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Supplemental Data

**Dominant Genetic Variation and Missing Heritability
for Human Complex Traits: Insights from Twin
versus Genome-wide Common SNP Models**

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Table S1. General characteristics of study participants

	All	Gender		Zygosity ^b		
		Male	Female	MZ	SSDZ	OSDZ
Phenotypes						
n_{total}	10682	5074	5608	2499	4154	4029
Age^a	64.89±8.08	65.45±7.99	64.38±8.13	63.67±7.49	65.45±8.47	65.06±7.95
n_{pair-match}	7740	3653	4087	2176	2886	2678
Age	65.03±7.75	65.58±7.69	64.54±7.77	63.54±7.31	65.63±8.09	65.60±7.56
Genotypes						
n_{pheno-match}	9606	4523	5083	1423	4154	4029
Age	65.04±8.15	65.48±8.05	64.65±8.22	63.76±7.62	65.45±8.47	65.06±7.95
n_{unrelated}	5779	2755	3024	1185	2316	2278
Age	64.91±8.33	65.51±8.21	64.37±8.40	63.96±7.71	65.38±8.69	64.93±8.22

^a Age of each subgroup is described as mean ± standard deviation;

^b Including monozygotic (MZ), same-sex dizygotic (SSDZ) and opposite-sex dizygotic (OSDZ) twins.

Table S2. Eighteen traits and units

Trait	Abbreviation	Unit
Total cholesterol	TC	mmol/L
High density lipoprotein	HDL	mmol/L
Low density lipoprotein	LDL	mmol/L
Apolipoprotein A1	ApoA1	g/L
Apolipoprotein B	ApoB	g/L
Triglyceride	TG	mmol/L
C-reactive Protein	CRP	mg/L
Glucose	Glu	mmol/L
Glycosylated hemoglobin A1c	HbA1c	%
Hemoglobin	HB	g/dL
Cystatin C	CysC	mg/L
Creatinine	Crea	μmol/L
Glomerular filtration rate	GFR	mL/min /1.73 m ²
Immunoglobulin A	IgA	g/L
Body mass index	BMI	kg/m ²
Weight	WT	kg
Waist circumference	WC	cm
Height		m

Table S3. Descriptive statistics of each trait

Trait	All	Gender ^a		Zygosity ^b		
		Male	Female	MZ	SSDZ	OSDZ
TC	5.77±1.12	5.52±1.10	6.00±1.09	5.77±1.12	5.79±1.12	5.76±1.13
n	10682	5074	5608	2499	4154	4029
HDL	1.41±0.42	1.24±0.34	1.56±0.42	1.40±0.43	1.42±0.42	1.39±0.42
n	10682	5074	5608	2499	4154	4029
LDL	3.76±0.99	3.65±0.98	3.86±0.99	3.78±0.98	3.76±0.99	3.74±0.99
n	10543	4985	5558	2467	4102	3974
ApoA1	1.64±0.30	1.53±0.26	1.75±0.30	1.64±0.31	1.64±0.30	1.64±0.30
n	10678	5073	5605	2497	4154	4027
ApoB	1.08±0.25	1.07±0.24	1.10±0.25	1.07±0.24	1.09±0.25	1.09±0.25
n	10678	5073	5605	2497	4154	4027
TG	1.37±0.82	1.44±0.92	1.30±0.72	1.33±0.78	1.36±0.83	1.39±0.83
n	10681	5073	5608	2499	4153	4029
CRP	3.13±6.61	3.29±7.95	3.00±5.10	3.05±6.80	3.14±6.84	3.18±6.24
n	10679	5074	5605	2498	4153	4028
Glu	5.59±1.22	5.76±1.33	5.44±1.08	5.53±1.09	5.60±1.25	5.63±1.26
n	10676	5073	5603	2499	4150	4027
HbA1c	4.82±0.68	4.85±0.74	4.78±0.61	4.77±0.60	4.82±0.67	4.84±0.72
n	10668	5069	5599	2498	4150	4020
HB	14.26±1.21	14.86±1.13	13.72±1.00	14.31±1.19	14.18±1.22	14.32±1.20
n	10664	5065	5599	2495	4148	4021
CysC	1.02±0.29	1.05±0.33	0.99±0.25	0.99±0.22	1.03±0.30	1.03±0.32
n	10405	4936	5469	2453	4020	3932
Crea	78.01±28.17	87.36±35.68	69.58±14.51	77.46±16.47	77.50±22.12	78.89±37.80
n	10405	4936	5469	2453	4020	3932
GFR	83.55±21.88	80.74±21.94	86.08±21.53	85.94±21.15	83.04±22.40	82.58±21.70
n	10404	4935	5469	2453	4020	3931
IgA	2.52±1.14	2.67±1.18	2.39±1.08	2.37±1.02	2.51±1.15	2.63±1.19
n	10621	5046	5575	2489	4139	3993
BMI	26.31±7.33	26.59±6.83	26.07±7.75	26.34±8.56	26.20±7.37	26.42±6.40
n	10562	5021	5541	2484	4110	3968
WT	74.94±13.81	81.77±12.33	68.75±12.05	75.11±13.95	74.18±13.59	75.62±13.91
n	10570	5027	5543	2487	4113	3970
WC	91.78±12.18	97.16±10.26	86.91±11.72	91.97±12.01	91.25±11.98	92.22±12.47
n	10556	5019	5537	2485	4106	3965
Height	1.69±0.10	1.76±0.09	1.63±0.08	1.70±0.10	1.69±0.10	1.70±0.10
n	10573	5026	5547	2486	4118	3969

