

“Beyond Twins”

Lindon Eaves,
VIPBG, Richmond
Boulder CO,
March 2012

The Twin Tool-Kit

- Continuous and categorical data
- Twins
- Univariate and Multivariate ACE
- Developmental Change
- Heterogeneity/Moderation
- Definition variables

THIS IS JUST A TOOL KIT TO GET STARTED

This week we have pretty much ignored

- Assortative Mating
- Explicit Specification of the Family Environment (e.g. environmental effects of parental genotype)
- Genotype-environment covariance (e.g. “passive” rGE)
- Causal pathways between measures
- Some aspects of development

The chances are...

...that your real questions don't fit
into this basic framework

BE CREATIVE...

IMAGINE...

If you can write the model...
...you can fit it

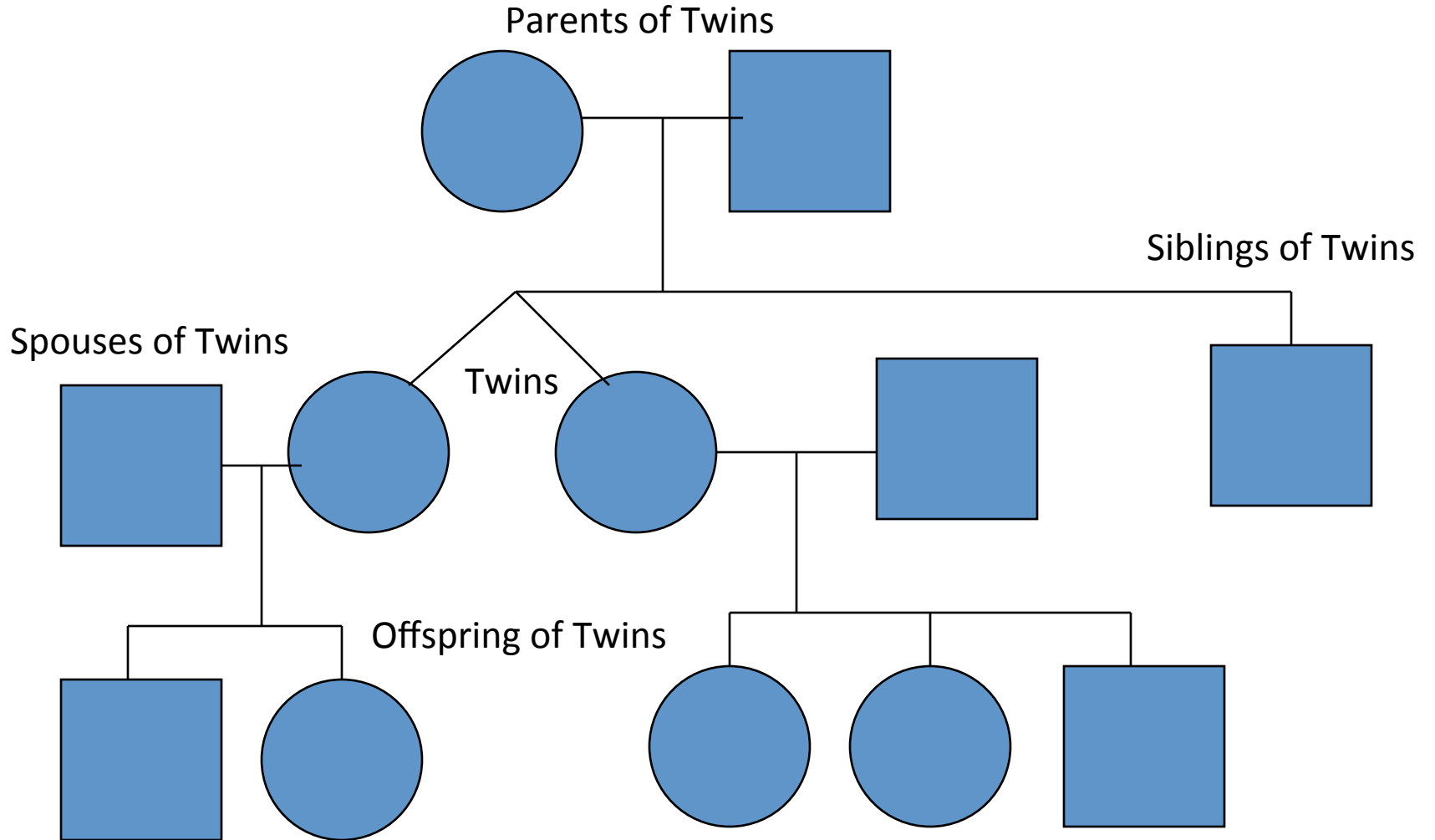
(If you can get the data)

