42 (0.34-0.50)
ω-6/total fatty acids [%]	34 [32-37]	34 [32-36]	35 [32-37]	0.43 (0.35-0.51)
ω-7, ω-9 and sat. fatty	62 [60-65]	62 [60-64]	61 [59-64]	0.46 (0.38-0.54)

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acids/total fatty acids [%]				
Esterified cholesterol	3.6 [3.2-4.0]	4.0 [3.6-4.6]	3.7 [3.3-4.1]	0.51 (0.43-0.59)
Free cholesterol	1.4 [1.2-1.5]	1.3 [1.2-1.5]	1.4 [1.3-1.6]	0.48 (0.40-0.56)
Phosphoglycerides	0.87 [0.78-0.99]	0.92 [0.82-1.1]	0.94 [0.84-1.1]	0.50 (0.42-0.58)
Phosphatidylcholine	2.1 [1.9-2.3]	2.2 [1.9-2.5]	2.2 [2.0-2.4]	0.51 (0.43-0.60)
Sphingomyelin	0.36 [0.32-0.40]	0.27 [0.22-0.32]	0.38 [0.33-0.42]	0.34 (0.26-0.42)
Methylene groups/ fatty acid chain	9.9 [9.7-10]	9.4 [9.2-9.6]	9.8 [9.7-10]	0.27 (0.19-0.35)
Methylene groups/ double bond	7.7 [7.3-8.1]	7.5 [7.1-7.9]	7.6 [7.3-8.0]	0.52 (0.44-0.60)
Double bonds/fatty acid	1.3 [1.2-1.3]	1.3 [1.2-1.3]	1.3 [1.2-1.4]	0.54 (0.46-0.62)
Bisallylic groups/ double bond	0.54 [0.52-0.56]	0.53 [0.51-0.55]	0.55 [0.53-0.57]	0.54 (0.46-0.62)
Bisallylic groups/ fatty acid	0.69 [0.64-0.75]	0.67 [0.62-0.73]	0.70 [0.65-0.77]	0.56 (0.48-0.64)
Fatty acid chain length	18.3 [18.1-18.4]	17.8 [17.6-18.0]	18.3 [18.1-18.4]	0.34 (0.26-0.43)