^a Sex-difference: TC, HDL, LDL, ApoA1, ApoB and GFR were significantly lower in males (P<0.05); TG, CRP, Glu, HbA1c, HB, CysC, Crea, IgA, BMI, weight, waist circumference and height were significantly higher in males (P<0.05);

^b HDL, ApoB, TG, Glu, HbA1c, HB, CysC, Crea, GFR, IgA, weight, waist circumference and height were significantly different among monozygotic (MZ), same-sex dizygotic (SSDZ) and opposite-sex dizygotic (OSDZ) twins (P<0.05).

Table S4. Estimates and parameters in SNP-based GREML(d) analyses

Trait	GRM ^a	V(G) ^b	V(e) ^c	Vp ^d	V(G)/Vp ^e	logL ^f	logL0 ^g	LRT ^h	df ⁱ	P ^j
TC	GREML	0.15	0.83	0.98	0.15	-2837.23	-2840.16	5.87	1	7.69E-3
(n=5779)	GREMLd	0.00	0.98	0.98	0.00	-2840.16	-2840.16	0.00	1	0.50
LDL	GREML	0.15	0.83	0.99	0.16	-2814.76	-2818.06	6.59	1	5.14E-3
(n=5704)	GREMLd	0.00	0.99	0.99	0.00	-2818.06	-2818.06	0.00	1	0.50
ApoB	GREML	0.14	0.85	0.99	0.14	-2861.98	-2864.65	5.33	1	0.01
(n=5776)	GREMLd	0.00	0.99	0.99	0.00	-2864.65	-2864.65	0.00	1	0.50
TG	GREML	0.31	0.68	0.99	0.31	-2841.81	-2856.49	29.35	1	3.02E-8
(n=5778)	GREMLd	0.28	0.71	0.99	0.28	-2851.29	-2856.49	10.40	1	6.29E-4
CRP	GREML	0.38	0.63	1.01	0.37	-2906.29	-2932.21	51.84	1	3.02E-13
(n=5777)	GREMLd	0.00	1.01	1.01	0.00	-2932.21	-2932.21	0.00	1	0.50
Glu	GREML	0.17	0.82	0.99	0.17	-2847.99	-2852.33	8.66	1	1.62E-3
(n=5775)	GREMLd	0.15	0.84	0.99	0.15	-2850.98	-2852.33	2.69	1	0.05
HbA1c	GREML	0.20	0.80	1.00	0.20	-2880.00	-2885.65	11.30	1	3.88E-4
(n=5770)	GREMLd	0.00	1.00	1.00	0.00	-2885.65	-2885.65	0.00	1	0.50
HB	GREML	0.21	0.80	1.01	0.21	-2921.46	-2927.49	12.07	1	2.56E-4
(n=5769)	GREMLd	0.00	1.01	1.01	0.00	-2927.49	-2927.49	0.00	1	0.50
CysC	GREML	0.28	0.74	1.02	0.27	-2877.14	-2886.99	19.71	1	4.51E-6
(n=5634)	GREMLd	0.05	0.97	1.02	0.05	-2886.82	-2886.99	0.34	1	0.28
Crea	GREML	0.18	0.83	1.01	0.18	-2848.49	-2853.10	9.21	1	1.20E-3
(n=5634)	GREMLd	0.01	1.01	1.01	0.01	-2853.09	-2853.10	0.00	1	0.48
GFR	GREML	0.33	0.69	1.02	0.32	-2869.81	-2883.10	26.59	1	1.26E-7
(n=5633)	GREMLd	0.04	0.99	1.02	0.03	-2883.03	-2883.10	0.14	1	0.35
BMI	GREML	0.20	0.78	0.98	0.21	-2792.70	-2799.26	13.11	1	1.47E-4
(n=5695)	GREMLd	0.02	0.96	0.98	0.02	-2799.22	-2799.26	0.08	1	0.39
WT	GREML	0.26	0.72	0.98	0.26	-2788.92	-2797.98	18.13	1	1.03E-5
(n=5699)	GREMLd	0.11	0.87	0.98	0.11	-2797.18	-2797.98	1.61	1	0.10
WC	GREML	0.16	0.81	0.97	0.16	-2763.68	-2767.08	6.81	1	4.55E-3
(n=5693)	GREMLd	0.19	0.78	0.97	0.19	-2764.65	-2767.08	4.86	1	0.01
HDL	GREML	0.24	0.77	1.01	0.24	-2911.87	-2919.78	15.83	1	3.47E-5
(n=5779)	GREMLd	0.01	1.00	1.01	0.01	-2919.77	-2919.78	0.03	1	0.44
ApoA1	GREML	0.17	0.84	1.00	0.17	-2899.83	-2903.44	7.23	1	3.58E-3
(n=5776)	GREMLd	0.09	0.92	1.00	0.09	-2902.92	-2903.44	1.05	1	0.15
IgA	GREML	0.25	0.77	1.02	0.24	-2916.66	-2925.59	17.88	1	1.18E-5
(n=5745)	GREMLd	0.00	1.01	1.02	0.00	-2925.59	-2925.59	0.00	1	0.49
Height	GREML	0.62	0.39	1.01	0.62	-2828.89	-2878.51	99.26	1	<0.01
(n=5701)	GREMLd	0.00	1.01	1.01	0.00	-2878.51	-2878.51	0.00	1	0.50