Choose the design and write the model to reflect your own scientific questions

You can combine different elements to answer your question

Here are a few examples but they do not exhaust the possibilities

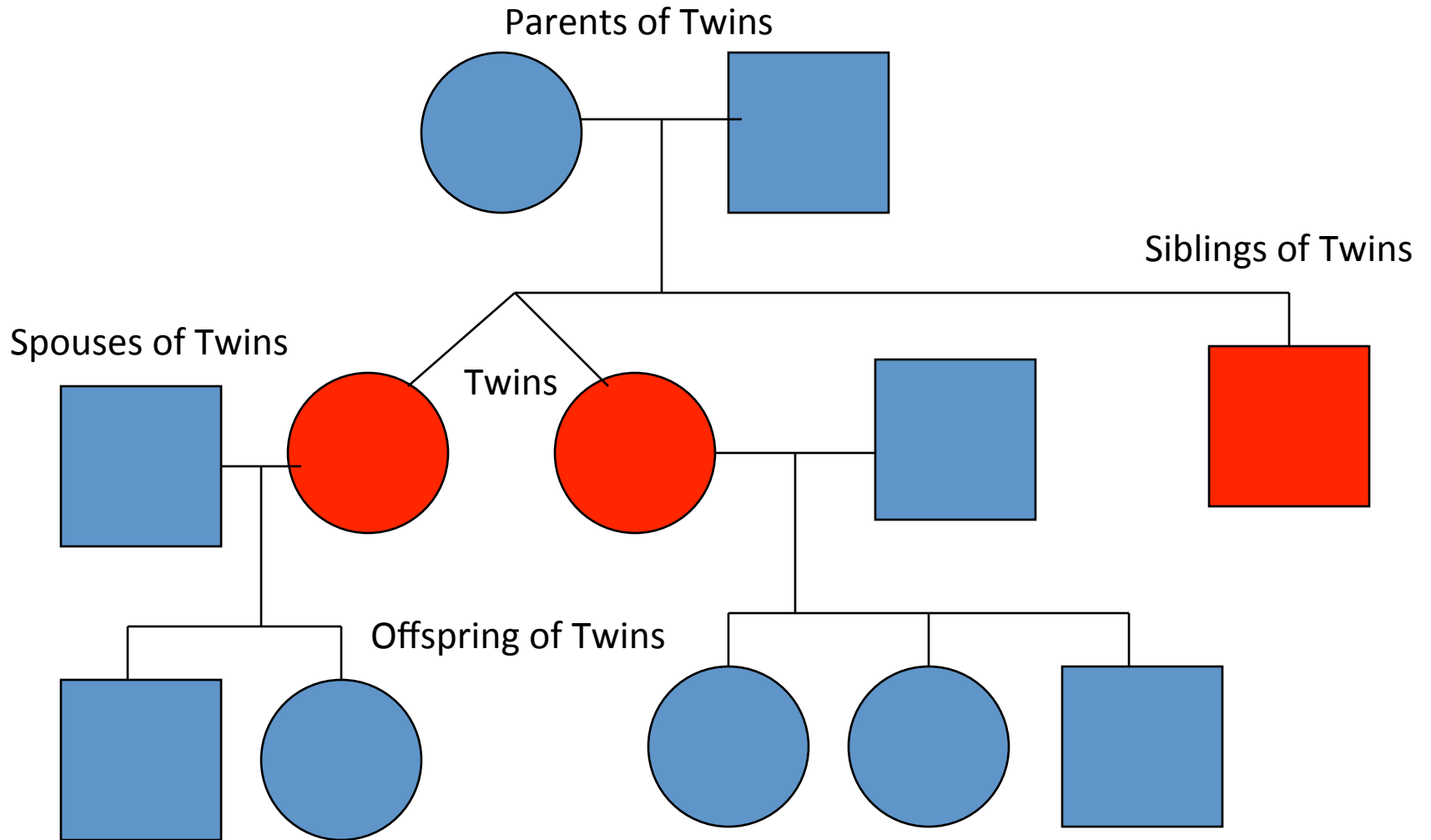
Extended Kinships of Twins



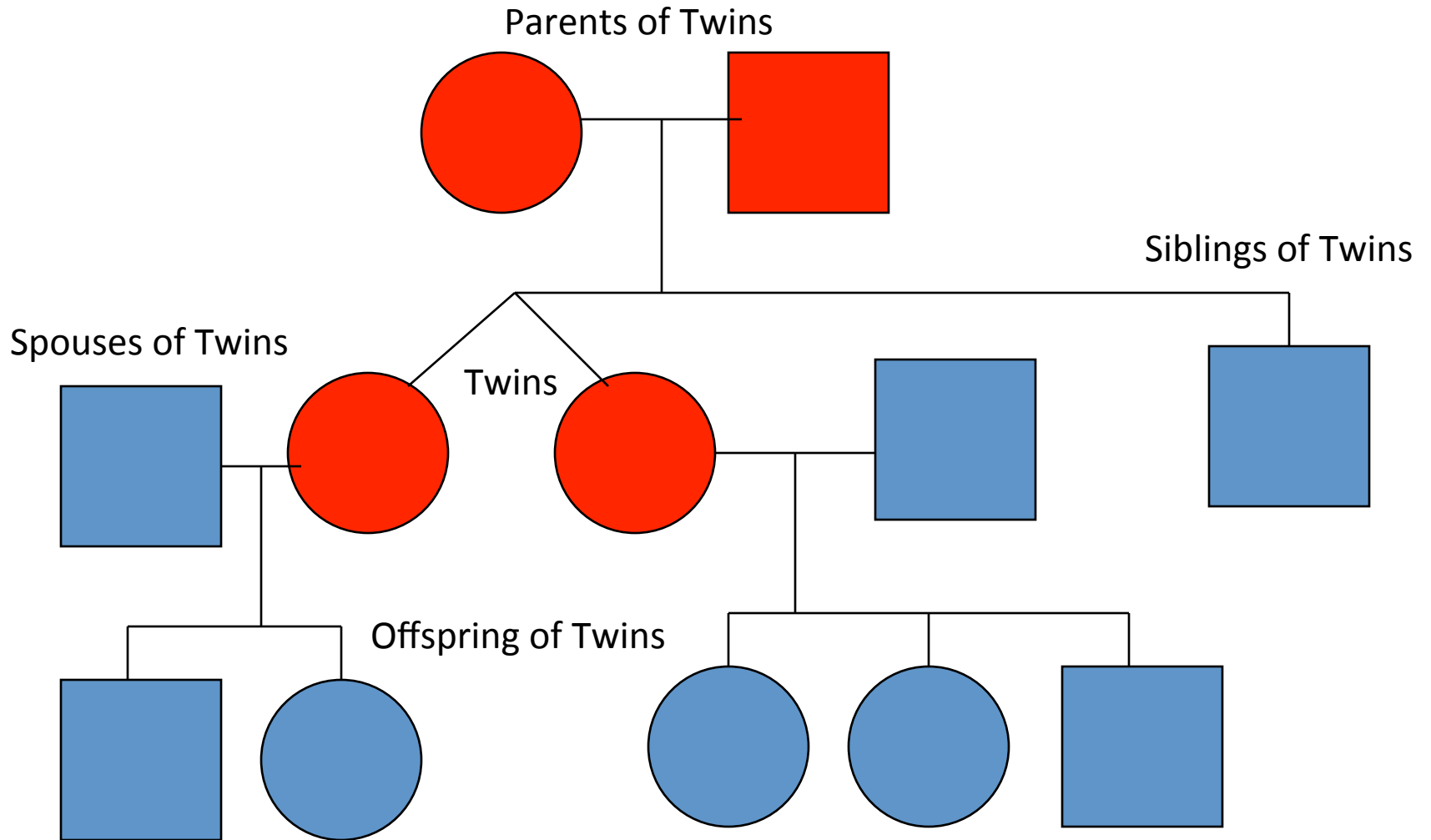
Can Extend Pedigrees by Using Reports by Relatives

**BUT NEED TO BE CAREFUL ABOUT
RATER BIASES**

Twins and Siblings



Twins and Parents (“TAP”)



Transmission of Attitudes Toward Abortion and Gay Rights: Effects of Genes, Social Learning and Mate Selection

Lindon J. Eaves · Peter K. Hatemi

Behav Genet. 2008 May;38(3):247-56.