Albumin [standardized concentration unit]	0.090 [0.088-0.093]	0.092 [0.089-0.098]	0.090 [0.086-0.093]	0.28 (0.20-0.36)

Metabolite concentrations are median (interquartile range) in mmol/l unless otherwise stated. Tracking (the likelihood to maintain the original fractile over time) was assessed by Spearman's correlation coefficients. $P<1\times10^{-10}$ for all.

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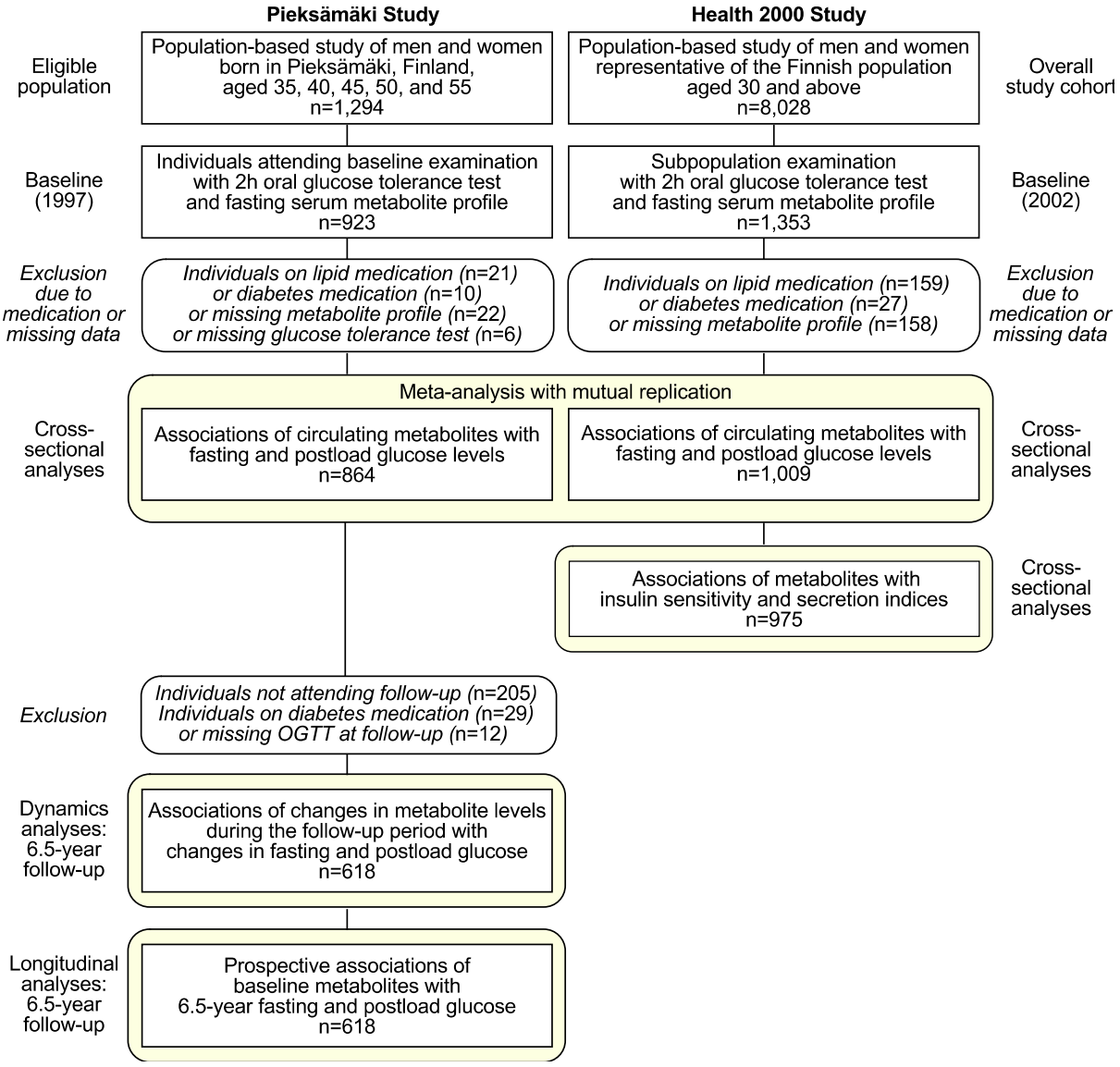
Supplementary Figure 1. Study flow chart