^a Genomic-relatedness-matrix (additive or dominant); ^b Genetic variance (additive or dominant); ^c Non-shared environmental variance; ^d Phenotypic variance; ^e Additive or dominant genetic variance, significant dominance were labeled in red; ^f Log likelihood for the full model; ^g Log likelihood for the reduced model; ^h Likelihood ratio test; ⁱ Degree of freedom; ^j P value.

Table S5. Model fitting for classic twin-based structural equation model

Trait	Model ^a	EP ^b	minus 2LL ^c	Df ^d	AIC ^e	diff LL ^f	diff df ^g	p ^h
TC	Saturated	10	21583.58	7730	6123.58	NA	NA	NA
	ACE	4	21597.89	7736	6125.89	14.32	6	2.63E-02
	ADE	4	21592.47	7736	6120.47	8.90	6	1.79E-01
	AE	3	21597.89	7737	6123.89	14.32	7	4.58E-02
LDL	Saturated	10	21272.02	7629	6014.02	NA	NA	NA
	ACE	4	21287.48	7635	6017.48	15.46	6	1.70E-02
	ADE	4	21279.49	7635	6009.49	7.47	6	2.79E-01
	AE	3	21287.48	7636	6015.48	15.46	7	3.05E-02
ApoB	Saturated	10	21413.46	7728	5957.46	NA	NA	NA
	ACE	4	21424.26	7734	5956.26	10.81	6	9.45E-02
	ADE	4	21421.19	7734	5953.19	7.74	6	2.58E-01
	AE	3	21424.26	7735	5954.26	10.81	7	1.47E-01
TG	Saturated	10	21310.31	7729	5852.31	NA	NA	NA
	ACE	4	21324.27	7735	5854.27	13.96	6	3.01E-02
	ADE	4	21320.95	7735	5850.95	10.64	6	1.00E-01
	AE	3	21324.27	7736	5852.27	13.96	7	5.20E-02
CRP	Saturated	10	21587.85	7728	6131.85	NA	NA	NA
	ACE	4	21599.75	7734	6131.75	11.90	6	6.43E-02
	ADE	4	21596.98	7734	6128.98	9.13	6	1.67E-01
	AE	3	21599.75	7735	6129.75	11.90	7	1.04E-01
Glu	Saturated	10	21521.28	7726	6069.28	NA	NA	NA
	ACE	4	21551.71	7732	6087.71	30.43	6	3.26E-05
	ADE	4	21537.24	7732	6073.24	15.96	6	1.40E-02
	AE	3	21551.71	7733	6085.71	30.43	7	7.93E-05
HbA1c	Saturated	10	20836.70	7717	5402.70	NA	NA	NA
	ACE	4	20876.72	7723	5430.72	40.02	6	4.51E-07
	ADE	4	20851.88	7723	5405.88	15.18	6	1.89E-02
	AE	3	20876.72	7724	5428.72	40.02	7	1.25E-06
HB	Saturated	10	21246.00	7716	5814.00	NA	NA	NA
	ACE	4	21256.52	7722	5812.52	10.51	6	1.05E-01
	ADE	4	21252.84	7722	5808.84	6.84	6	3.36E-01
	AE	3	21256.52	7723	5810.52	10.51	7	1.61E-01
CysC	Saturated	10	20534.11	7524	5486.11	NA	NA	NA
	ACE	4	20552.35	7530	5492.35	18.23	6	5.67E-03
	ADE	4	20546.69	7530	5486.69	12.57	6	5.04E-02
	AE	3	20552.35	7531	5490.35	18.23	7	1.10E-02
Crea	Saturated	10	20720.13	7524	5672.13	NA	NA	NA
	ACE	4	20735.30	7530	5675.30	15.18	6	1.89E-02
	ADE	4	20725.89	7530	5665.89	5.76	6	4.51E-01
	AE	3	20735.30	7531	5673.30	15.18	7	3.38E-02
GFR	Saturated	10	20597.48	7524	5549.48	NA	NA	NA
	ACE	4	20612.62	7530	5552.62	15.14	6	1.92E-02
	ADE	4	20605.68	7530	5545.69	8.20	6	2.24E-01