Table 2 Polychoric correlations for attitudes to abortion and gay rights

Relationship	Correlation		<i>N</i> (pairs)
	Abortion	Gay rights	
Husband–wife	0.632	0.581	5162
Mother–daughter	0.500	0.469	4802
Mother–son	0.373	0.391	3233
Father–daughter	0.428	0.365	3166
Father–son	0.398	0.389	2315
Male siblings	0.420	0.309	1564
Female siblings	0.463	0.453	3701
Unlike-sex siblings	0.405	0.346	4462
Male DZ twins	0.423	0.371	610
Female DZ twins	0.557	0.491	1273
Unlike-sex DZ twins	0.425	0.393	1397
Male MZ twins	0.553	0.574	814
Female MZ twins	0.676	0.599	1982
Retest male	0.801	0.774	1019
Retest female	0.864	0.806	2912

Path model for biological and cultural inheritance

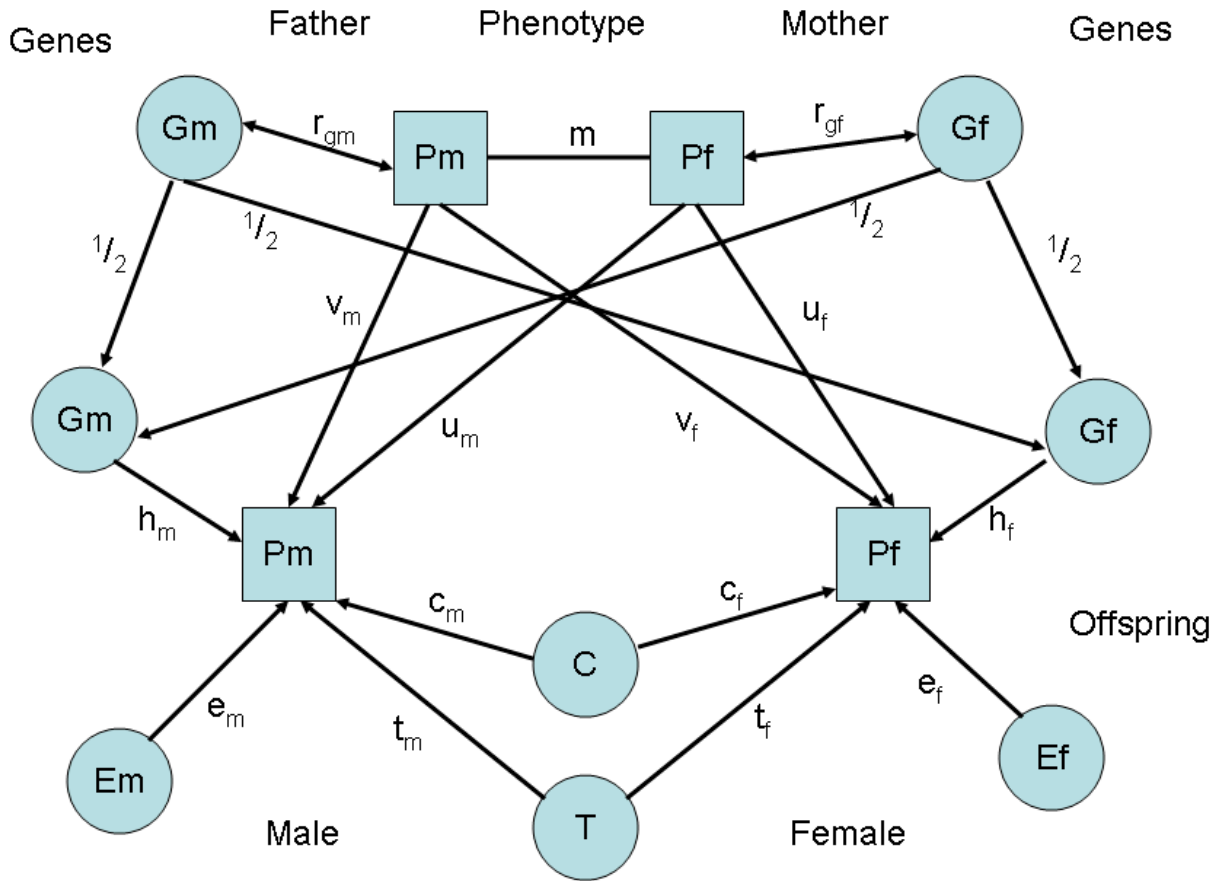


Table 4: Estimates of path coefficients

Parameter	Abortion	Gay Rights	Path
h_m	0.756	0.834	Additive genetic effects to male phenotype
h_f	0.716	0.710	Additive genetic effects to female phenotype
h_s	0	0	Sex-specific genetic effects
c_m	0.370	0.051	Non-transmitted shared environment to male siblings
c_f	0.255	0.341	Non-transmitted shared environment to female siblings
t_m	0.048	0.301	Additional twin shared environment (males)
t_f	0.355	0.203	Additional twin shared environment (females)
u_f	0.184	0.261	Mother-daughter cultural inheritance
u_m	-0.140	-0.033	Mother-son cultural inheritance
v_f	-0.100	-0.203	Father-daughter cultural inheritance
v_m	0.107	-0.040	Father-son cultural inheritance
m	0.761	0.734	Phenotypic correlation between spouses
r_{gm}	0.895	0.881	Reliability (male)
r_{gf}	0.929	0.898	Reliability (female)

Note: “reliabilities” are estimated as the path from “true” score to observed score. Test-retest correlations are the squares of the path coefficients.

Table 5: Proportions of reliable variation explained by sources of variance (full model)

Component of variance	Proportion of reliable variance			
	Abortion		Gay Rights	
	Males	Females	Males	Female
Additive genetic	0.572	0.513	0.696	0.505
Non-shared environment	0.316	0.213	0.288	0.253
Shared sibling environment	0.137	0.065	0.003	0.116
Extra-shared twin environment	0.002	0.112	0.091	0.041
Vertical cultural inheritance	0.008	0.016	0.005	0.031
Genotype-environment covariance	-0.035	0.080	-0.081	0.053
Total shared environment	0.147	0.193	0.099	0.188
Reliability (retest)	0.801	0.863	0.776	0.806

The mediating effect of parental neglect on adolescent and young adult anti-sociality: A longitudinal study of twins and their parents (LTAP).

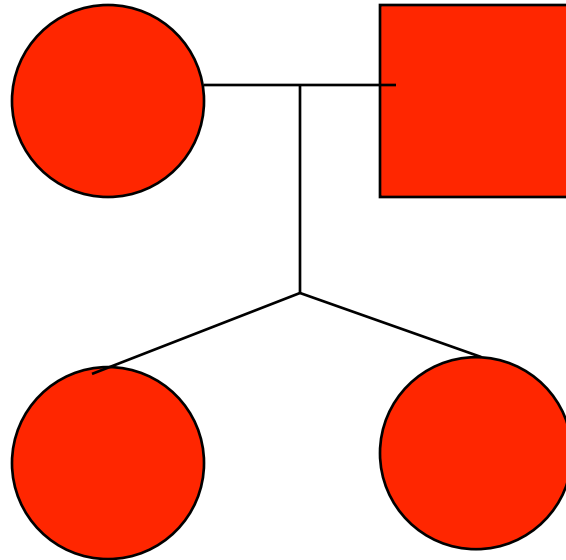
Running title: Childhood adversity and anti-social behavior.

Lindon J Eaves, Elizabeth C Prom, Judy L Silberg

Behav Genet. 2010 Jul;40(4):425-37.

