Supplemental Methods

MZ twins are derived from a single fertilized egg cell (zygote) and therefore share (nearly) 100% of their segregating genes. DZ twins (who are derived from two zygotes) and non-twin siblings share on average 50% of their segregating genes. Parents share 50% of their genetic material with their children. Common environmental influences may be shared by siblings ("sibling-shared environmental effects") or by individuals who share a household ("shared household effects"). In our study, the parents of twins who live together may share household effects, but household effects are not likely to contribute largely to the similarity of siblings and of parents with their offspring because the offspring in our study are adults, thus most live on their own. All family members share 0% of V_E by definition. Assuming that the variation of a trait is caused by A, D, C (sibling-shared) and E ($V_P = V_A + V_D + V_C + V_E$), the phenotypic covariance of family members can be expressed as a function of V_A, V_D, V_C and V_E (i.e. covariance MZ twins= $V_A + V_D + V_C$, covariance DZ twins and sibs=1/2 V_A + 1/4 V_D+ V_C, and covariance parent-offspring=1/2 V_A). Correlations, which represent a standardized measure of the shared variance between variables, are also frequently used to summarize the similarity of family members. Following from the equations for the covariances explained above, the phenotypic correlations among relatives can be written as:

Phenotypic correlation MZ twins = $h^2 + d^2 + c^2$

Phenotypic correlation Parent-offspring = ½ h^2

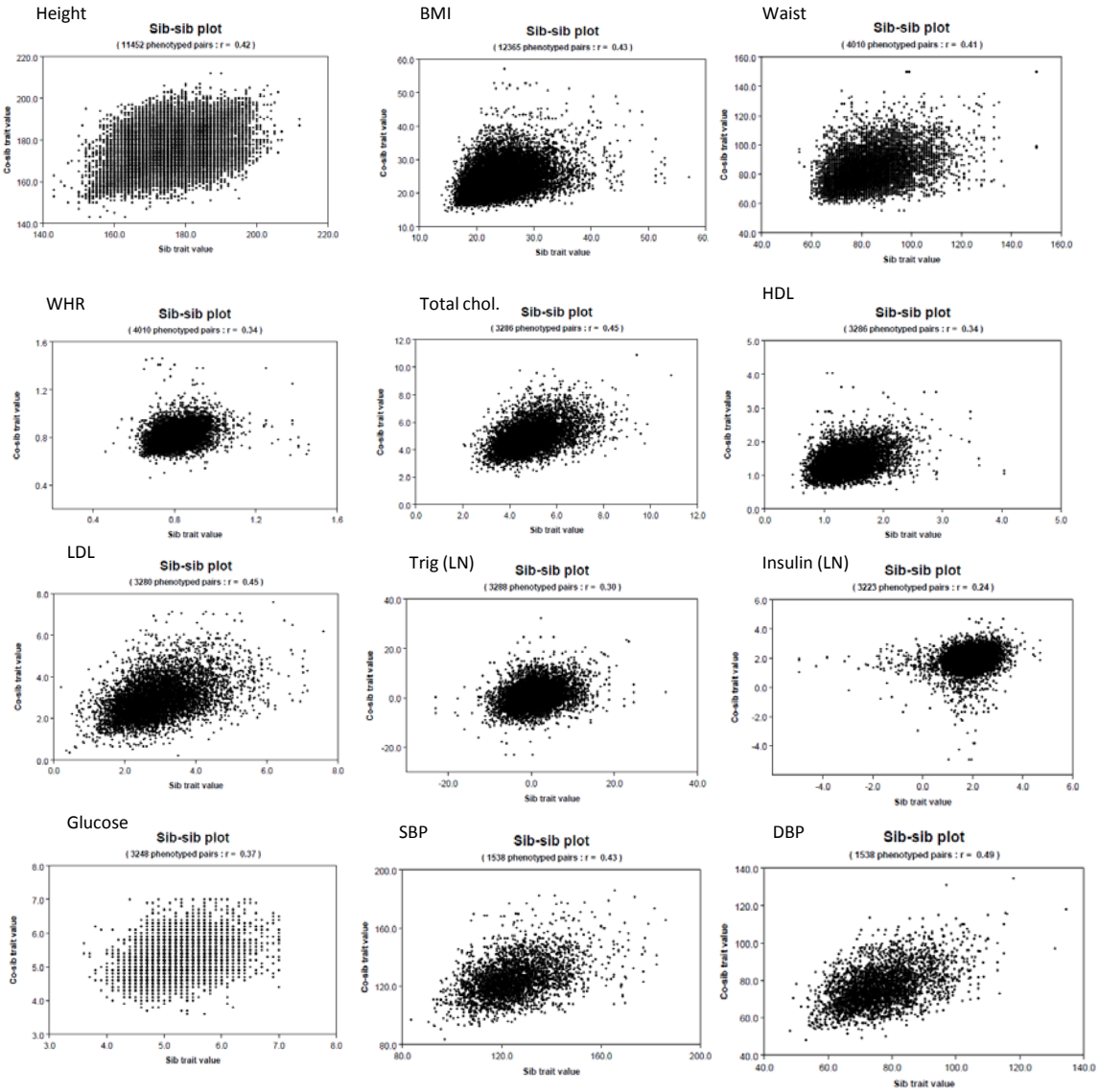
Phenotypic correlation DZ twin / siblings = ½ h^2 + ¼ d^2 + c^2

Where h^2= proportion of variance due to additive genetic effects (V_A / V_P), d^2= proportion of variance due to non-additive genetic effects (V_D/ V_P), c^2 =proportion of variance due to sibling shared environment (V_C / V_P).