	AE	3	20612.62	7531	5550.62	15.14	7	3.43E-02
BMI	Saturated	10	20876.61	7669	5538.61	NA	NA	NA
	ACE	4	20912.53	7675	5562.53	35.92	6	2.85E-06
	ADE	4	20881.45	7675	5531.45	4.84	6	5.64E-01
	AE	3	20912.53	7676	5560.53	35.92	7	7.50E-06
WT	Saturated	10	20721.53	7674	5373.54	NA	NA	NA
	ACE	4	20755.37	7680	5395.37	33.83	6	7.24E-06
	ADE	4	20730.42	7680	5370.42	8.89	6	1.80E-01
	AE	3	20755.37	7681	5393.37	33.83	7	1.85E-05
WC	Saturated	10	21035.29	7661	5713.29	NA	NA	NA
	ACE	4	21082.82	7667	5748.82	47.52	6	1.47E-08
	ADE	4	21040.72	7667	5706.73	5.43	6	4.90E-01
	AE	3	21082.82	7668	5746.82	47.52	7	4.41E-08
HDL	Saturated	10	20977.12	7730	5517.12	NA	NA	NA
	ACE	4	20988.98	7736	5516.98	11.86	6	6.51E-02
	ADE	4	20987.38	7736	5515.38	10.26	6	1.14E-01
	AE	3	20988.98	7737	5514.98	11.86	7	1.05E-01
ApoA1	Saturated	10	21035.10	7728	5579.10	NA	NA	NA
	ACE	4	21047.81	7734	5579.81	12.71	6	4.79E-02
	ADE	4	21048.01	7734	5580.01	12.91	6	4.44E-02
	AE	3	21048.01	7735	5578.01	12.91	7	7.42E-02
IgA	Saturated	10	21121.74	7681	5759.74	NA	NA	NA
	ACE	4	21187.33	7687	5813.34	65.59	6	3.26E-12
	ADE	4	21190.83	7687	5816.83	69.09	6	6.29E-13
	AE	3	21190.83	7688	5814.83	69.09	7	2.26E-12
Height	Saturated	10	19587.10	7675	4237.10	NA	NA	NA
	ACE	4	19596.82	7681	4234.82	9.72	6	1.37E-01
	ADE	4	19606.82	7681	4244.82	19.72	6	3.11E-03
	AE	3	19606.82	7682	4242.82	19.72	7	6.21E-03

^a Each model is compared with saturated model, and the model in bold is the best fitted model according to Akaike information criterion;

^b EP: number of estimated parameters;

^c minus 2LL: minus 2 log likelihood;

^d df: degree of freedom;

^e AIC: Akaike information criterion;

^f diff LL: difference of log likelihood;

^g diff df: difference of df;

^h P: P value.

Table S6. Intra-pair correlation and Falconer estimation for each trait

Trait	Intra-pair correlation ^a				Falconer Equation ^b		
	r_{MZ}	r_{DZ}	r_{SSDZ}	r_{OSDZ}	A	C	E
TC	0.48	0.19	0.20	0.18	0.58	-0.10	0.52
95% CI	(0.43-0.52)	(0.15-0.23)	(0.15-0.25)	(0.12-0.23)			
LDL	0.46	0.18	0.19	0.16	0.56	-0.10	0.54
95% CI	(0.41-0.51)	(0.14-0.21)	(0.14-0.24)	(0.11-0.22)			
ApoB	0.52	0.23	0.26	0.20	0.58	-0.06	0.48
95% CI	(0.48-0.57)	(0.20-0.27)	(0.21-0.31)	(0.15-0.25)			
TG	0.55	0.24	0.27	0.21	0.62	-0.07	0.45
95% CI	(0.51-0.59)	(0.21-0.28)	(0.23-0.32)	(0.16-0.26)			
CRP	0.42	0.19	0.21	0.17	0.46	-0.04	0.58
95% CI	(0.37-0.46)	(0.15-0.23)	(0.16-0.26)	(0.12-0.22)			
Glu	0.51	0.20	0.23	0.17	0.62	-0.11	0.49
95% CI	(0.46-0.55)	(0.16-0.24)	(0.18-0.28)	(0.11-0.22)			
HbA1c	0.69	0.28	0.27	0.28	0.82	-0.13	0.31
95% CI	(0.66-0.72)	(0.24-0.31)	(0.23-0.32)	(0.23-0.33)			
HB	0.55	0.24	0.27	0.21	0.62	-0.07	0.45
95% CI	(0.50-0.59)	(0.21-0.28)	(0.23-0.32)	(0.16-0.26)			
CysC	0.57	0.26	0.27	0.26	0.62	-0.05	0.43
95% CI	(0.53-0.61)	(0.23-0.30)	(0.22-0.32)	(0.20-0.31)			
Crea	0.58	0.24	0.27	0.21	0.68	-0.10	0.42
95% CI	(0.54-0.62)	(0.20-0.28)	(0.22-0.32)	(0.16-0.26)			
GFR	0.57	0.24	0.24	0.24	0.66	-0.09	0.43
95% CI	(0.53-0.61)	(0.21-0.28)	(0.19-0.29)	(0.19-0.29)			
BMI	0.68	0.24	0.29	0.18	0.88	-0.20	0.32
95% CI	(0.64-0.71)	(0.21-0.28)	(0.25-0.34)	(0.13-0.24)			
WT	0.73	0.27	0.33	0.21	0.92	-0.19	0.27
95% CI	(0.70-0.75)	(0.24-0.31)	(0.28-0.37)	(0.16-0.26)			
WC	0.63	0.20	0.27	0.13	0.86	-0.23	0.37
95% CI	(0.59-0.67)	(0.16-0.24)	(0.22-0.31)	(0.08-0.19)			
HDL	0.67	0.31	0.34	0.28	0.72	-0.05	0.33
95% CI	(0.64-0.70)	(0.28-0.34)	(0.29-0.38)	(0.23-0.33)			
ApoA1	0.65	0.34	0.38	0.29	0.62	0.03	0.35
95% CI	(0.61-0.68)	(0.30-0.37)	(0.33-0.42)	(0.24-0.34)			
IgA	0.43	0.28	0.31	0.26	0.30	0.13	0.57
95% CI	(0.38-0.48)	(0.25-0.32)	(0.26-0.35)	(0.21-0.31)			
Height	0.87	0.48	0.49	0.46	0.78	0.09	0.13
95% CI	(0.85-0.88)	(0.45-0.51)	(0.45-0.53)	(0.42-0.51)			