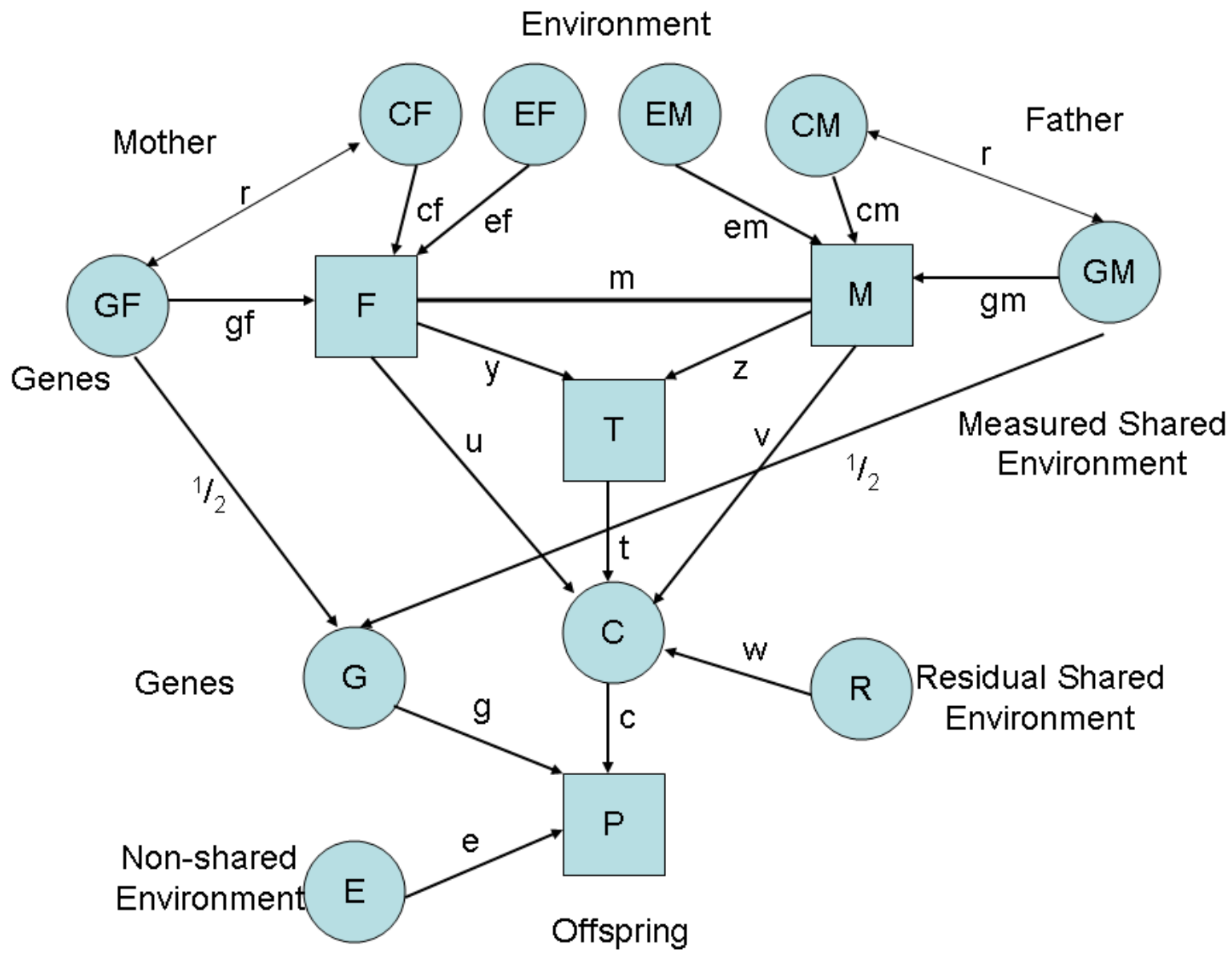
Twins and Parents (“TAP”)

ADULTS



TWINS MEASURED
AS JUVENILES AND ADULTS

Conceptual model for the effects of genes and the family environment on anti-social behavior.



Polychoric correlations between childhood adversity and anti-social behavior of adult and juvenile offspring

Outcome	Statistic		
	N	r	a.s.e.
Adult male	476	0.1506	0.0770
Adult female	513	0.2986	0.0659
Juvenile male	364	0.2276	0.1045
Juvenile female	406	0.3183	0.0824

Polychoric correlations between parental (adult) anti-social behavior (ASP) and childhood adversity

Relationship	Statistic		
	N	R	a.s.e.
Mother-Father ASP	942	0.4006	0.0370
Father ASP-Adversity	489	0.2805	0.0707
Mother ASP.-Adversity	577	0.4121	0.0565

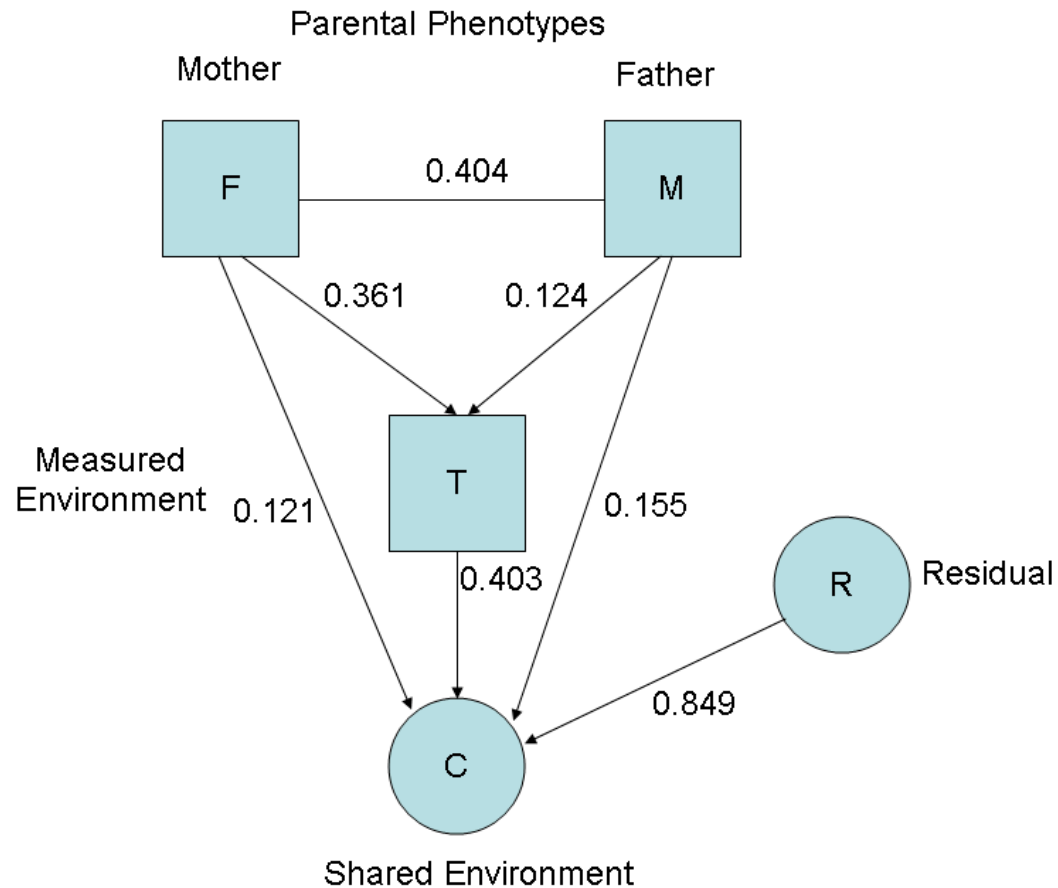
Polychoric correlations between anti-social behavior of (adult) parents adult (ASP) and juvenile (CD) anti-social behavior of their offspring.

