SUPPLEMENTARY DATA

Bilirubin as a potential causal factor in type 2 diabetes risk: a Mendelian randomization study

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Short title: Bilirubin and type 2 diabetes

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Supplementary Table 1. Measurement of markers

Marker	**Assay**
Total cholesterol	Dry chemistry (Eastman Kodak, Rochester, New York)
Glucose	Dry chemistry (Eastman Kodak, Rochester, New York)
High density lipoprotein cholesterol	Homogeneous method (direct HDL, Aeroset TM System, Abbott Laboratories, Abbott Park, Illinois)
Triglycerides	Enzymatically
High-sensitivity C-reactive protein	Nephelometry (BN II, Dade Behring, Marburg, Germany)
Urinary albumin concentration	Nephelometry (Dade Behring Diagnostic, Marburg, Germany)
Gamma-glutamyltransferase	Standardized enzymatic method (Modular P; Roche Diagnostics, Indianapolis, IN)
Alanine aminotransferase	Standardized enzymatic method (Modular P; Roche Diagnostics, Indianapolis, IN)
Aspartate aminotransferase	Standardized enzymatic method (Modular P; Roche Diagnostics, Indianapolis, IN)
Alkaline phosphatase	Standardized enzymatic method (Modular P; Roche Diagnostics, Indianapolis, IN)
Albumin	Standardized enzymatic method (Modular P; Roche Diagnostics, Indianapolis, IN)

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Supplementary Table 2. Association of individual SNPs with bilirubin, type 2 diabetes and glycemic traits in genome-wide association study summary statistics

SNP			Association with Bilirubin*		Association with T2D or glycemic traits†							
					T2D		Glucose		Insulin		HOMA-IR	
	Gene	Alleles	Effect (SE)	*P*	Effect (SE)	*P*	Effect (SE)	*P*	Effect (SE)	*P*	Effect (SE)	*P*
rs6742078	*UGT1A1*	T/G	0.23 (0.01)	5×10^{-324}	0.030 (0.020)	0.1	-0.009 (0.004)	0.02	-0.009 (0.004)	0.03	-0.009 (0.004)	0.03
rs4149056	*SLCO1B1*	C/T	0.05 (0.01)	1×10^{-13}	-0.020 (0.022)	0.31	0.0003 (0.005)	0.94	0.006 (0.005)	0.25	0.004 0.005)	0.47
rs16928809	*SLC22A18*	A/G	0.06 (0.01)	1×10^{-7}	-0.049 (0.03)	0.13	-0.003 (0.007)	0.67	-0.002 (0.007)	0.76	-0.004 (0.008)	0.63

*The estimated SNP effects for serum total bilirubin levels (umol/L increase in log-transformed levels) were obtained from GWA meta-analysis among up to 9,464 individuals, Johnson et al. (17). The *UGT1A1* SNP, rs6742078, explained 16.7-18.1% of the total variance in bilirubin levels as reported in Johnson et al. (17). Two other SNPs, rs4149056 and rs16928809, explained less than 1% (e.g, the *SLCO1B1* SNP, rs4149056:0.5-0.6%) of the total variance in bilirubin levels. †The estimated SNP effects for T2D and glycemic traits were obtained from the DIGRAM consortium (among up to 12,171 case subjects and 56,862 controls), Morris et al. (45), and MAGIC (among up to 46,186 individuals), Dupuis et al. (27), respectively.