^a All intra-pair correlations of each biomarker in each group were significant ($P < 0.0001$);

^b Falconer equations: $A = 2(r_{MZ} - r_{DZ})$; $C = r_{MZ} - A$; $E = 1 - r_{MZ}$; A: additive genetic variance, C: shared environmental variance, E: non-shared/unique environmental variance.

Table S7. Estimates from classic and sex-limitation structural equation model

Traits		ACE model				ADE model				AE model	
		h ²	95% CI	c ²	95%CI	h ²	95% CI	d ²	95%CI	h ²	95% CI
Total cholesterol	All	0.45	(0.40,0.49)	0.00	(0.00,0.03)	0.28	(0.13,0.43)	0.19	(0.03,0.36)	0.45	(0.41,0.49)
	Male	0.42	(0.22,0.48)	0.00	(0.00,0.17)	0.43	(0.11,0.48)	0.00	(0.00,0.33)	0.43	(0.36,0.48)
	Female	0.51	(0.42,0.56)	0.00	(0.00,0.06)	0.28	(0.01,0.53)	0.25	(0.00,0.53)	0.51	(0.45,0.56)
LDL	All	0.43	(0.39,0.47)	0.00	(0.00,0.03)	0.23	(0.08,0.38)	0.24	(0.07,0.41)	0.43	(0.39,0.47)
	Male	0.38	(0.17,0.45)	0.00	(0.00,0.17)	0.38	(0.04,0.45)	0.00	(0.00,0.36)	0.38	(0.32,0.45)
	Female	0.52	(0.45,0.57)	0.00	(0.00,0.05)	0.20	(0.00,0.46)	0.34	(0.07,0.59)	0.52	(0.46,0.57)
Apolipoprotein B	All	0.51	(0.46,0.55)	0.00	(0.00,0.03)	0.39	(0.25,0.53)	0.14	(0.00,0.30)	0.51	(0.48,0.55)
	Male	0.40	(0.21,0.51)	0.05	(0.00,0.20)	0.46	(0.23,0.51)	0.00	(0.00,0.24)	0.46	(0.40,0.51)
	Female	0.61	(0.52,0.65)	0.00	(0.00,0.06)	0.42	(0.17,0.63)	0.19	(0.00,0.46)	0.61	(0.56,0.65)
Triglyceride	All	0.54	(0.49,0.58)	0.00	(0.00,0.03)	0.42	(0.27,0.55)	0.14	(0.00,0.30)	0.54	(0.51,0.58)
	Male	0.55	(0.40,0.60)	0.00	(0.00,0.12)	0.51	(0.22,0.60)	0.04	(0.00,0.35)	0.55	(0.50,0.60)
	Female	0.56	(0.46,0.61)	0.00	(0.00,0.08)	0.45	(0.20,0.61)	0.12	(0.00,0.39)	0.56	(0.51,0.61)
C-reactive protein	All	0.42	(0.36,0.46)	0.00	(0.00,0.04)	0.30	(0.15,0.44)	0.14	(0.00,0.31)	0.42	(0.38,0.46)
	Male	0.40	(0.27,0.46)	0.00	(0.00,0.10)	0.24	(0.00,0.45)	0.18	(0.00,0.46)	0.40	(0.33,0.46)
	Female	0.47	(0.31,0.53)	0.00	(0.00,0.00)	0.44	(0.18,0.53)	0.04	(0.00,0.32)	0.47	(0.41,0.53)
Glucose	All	0.50	(0.46,0.54)	0.00	(0.00,0.02)	0.24	(0.09,0.38)	0.30	(0.15,0.46)	0.50	(0.46,0.54)
	Male	0.54	(0.45,0.59)	0.00	(0.00,0.07)	0.28	(0.00,0.56)	0.27	(0.00,0.58)	0.54	(0.48,0.59)
	Female	0.52	(0.41,0.57)	0.00	(0.00,0.08)	0.38	(0.13,0.56)	0.15	(0.00,0.42)	0.52	(0.46,0.57)
HbA1c	All	0.70	(0.67,0.72)	0.00	(0.00,0.01)	0.37	(0.24,0.51)	0.35	(0.21,0.49)	0.70	(0.67,0.72)
	Male	0.72	(0.68,0.76)	0.00	(0.00,0.03)	0.18	(0.00,0.47)	0.56	(0.26,0.76)	0.72	(0.68,0.76)
	Female	0.69	(0.61,0.73)	0.00	(0.00,0.06)	0.54	(0.30,0.72)	0.15	(0.00,0.40)	0.69	(0.65,0.73)
Hemoglobin	All	0.54	(0.49,0.57)	0.00	(0.00,0.03)	0.41	(0.26,0.55)	0.15	(0.00,0.30)	0.54	(0.50,0.57)
	Male	0.53	(0.42,0.58)	0.00	(0.00,0.09)	0.38	(0.07,0.58)	0.16	(0.00,0.49)	0.53	(0.48,0.58)
	Female	0.54	(0.39,0.63)	0.04	(0.00,0.16)	0.58	(0.40,0.63)	0.00	(0.00,0.19)	0.58	(0.53,0.63)
Cystatin C	All	0.59	(0.54,0.62)	0.00	(0.00,0.03)	0.42	(0.28,0.56)	0.18	(0.03,0.34)	0.59	(0.55,0.62)
	Male	0.53	(0.45,0.58)	0.00	(0.00,0.06)	0.21	(0.00,0.51)	0.34	(0.03,0.59)	0.53	(0.47,0.58)