Relationship	Statistic		
	N	r	a.s.e.
Mother-adult son	977	0.2368	0.0398
Mother-adult daughter	1158	0.2126	0.0380
Mother-juvenile son	662	0.1475	0.0583
Mother-juvenile daughter	746	0.2454	0.0558
Father-adult son	761	0.1507	0.0471
Father-adult daughter	869	0.2558	0.0442
Father-juvenile son	525	0.2035	0.0671
Father-juvenile daughter	568	0.1450	0.0681

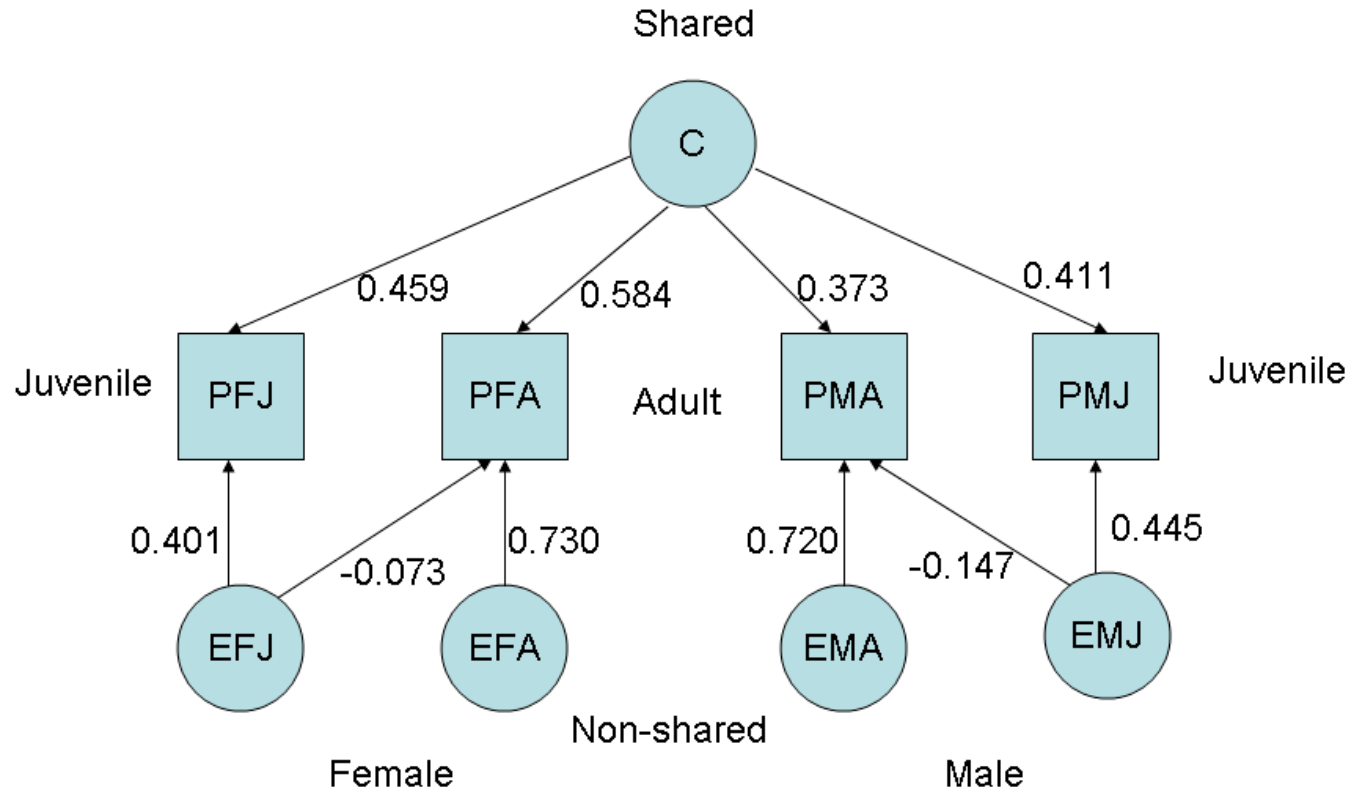
Polychoric correlations for juvenile conduct disorder and adult anti-social personality in YAFU/VTSABD twins.

Relationship		Statistic		
		N	r	a.s.e.
Twins (as adults)	MZm	243	0.5654	0.0615
	MZf	333	0.5093	0.0611
	DZm	137	0.2646	0.1078
	DZf	154	0.4069	0.0960
	DZmf	209	0.3069	0.0875
Twins (as juveniles)	MZm	169	0.8003	0.0572
	MZf	225	0.8023	0.0552
	DZm	101	0.5153	0.1498
	DZf	92	0.4189	0.1565
	DZmf	132	0.0150	0.1809
Twins (adult-juvenile)	MZm	288	0.1751	0.0879
	MZf	394	0.1126	0.0848
	DZm	168	0.1526	0.1284
	DZf	164	0.3596	0.1101
	DZmf	115	0.0595	0.1474
	DZfm	113	0.0647	0.1630
Within subject (adult-juvenile)	Males	569	0.2452	0.0632
	Females	674	0.1103	0.0643