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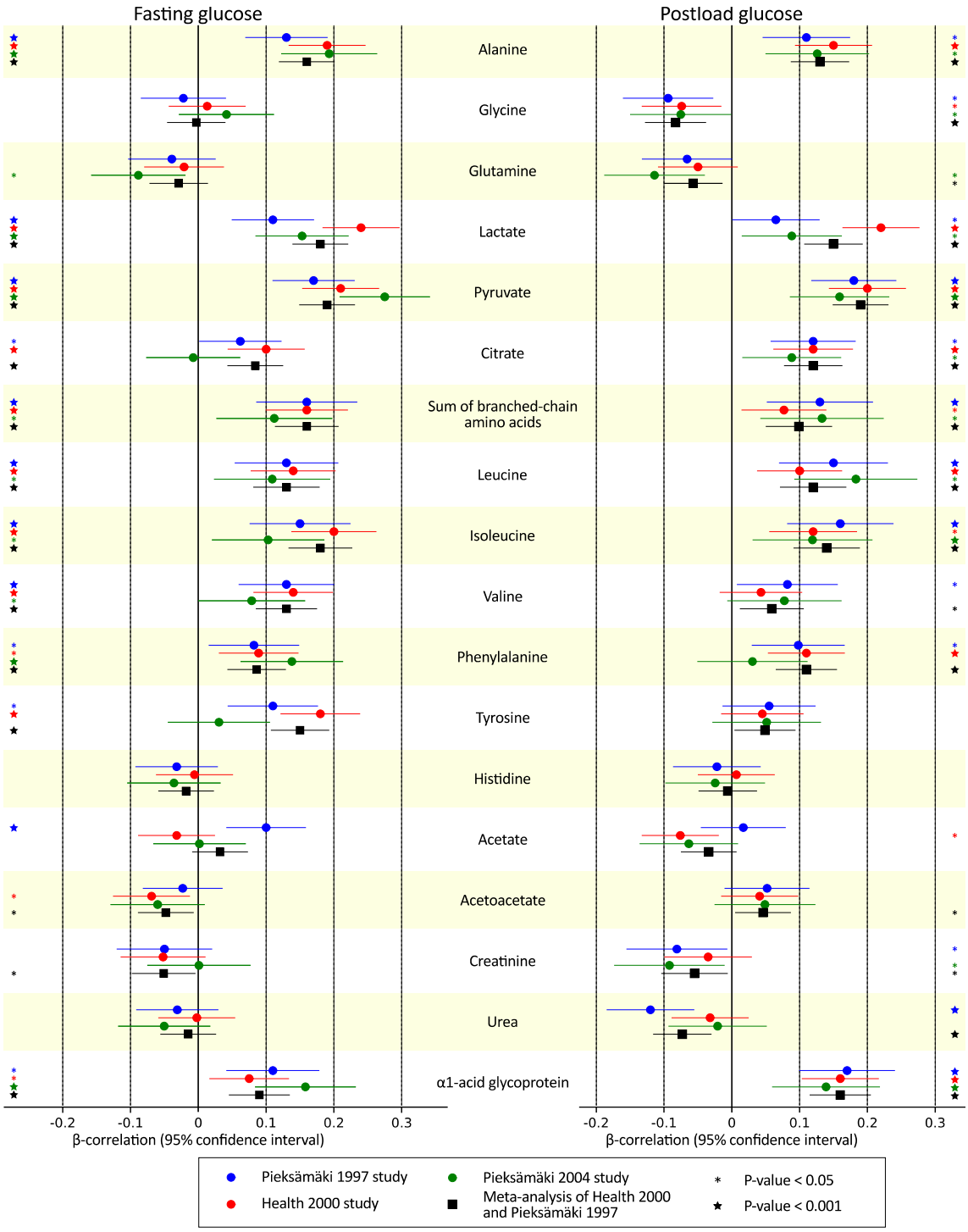
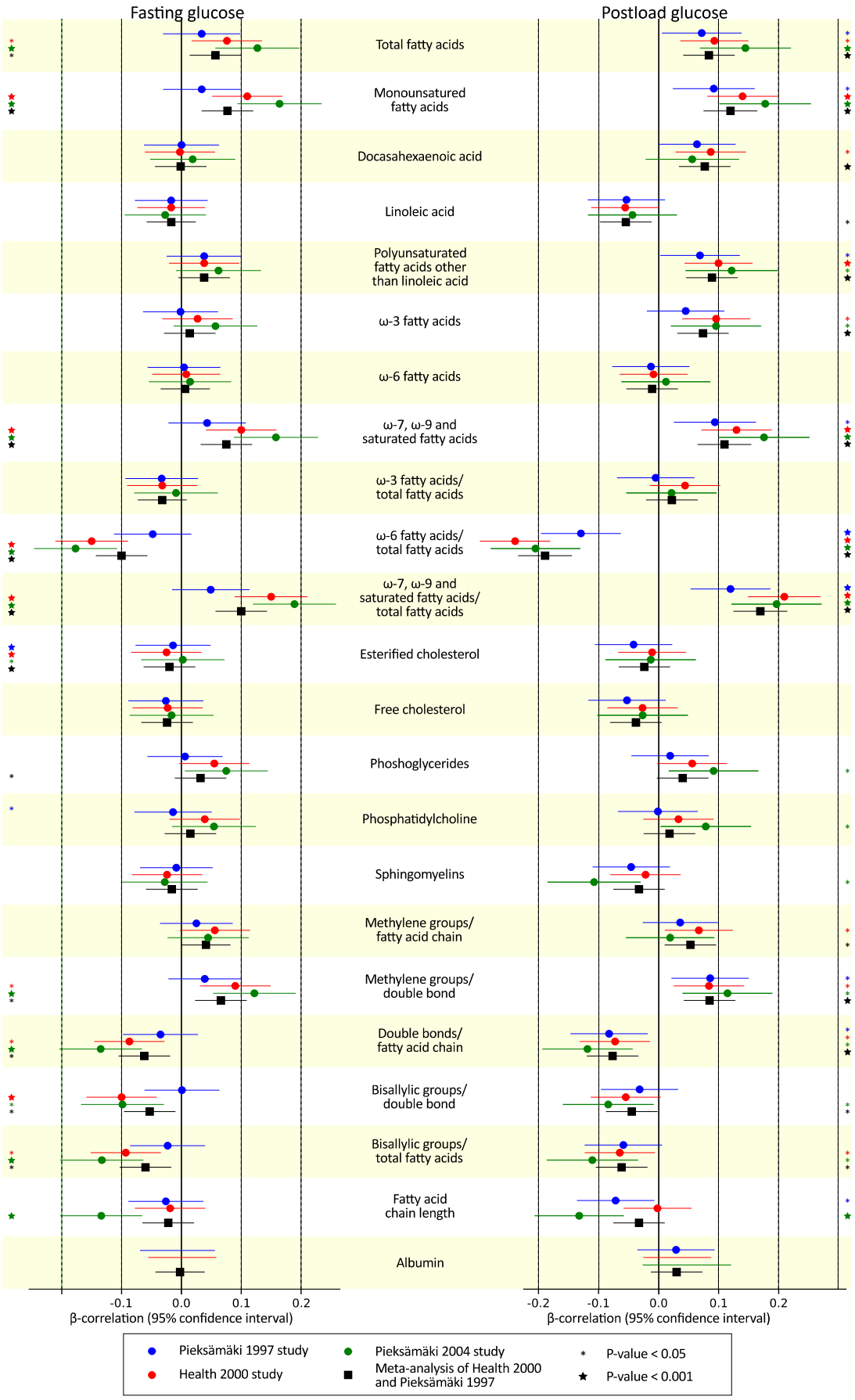
Supplementary Figure 2. Cross-sectional associations of all assayed metabolites with fasting and postload glucose



Associations of metabolites with glucose levels adjusted for sex, age, body mass index and systolic blood pressure. Assocation magnitudes are in units of 1-SD glucose per 1-SD metabolite concentration. Blue, red and green circles indicate individual field surveys and balck squares meta-analysis of the Health 2000 Study (n=1,009) and the Pieksämäki 1997 study (n=864).