	Female	0.68	(0.58,0.71)	0.00	(0.00,0.08)	0.59	(0.34,0.71)	0.09	(0.00,0.35)	0.68	(0.63,0.71)
Creatinine	All	0.57	(0.53,0.60)	0.00	(0.00,0.02)	0.35	(0.21,0.50)	0.24	(0.09,0.40)	0.57	(0.53,0.60)
	Male	0.56	(0.49,0.61)	0.00	(0.00,0.04)	0.09	(0.00,0.39)	0.50	(0.18,0.63)	0.56	(0.50,0.61)
	Female	0.49	(0.35,0.64)	0.12	(0.00,0.24)	0.63	(0.52,0.67)	0.00	(0.00,0.11)	0.63	(0.58,0.67)
GFR	All	0.56	(0.52,0.60)	0.00	(0.00,0.03)	0.38	(0.23,0.52)	0.21	(0.05,0.36)	0.56	(0.53,0.60)
	Male	0.51	(0.44,0.57)	0.00	(0.00,0.05)	0.08	(0.00,0.38)	0.46	(0.14,0.59)	0.51	(0.45,0.57)
	Female	0.63	(0.50,0.67)	0.00	(0.00,0.11)	0.61	(0.35,0.67)	0.03	(0.00,0.29)	0.63	(0.59,0.67)
Body mass index	All	0.65	(0.62,0.68)	0.00	(0.00,0.01)	0.28	(0.13,0.42)	0.41	(0.26,0.56)	0.65	(0.62,0.68)
	Male	0.66	(0.59,0.70)	0.00	(0.00,0.06)	0.37	(0.06,0.66)	0.30	(0.01,0.62)	0.66	(0.61,0.70)
	Female	0.68	(0.60,0.72)	0.00	(0.00,0.07)	0.56	(0.32,0.71)	0.12	(0.00,0.38)	0.68	(0.64,0.72)
Weight	All	0.70	(0.68,0.73)	0.00	(0.00,0.01)	0.37	(0.23,0.51)	0.35	(0.21,0.50)	0.70	(0.68,0.73)
	Male	0.73	(0.63,0.76)	0.00	(0.00,0.09)	0.63	(0.34,0.76)	0.10	(0.00,0.40)	0.73	(0.70,0.76)
	Female	0.71	(0.62,0.74)	0.00	(0.00,0.08)	0.61	(0.36,0.74)	0.10	(0.00,0.36)	0.71	(0.67,0.74)
Waist circumference	All	0.60	(0.56,0.63)	0.00	(0.00,0.01)	0.15	(0.01,0.29)	0.49	(0.34,0.65)	0.60	(0.56,0.63)
	Male	0.63	(0.56,0.68)	0.00	(0.00,0.06)	0.32	(0.01,0.62)	0.32	(0.02,0.65)	0.63	(0.59,0.68)
	Female	0.63	(0.54,0.67)	0.00	(0.00,0.08)	0.51	(0.25,0.67)	0.13	(0.00,0.40)	0.63	(0.58,0.67)
HDL	All	0.66	(0.61,0.69)	0.00	(0.00,0.04)	0.58	(0.44,0.68)	0.09	(0.00,0.23)	0.66	(0.63,0.69)
	Male	0.60	(0.44,0.68)	0.05	(0.00,0.18)	0.65	(0.44,0.69)	0.00	(0.00,0.21)	0.65	(0.60,0.69)
	Female	0.67	(0.56,0.71)	0.00	(0.00,0.10)	0.63	(0.39,0.71)	0.04	(0.00,0.29)	0.67	(0.63,0.71)
Apolipoprotein A1	All	0.64	(0.55,0.68)	0.02	(0.00,0.08)	0.66	(0.55,0.68)	0.00	(0.00,0.11)	0.66	(0.63,0.68)
	Male	0.55	(0.40,0.67)	0.07	(0.00,0.20)	0.63	(0.46,0.67)	0.00	(0.00,0.17)	0.63	(0.59,0.67)
	Female	0.60	(0.47,0.71)	0.07	(0.00,0.18)	0.68	(0.55,0.71)	0.00	(0.00,0.13)	0.68	(0.64,0.71)
Immunoglobulin A	All	0.40	(0.29,0.51)	0.07	(0.00,0.15)	0.50	(0.43,0.54)	0.00	(0.00,0.07)	0.50	(0.46,0.54)
	Male	0.13	(0.00,0.32)	0.26	(0.11,0.39)	0.43	(0.33,0.48)	0.00	(0.00,0.09)	0.43	(0.37,0.48)
	Female	0.59	(0.47,0.64)	0.00	(0.00,0.10)	0.52	(0.27,0.63)	0.07	(0.00,0.34)	0.59	(0.53,0.64)
Height	All	0.77	(0.71,0.83)	0.09	(0.04,0.15)	0.87	(0.83,0.88)	0.00	(0.00,0.03)	0.87	(0.85,0.88)
	Male	0.72	(0.62,0.84)	0.14	(0.03,0.24)	0.86	(0.77,0.88)	0.00	(0.00,0.09)	0.86	(0.85,0.88)
	Female	0.75	(0.65,0.86)	0.12	(0.01,0.21)	0.87	(0.78,0.89)	0.00	(0.00,0.09)	0.87	(0.85,0.89)