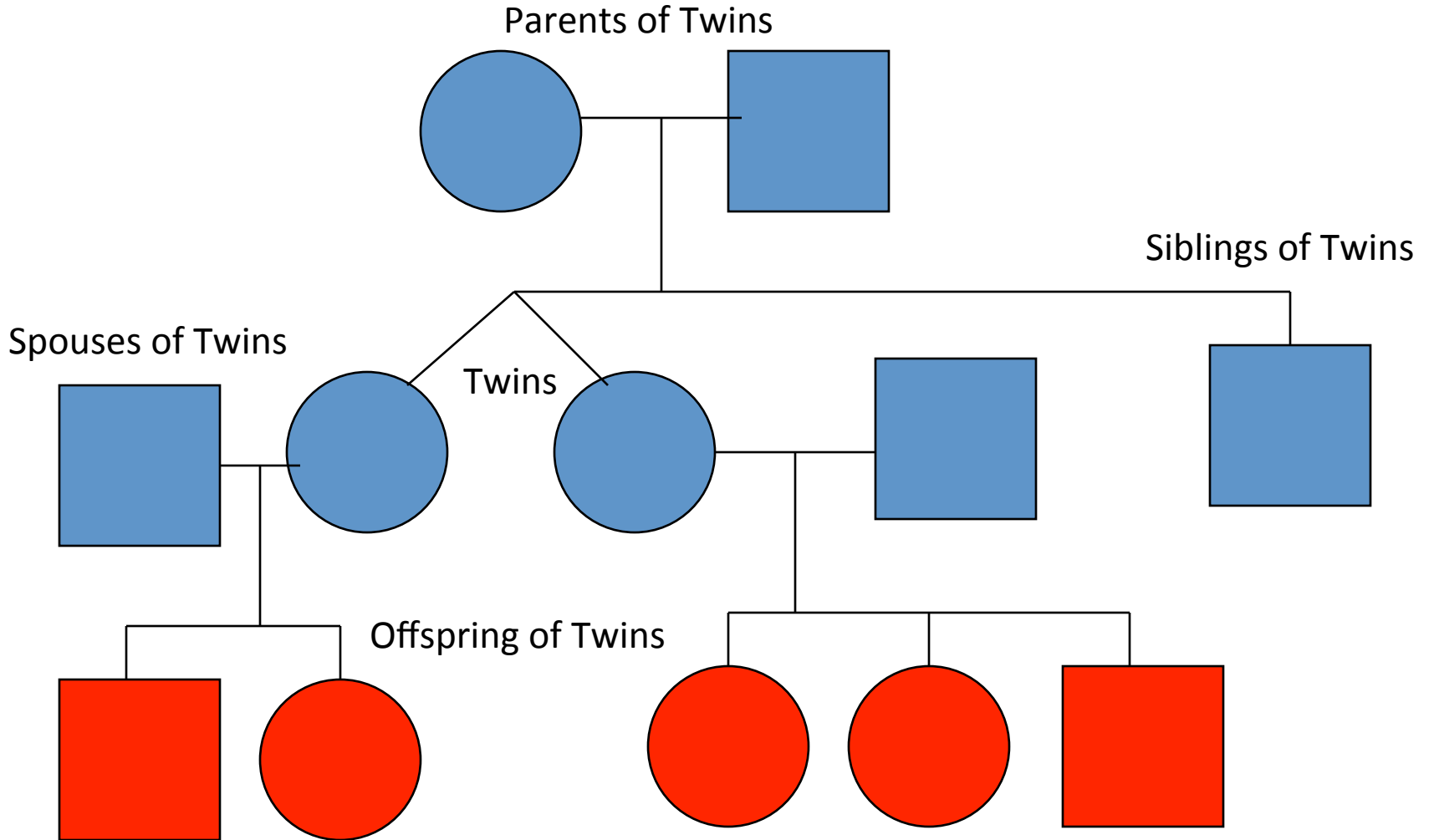
Estimated contributions of parents and residual effects to the shared environment of twin offspring.



Effects of the unique and shared environment on adult and juvenile anti-social behavior and females.



Children of Twins ("COT")



Gestational Age

Racial Differences in Genetic and Environmental Risk to Preterm Birth

Timothy P. York, Jerome F. Strauss,
Michael C. Neale, Lindon J. Eaves

PLoS One. 2010 Aug 25;5(8):e12391.

Table 2. Sample frequencies by parental relationship and race.

Parental relationship	European American		African American	
	N. Families	N. Births	N. Families	N. Births
Sibship	284,446	575,709	66,983	119,791
Maternal half-sibship	6,736	12,269	2,431	4,515
Paternal half-sibship	5,419	9,800	2,839	5,292
MZ male twin	595	1,092	69	99
MZ female twin	618	1,212	98	144
DZ male twin	393	700	52	77
DZ female twin	368	696	72	119
DZ male-female twin	936	1,614	139	210
<i>Total</i>	299,511	603,092	72,683	130,247

Table 1. Expected covariance of gestational age expressed as variance components between pregnancy outcomes as a function of relationship between offspring.

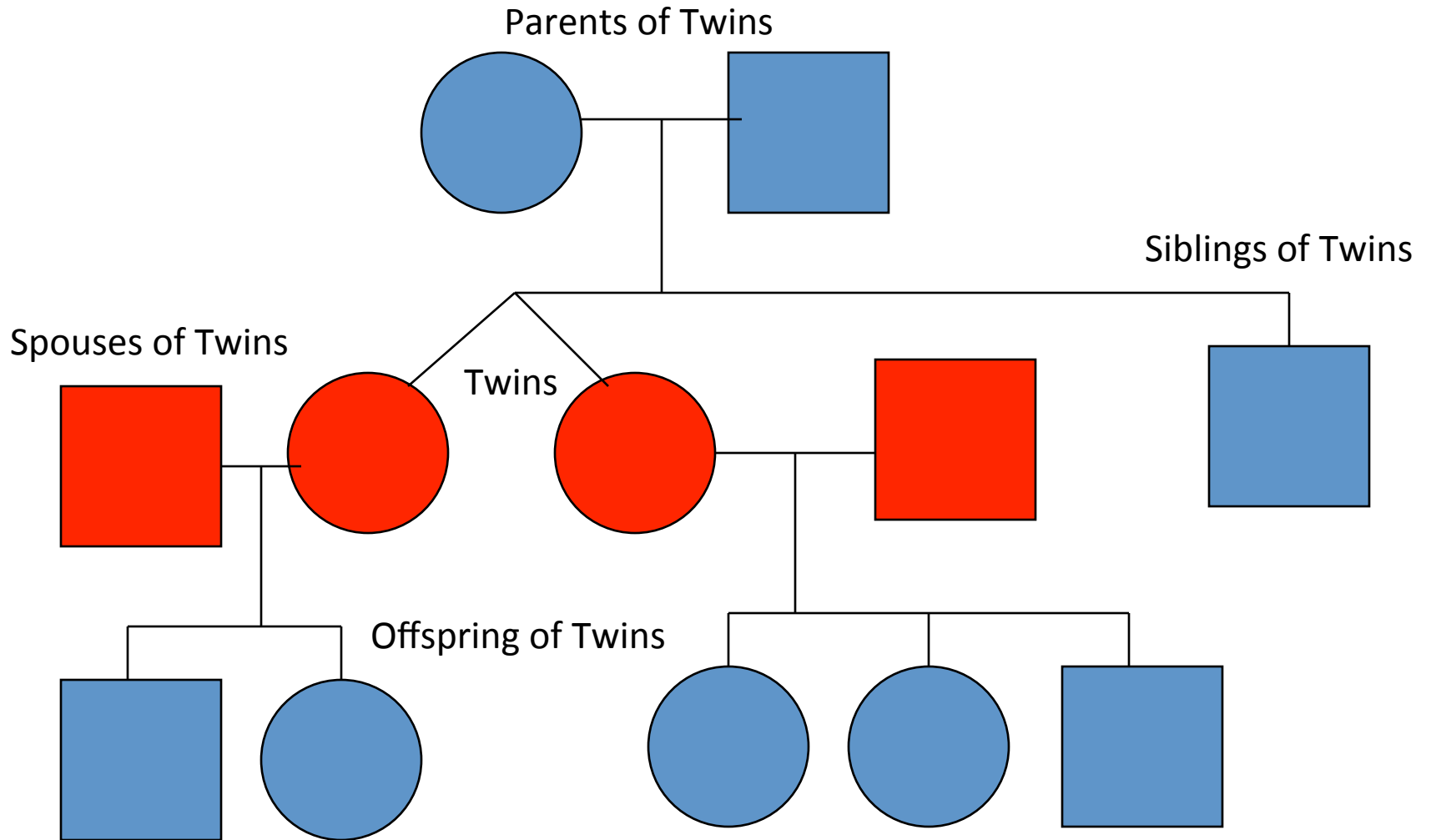
Parental relationship	Fetal relationship	Expected covariance
MZ female twins	Half-sibling	$\frac{1}{4} f^2 + m^2$
DZ female twins	Cousin	$\frac{1}{8} f^2 + \frac{1}{2} m^2$
MZ male twins	Half-sibling	$\frac{1}{4} f^2$
DZ male twins	Cousin	$\frac{1}{8} f^2$
DZ male-female twins	Cousin	$\frac{1}{8} f^2$
Sibship	Sibling	$\frac{1}{2} f^2 + m^2 + c^2$
Maternal half-sibship	Half-sibling	$\frac{1}{4} f^2 + m^2 + hc^2$
Paternal half-sibship	Half-sibling	$\frac{1}{4} f^2 + hc^2$