Prior exploratory analyses of the twin family data in Mx indicated the absence of sibling-shared environmental effects for the vast majority of traits in our study; these effects were therefore not included in further analyses. Sex or age differences in V_A , $V_{D.}$,V_C or V_E are indicated by differences in the pattern of phenotypic correlations in male versus female relatives ("quantitative sex difference") or young versus old relatives ("quantitative age difference"). A smaller correlation in opposite-sex relatives compared to same-sex relatives indicates that different factors (e.g. different genes or different environmental factors) contribute to variation in males and females ("qualitative sex difference"). Similarly, if the phenotypic correlation decreases with increasing age difference between relatives, this is an indication that different factors may play a role at different ages ("qualitative age difference").

Supplemental Figures

Supplemental Figure 1: Sib-pair resemblance for metabolic syndrome traits. The figure shows scatterplots of trait values for all sib-sib relations in the sample (including DZ twins).



Supplemental Tables

Supplemental Table 1: Numbers and age of twins and family members

	Descriptives total sample			*Descriptives of twins by zygosity*			
	N	Age Men (SD)	Age women (SD)		N twins in pairs	Total N twins	Age (SD)
BMI							
Twins	12877 (*M*: 4666, *F:*8211)	28.79 (11.93)	30.71 (12.84)	MZM	1660	1901	29.83 (12.51)
Sisters	2065 (*first*: 1759, *second*: 306)		35.32 (12.87)	DZM	1088	1326	28.04 (11.87)
Brothers	1550 (*first*: 1333, *second*: 217)	33.86 (12.88)		MZF	3656	4060	32.60 (13.68)
Parents	10529 (*Mo*: 6036; *Fa*:4493)	54.81 (8.37)	52.24 (8.86)	DZF	2020	2345	29.90 (12.09)
Total	27021 (*M:* 10709, *F:* 16312)	40.44 (16.35)	39.26 (15.30)	DOS	2462	3245	27.77 (11.02)
Waist, WHR							
Twins	4305 (*M*: 1496 , *F:* 2809)	33.95 (11.62)	35.45 (11.58)	MZM	568	684	35.17 (12.66)
Sisters	869 (*first*: 725, *second*: 144)		41.35 (12.88)	DZM	286	395	32.99 (11.20)
Brothers	575 (*first:* 500, *second*: 75)	40.03 (13.72)		MZF	1278	1514	36.52 (11.92)
Parents	3216 (*Mo*: 2052, *Fa*: 1164)	61.57 (7.34)	55.87 (10.60)	DZF	670	818	34. 89 (11.51)
Total	8965 (*M*: 3235, *F:* 5730)	44.97 (16.58)	43.66 (14.78)	DOS	630	894	32.94 (10.00)
Glucose and insulin							
Twins	3724(*M*: 1262 , *F:* 2462)	33.95 (10.99)	35.84 (11.44)	MZM	398	579	35.07 (11.93)
Sisters	1143 (*first*: 818, *second*: 325)		42.12(10.58)	DZM	206	325	33.29(11.05)
Brothers	470 (*first:* 416 *second*: 54)	39.69 (13.12)		MZF	1018	1366	36.96 (11.80)
Parents	2226 (*Mo*: 1263, *Fa*: 963)	61.88 (7.05)	60.15(7.57)	DZF	526	695	35.12 (11.34)
Total	7563 (*M*: 2697, *F:* 4866)	44.94 (16.38)	43.61 (14.47)	DOS	498	759	33.01 (9.40)
Lipids							
Twins	3721 (*M*: 1273 , *F*: 2448)	33.92 (11.02)	35.56 (11.16)	MZM	394	583	34.87 (11.89)
Sisters	1185 (*first*: 842, *second*: 343)		41.93 (10.47)	DZM	212	329	33.49 (11.32)