The values in bold black are the estimates from the best fitting model.

Table S8. Model fitting for sex-limitation structural equation model

Trait	Model ^a	EP ^b	minus 2LL ^c	Df ^d	AIC ^e	diff LL ^f	diff df ^g	p ^h
TC	ACE	17	21580.91	7723	6134.914	NA	NA	NA
	ADE	17	21577.63	7723	6131.626	-3.29	0	1
	AE	15	21580.92	7725	6130.918	0.00	2	1
LDL	ACE	17	21263.85	7622	6019.847	NA	NA	NA
	ADE	17	21257.72	7622	6013.719	-6.13	0	1
	AE	15	21263.85	7624	6015.847	0.00	2	1
ApoB	ACE	17	21396.60	7721	5954.595	NA	NA	NA
	ADE	17	21394.70	7721	5952.696	-1.90	0	1
	AE	15	21396.95	7723	5950.949	0.35	2	0.84
TG	ACE	17	21055.15	7722	5611.154	NA	NA	NA
	ADE	17	21054.26	7722	5610.256	-0.90	0	1
	AE	15	21055.15	7724	5607.154	0.00	2	1
CRP	ACE	17	21488.40	7721	6046.404	NA	NA	NA
	ADE	17	21487.23	7721	6045.231	-1.17	0	1
	AE	15	21488.40	7723	6042.404	0.00	2	1
Glu	ACE	17	21345.34	7719	5907.342	NA	NA	NA
	ADE	17	21341.11	7719	5903.110	-4.23	0	1
	AE	15	21345.34	7721	5903.342	0.00	2	1
HbA1c	ACE	17	20747.08	7710	5327.083	NA	NA	NA
	ADE	17	20730.82	7710	5310.823	-16.26	0	1
	AE	15	20747.08	7712	5323.083	0.00	2	1
HB	ACE	17	21190.62	7709	5772.621	NA	NA	NA
	ADE	17	21189.98	7709	5771.978	-0.64	0	1
	AE	15	21190.97	7711	5768.968	0.35	2	0.84
CysC	ACE	17	20468.89	7517	5434.887	NA	NA	NA
	ADE	17	20463.73	7517	5429.728	-5.16	0	1
	AE	15	20468.89	7519	5430.887	0.00	2	1
Crea	ACE	17	20505.86	7517	5471.856	NA	NA	NA
	ADE	17	20499.42	7517	5465.422	-6.43	0	1
	AE	15	20509.35	7519	5471.350	3.49	2	0.17
GFR	ACE	17	20580.29	7517	5546.288	NA	NA	NA
	ADE	17	20571.89	7517	5537.887	-8.40	0	1
	AE	15	20580.29	7519	5542.288	0.00	2	1
BMI	ACE	17	20782.26	7662	5458.262	NA	NA	NA
	ADE	17	20777.22	7662	5453.224	-5.04	0	1
	AE	15	20782.26	7664	5454.262	0.00	2	1
WT	ACE	17	20697.38	7667	5363.382	NA	NA	NA
	ADE	17	20696.19	7667	5362.193	-1.19	0	1
	AE	15	20697.38	7669	5359.382	0.00	2	1
WC	ACE	17	20979.99	7654	5671.987	NA	NA	NA
	ADE	17	20974.49	7654	5666.491	-5.50	0	1
	AE	15	20979.99	7656	5667.987	0	2	1