f^2 =fetal genetic, m^2 =maternal genetic, c^2 =shared familial environment
 h = parameter to allow for differences in half-sibling versus full-sibling shared environment (“fudge factor”)

Table 4. Estimated variance components from model 2 with empirically derived 95% bootstrap confidence intervals adjusted for covariates (birth order, maternal age, fetal sex, source of care, smoking, maternal education).

Source	Full Genetic Model (Model 2)			Reduced Genetic Model (Model 8)		
	Estimate	95% CI	Percentage	Estimate	95% CI	Percentage
<i>African American</i>						
Fetal genetic	0.264	(0.0, 2.302)	3.7	-	-	-
Maternal genetic	0.976	(0.274, 1.357)	13.8	1.040	(0.531, 1.445)	14.7
Shared environment	1.215	(0.499, 1.666)	17.1	1.281	(0.872, 1.781)	18.0
Unique environment	4.642	(3.559, 4.899)	65.4	4.777	(4.625, 4.927)	67.3
<i>European American</i>						
Fetal genetic	1.325	(0.640, 1.927)	35.2	1.325	(0.695, 1.964)	35.2
Maternal genetic	0.503	(0.263, 0.767)	13.4	0.503	(0.235, 0.758)	13.4
Shared environment	0.263	(0.006, 0.537)	7.0	0.264	(0.027, 0.537)	7.0
Unique environment	1.673	(1.355, 2.024)	44.4	1.674	(1.355, 1.990)	44.5

Spouses of Twins (“SPOT”)



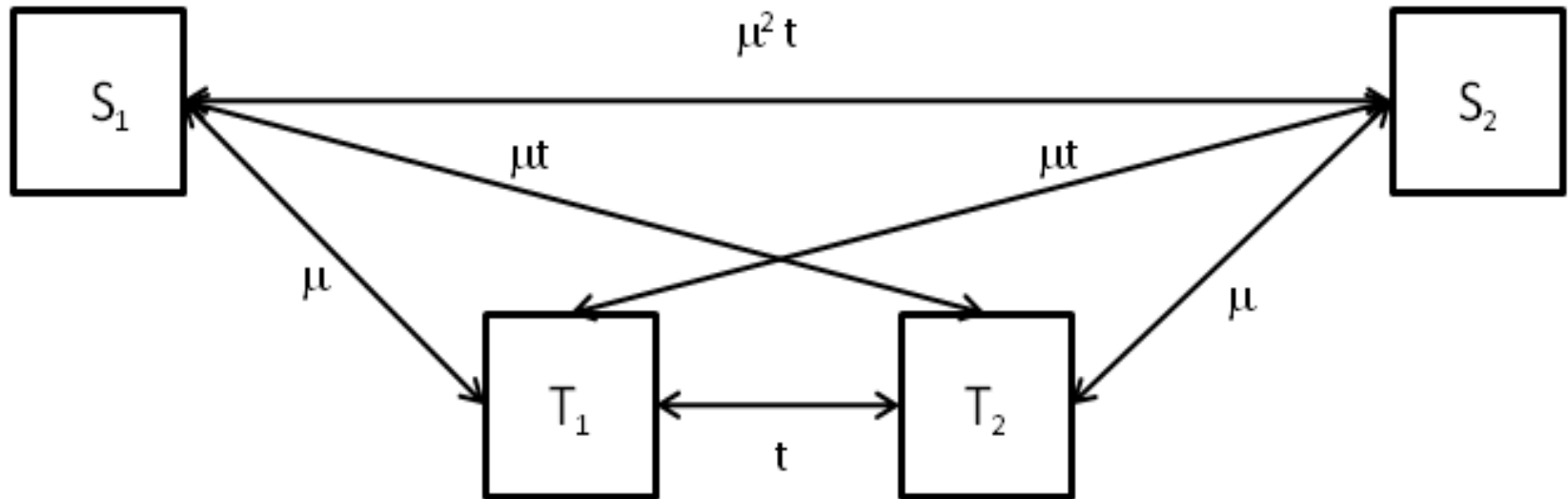
Modeling the Cultural and Biological Inheritance of Social and Political Behavior in Twins and Nuclear Families

**Lindon J. Eaves, Peter K. Hatemi,
Andrew C. Heath, Nicholas G. Martin**

***In P.Hatemi and R.McDermott (2011) "Man is by Nature a Political
Animal", Chicago, IL: University of Chicago Press.***