Brothers	480 (*first*: 424, *second*: 56))	39.46(12.66)		MZF	1004	1352	36.61 (11.57)
Parents	2083 (*Mo*: 1210, *Fa*: 873)	61.62 (6.98)	60.26 (7.70)	DZF	526	694	32.91 (11.00)
Total	7469 (*M*:2628 , *F*: 4841)	44.15 (16.14)	43.28 (14.39)	DOS	502	763	32.95 (9.23)
Blood pressure							
Twins	2002 (*M*: 765 , *F*: 1237)	32.65 (10.46)	32.83 (10.72)	MZM	388	416	32.53 (9.83)
Sisters	243 (*first*: 213, *second*: 30)		35.23 (11.81)	DZM	196	213	32.38 (11.42)
Brothers	185 (*first*: 166, *second*: 19)	33.85 (12.02)		MZF	704	760	33.24 (10.72)
Parents	362 (*Mo*: 185, *Fa*: 177)	47.68 (6.33)	45.28 (5.70)	DZF	284	324	31.88 (10.66)
Total	2792 (*M*: 1127 , *F*: 1665)	35.21 (11.54)	34.57 (11.15)	DOS	238	289	33.10 (10.78)

M= Male, F=Female, Mo=Mother, Fa=Father, N=Number of subjects

Supplemental Table 2: Twin correlations for metabolic syndrome traits stratified by age and sex.

	Height	BMI	Waist	WHR	TC	HDL	LDL	Trig	Insulin	Glucose	SBP	DBP
Young												
MZ twins												
MZ males	0.91	0.73	0.65	0.48	0.78	0.79	0.74	0.72	0.40	0.54	0.59	0.63
MZ females	0.90	0.72	0.66	0.41	0.70	0.70	0.74	0.57	0.39	0.53	0.57	0.54
DZ twins												
DZ males	0.55	0.58	0.47	0.50	0.43	0.36	0.43	0.32	0.26	0.42	0.48	0.25
DZ females	0.54	0.33	0.20	0.26	0.41	0.38	0.43	0.12	0.09	0.35	0.56	0.49
DZ opposite sex	0.39	0.39	0.40	0.24	0.07	0.14	0.07	0.26	0.34	0.39	0.41	0.40
Older twins												
MZ twins												
MZ males	0.89	0.75	0.76	0.57	0.67	0.58	0.64	0.69	0.56	0.43	0.67	0.69
MZ females	0.88	0.70	0.68	0.51	0.71	0.58	0.71	0.57	0.44	0.50	0.64	0.68
DZ twins												
DZ males	0.42	0.38	0.40	0.36	0.17	0.44	0.11	0.25	0.15	0.20	0.10	0.17
DZ females	0.55	0.32	0.42	0.38	0.47	0.34	0.40	0.30	0.22	0.35	0.50	0.48
DZ opposite sex	0.57	0.19	0.27	0.34	0.47	0.34	0.41	0.21	0.25	0.25	0.22	0.26

Age categories were defined based on the median age of twins (young twins=twins with an age below the median and older twins=twins with an age above the median). The median age of twins was 32 years for all metabolic syndrome variables. For height only, birth year (median=1973) instead of age was used to define categories. TC= Total cholesterol. Trig= Triglycerides.

Supplemental Table 3: Age-specific heritability estimates of metabolic syndrome traits and height.

	Height	BMI	Waist	WHR	TC	HDL	LDL	Trig	Insulin	Glucose	SBP	DBP
Young												
V_P	42.47	11.92	104.68	0.0045	0.81	0.12	0.65	20.53	0.51	0.25	132.68	92.72
a^2	0.84	0.33	0.37	0.29	0.39	0.36	0.42	0.25	0.23	0.58	0.61	0.62
d^2	0.07	0.47	0.38	0.16	0.28	0.27	0.27	0.32	0.25	0.00	0.00	0.00
H^2	0.91	0.79	0.75	0.45	0.67	0.63	0.69	0.57	0.48	0.58	0.61	0.62
SE	0.03	0.04	0.06	0.10	0.06	0.08	0.06	0.06	0.06	0.06	0.13	0.12
Old												
V_P	43.43	16.15	135.02	0.01	1.07	0.15	0.90	22.06	0.50	0.33	211.23	120.78
a^2	0.83	0.34	0.41	0.43	0.40	0.53	0.41	0.34	0.23	0.48	0.61	0.64
d^2	0.07	0.34	0.30	0.13	0.21	0.21	0.19	0.30	0.26	0.00	0.00	0.00
H^2	0.90	0.68	0.70	0.56	0.61	0.74	0.60	0.63	0.49	0.48	0.61	0.64
SE	0.03	0.03	0.05	0.10	0.06	0.07	0.05	0.06	0.07	0.05	0.08	0.10
r_A Young-Old	0.96	1.00	1.00	0.85	1.00	0.90	1.00	1.00	1.00	0.64	0.24	0.56

The estimates were obtained from a model in which V_P, V_A and V_E were allowed to differ between young and old subjects, whereas V_D was constant. Age categories were defined based on the median age of subjects (young=subjects with an age below the median and old=subjects with an age above the median). The median age was 35 years for SBP and DBP, 39 years for BMI, 40 years for HDL, LDL, total cholesterol and triglycerides, and 41 for insulin, glucose, waist and WHR. For height only, birth year (median=1966) instead of age was used to define categories. TC= Total cholesterol. Trig= Triglycerides. SE=Robust standard error of the broad heritability estimate from poly. r_A Young-Old=Correlation between additive genetic effects in young and old subjects.