HDL	ACE	17	20813.13	7723	5367.129	NA	NA	NA
	ADE	17	20813.46	7723	5367.459	0.33	0	0
	AE	15	20813.57	7725	5363.575	0.45	2	0.80
ApoA1	ACE	17	20986.29	7721	5544.293	NA	NA	NA
	ADE	17	20988.84	7721	5546.838	2.55	0	0
	AE	15	20988.84	7723	5542.838	2.55	2	0.28
IgA	ACE	17	21088.02	7674	5740.018	NA	NA	NA
	ADE	17	21098.33	7674	5750.325	10.31	0	0
	AE	15	21098.64	7676	5746.638	10.62	2	0.00
Height	ACE	17	19551.80	7668	4215.802	NA	NA	NA
	ADE	17	19562.34	7668	4226.342	10.54	0	0
	AE	15	19562.34	7670	4222.342	10.54	2	0.01

^a The model in bold is the best fitted model according to Akaike information criterion;

^b EP: number of estimated parameters;

^c minus 2LL: minus 2 log likelihood;

^d df: degree of freedom;

^e AIC: Akaike information criterion;

^f diff LL: difference of log likelihood;

^g diff df: difference of df;

^h P: P value.

Table S9. Distributions of the contact frequency and separation age by zygosity and sex

	MZ			SSDZ			OSDZ
	All	Male	Female	All	Male	Female	
Contact frequency							
n_{pair}	1066	549	517	1424	596	828	1325
Mean	3.03	3.04	3.03	2.71	2.64	2.76	2.45
Standard Deviation	0.82	0.82	0.81	0.82	0.81	0.82	0.69
Separation age							
n_{pair}	1027	518	509	1393	579	814	1302
Mean	19.80	20.29	19.30	18.55	19.30	18.02	18.25
Standard Deviation	3.43	3.59	3.20	3.59	3.76	3.37	3.75

Contact frequency was defined by the replies to questions about how often the participants usually met with their co-twin, and it was divided into four levels: 1-less than once a year; 2-on a yearly basis; 3-on a monthly basis; or 4-on a weekly basis; the measure here is used as a continuous variable. Contact frequency and separation age are significantly different between monozygotic (MZ) and same-sex dizygotic (SSDZ) twins ($P < 0.001$), MZ and opposite-sex dizygotic (OSDZ) twins ($P < 0.001$), SSDZ and OSDZ ($P < 0.05$); Contact frequency is not significantly different between males and females in MZ ($P = 0.94$), but significantly in SSDZ ($P = 0.007$); separation ages are significantly different between males and females both in MZ and in SSDZ ($P < 0.001$); Contact frequency and separation age are both significantly different between males of MZ and SSDZ ($P < 0.001$), and females of MZ and SSDZ ($P < 0.001$).

Table S10. Intra-pair correlation stratified by level of shared environment in monozygotic twins

Trait	1) Contact frequency ^a				2) Separation age ^b			
	r _{Low}	n _{pair}	r _{High}	n _{pair}	r _{Low}	n _{pair}	r _{High}	n _{pair}
Total cholesterol	0.461	619	0.482	447	0.497	530	0.440	497
High density lipoprotein	0.657	619	0.690	447	0.658	530	0.690	497
Low density lipoprotein	0.442	610	0.479	434	0.484	523	0.430	484
Apolipoprotein A1	0.625	618	0.677	447	0.647	529	0.663	497
Apolipoprotein B	0.504	618	0.542	447	0.521	529	0.521	497
Triglyceride	0.547	619	0.575	447	0.484	530	0.613	497
C-reactive protein	0.384	619	0.471	446	0.458	529	0.389	497
Glucose	0.512	619	0.501	447	0.487	530	0.516	497
Glycosylated hemoglobin A1c	0.644	618	0.750	447	0.657	529	0.737	497
Hemoglobin	0.543	616	0.539	447	0.537	528	0.559	496
Cystatin C	0.530	600	0.635	429	0.546	514	0.596	479
Creatinine	0.541	600	0.630	429	0.567	514	0.606	479
Glomerular filtration rate	0.533	600	0.623	429	0.544	514	0.588	479
Immunoglobulin A	0.447	614	0.402	444	0.474	529	0.395	491
Body mass index	0.641	614	0.727	447	0.647	527	0.708	495
Weight	0.676	617	0.794	447	0.700	529	0.753	496
Waist circumference	0.602	619	0.689	444	0.620	528	0.645	496
Height	0.846	616	0.882	447	0.820	528	0.906	496

^a Low contact frequency was defined as ≤ 3 (on the monthly basis), high contact frequency was defined as > 3 ; contact frequency in low group (mean=2.43, standard deviation=0.48) was significantly lower than high group (mean=3.88, standard deviation=0.22), $P < 0.0001$; r is the intra-pair correlation coefficient, all of them were significant ($P < 0.0001$);

^b Low separation age was defined as ≤ 19.5 years old (median age), while high separation age was defined as > 19.5 years old; separation age in low group (mean=17.46, standard deviation=2.23) was significantly younger than high group (mean=22.30, standard deviation=2.63), $P < 0.0001$; r is the intra-pair correlation coefficient, all of them were significant ($P < 0.0001$).