SUPPLEMENTARY DATA



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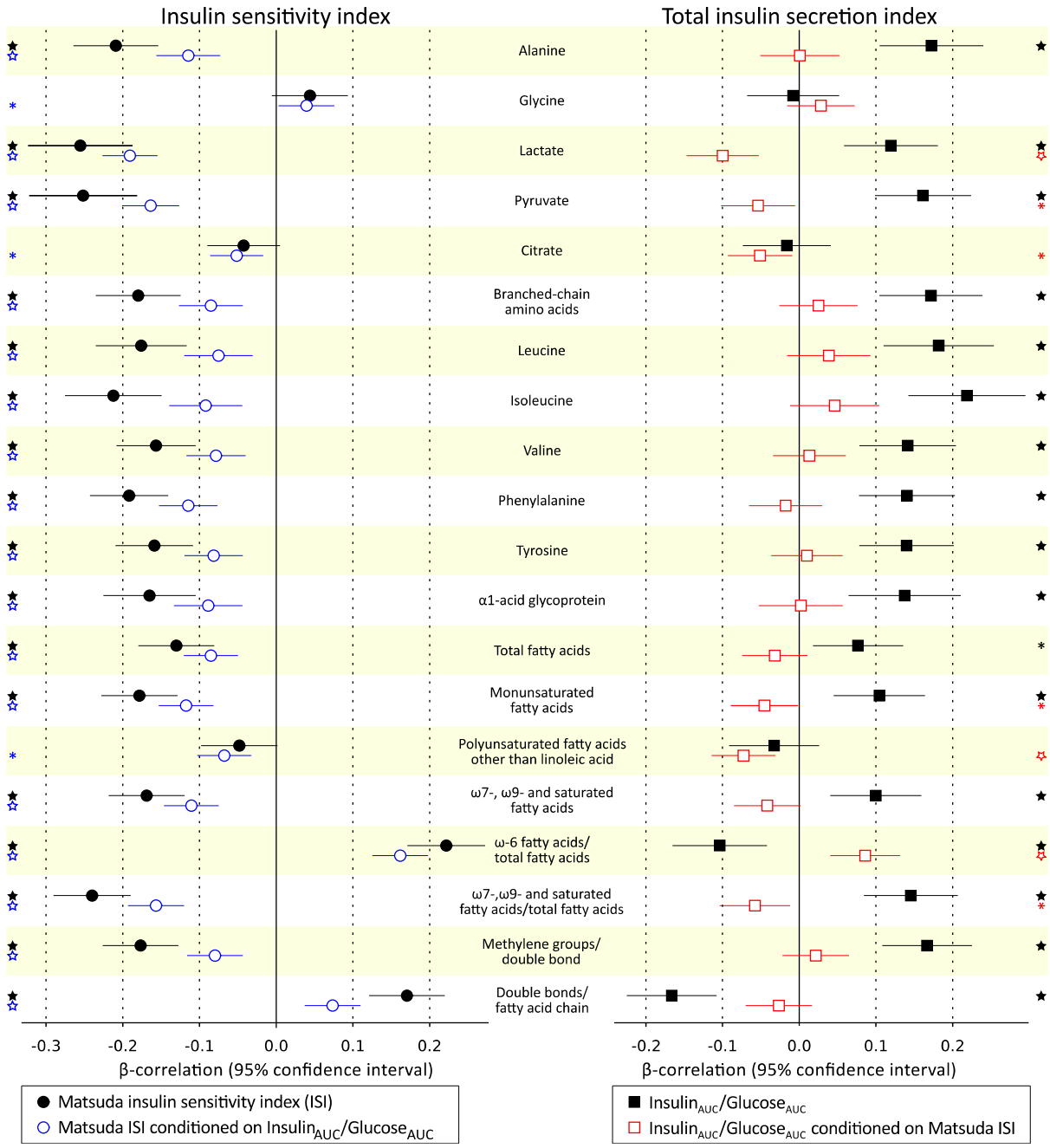
Supplementary Figure 3. Metabolites vs insulin sensitivity and insulin secretion indices



Associations of metabolites with markers of insulin sensitivity (Matsuda ISI; circles) and total phase insulin secretion (Insulin$_{AUC}$/Glucose$_{AUC}$; squares) in the Finnish Health 2000 Study (n=975). Association magnitudes are in units of 1-SD change in insulin sensitivity/secretion index per 1-SD metabolite concentration. All associations were adjusted for age, sex, body mass index and systolic blood pressure. Metabolites quantified from native serum were further adjusted for triglycerides and HDL-C. *: P-value < 0.05; ★: P-value < 0.001.