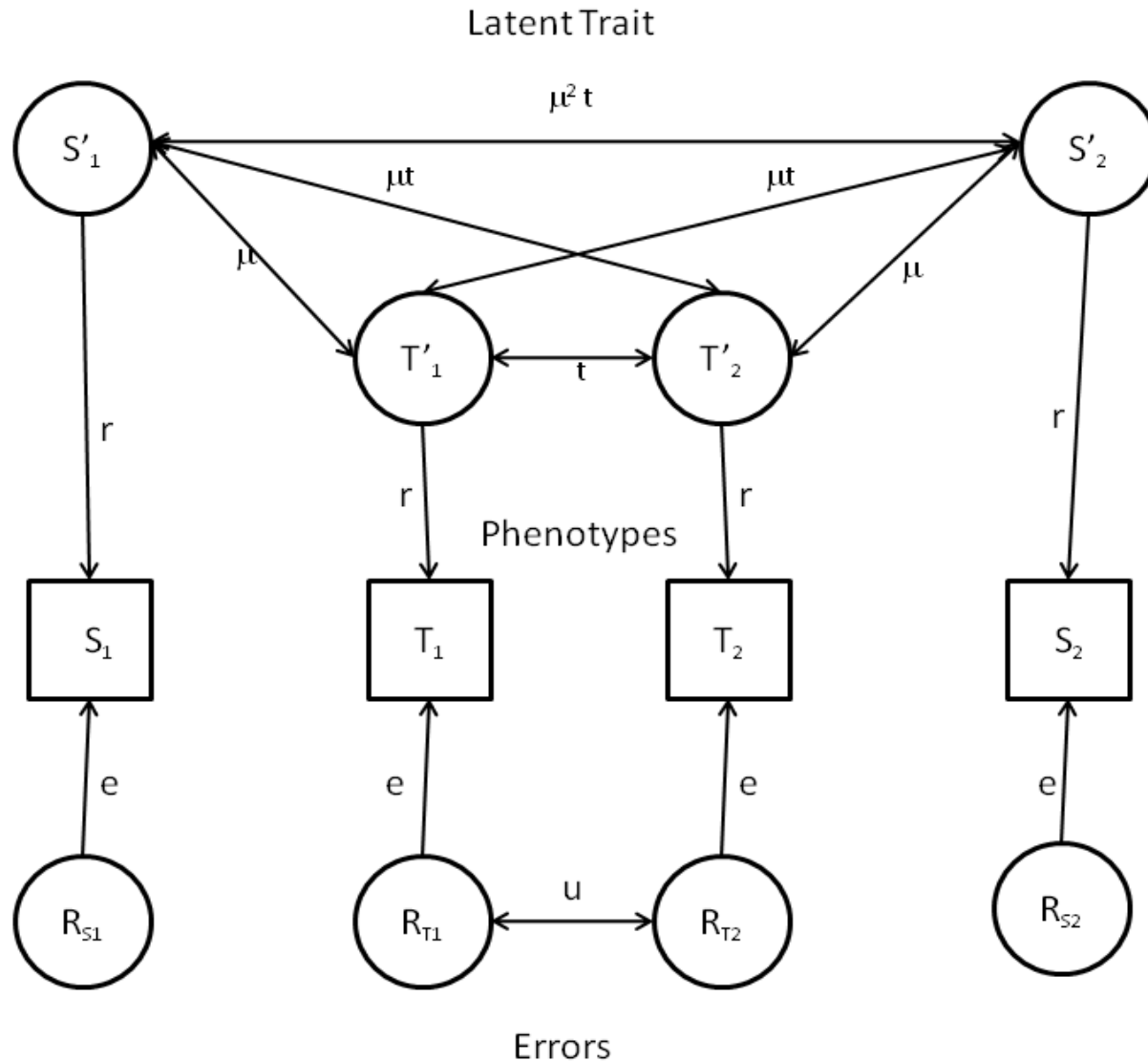
Phenotypic Assortment

Spouses of Twins

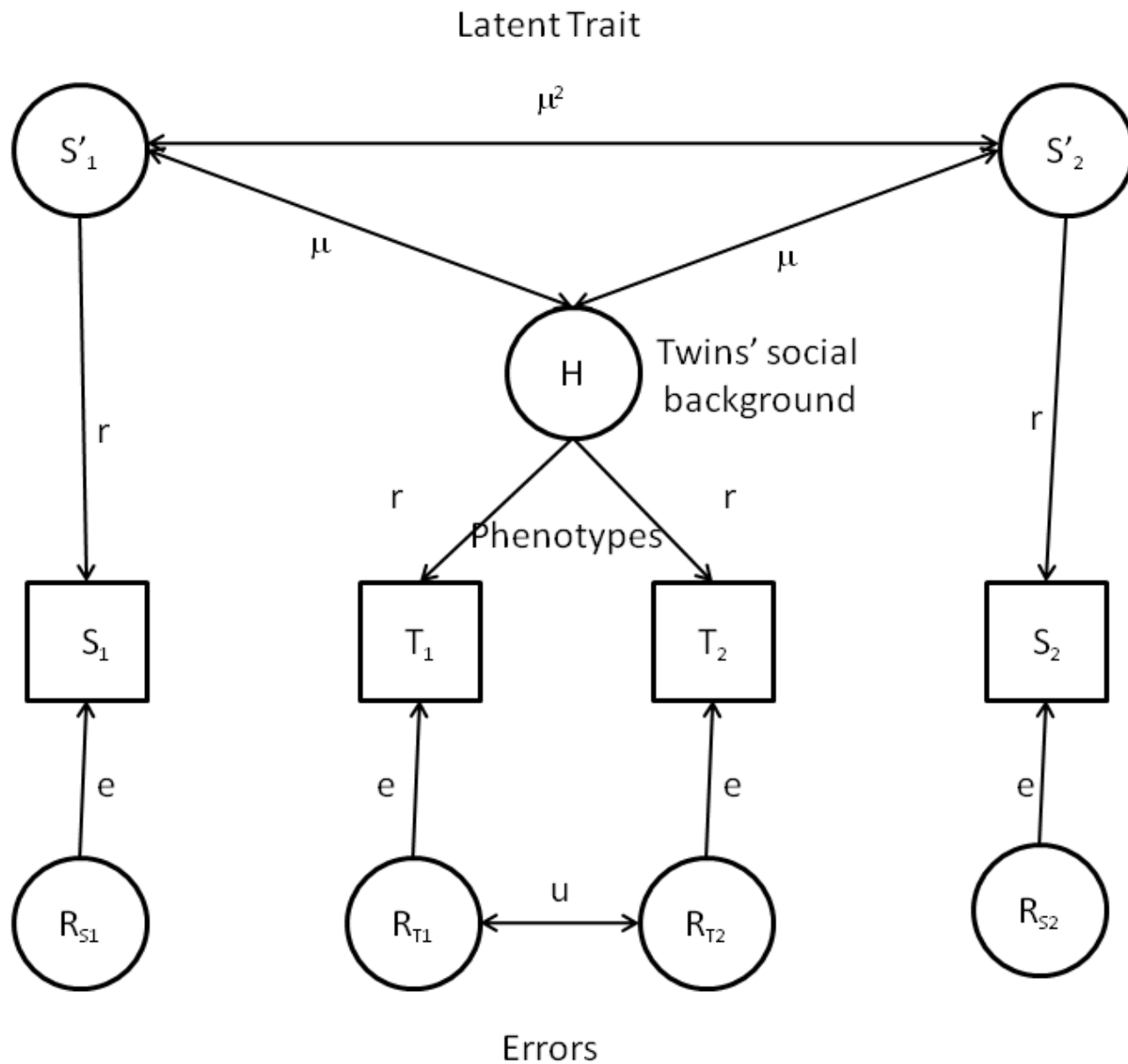


Twins

Latent Variable Assortment (Phenotype subject to error)



“Social Homogamy”



Spousal Interaction

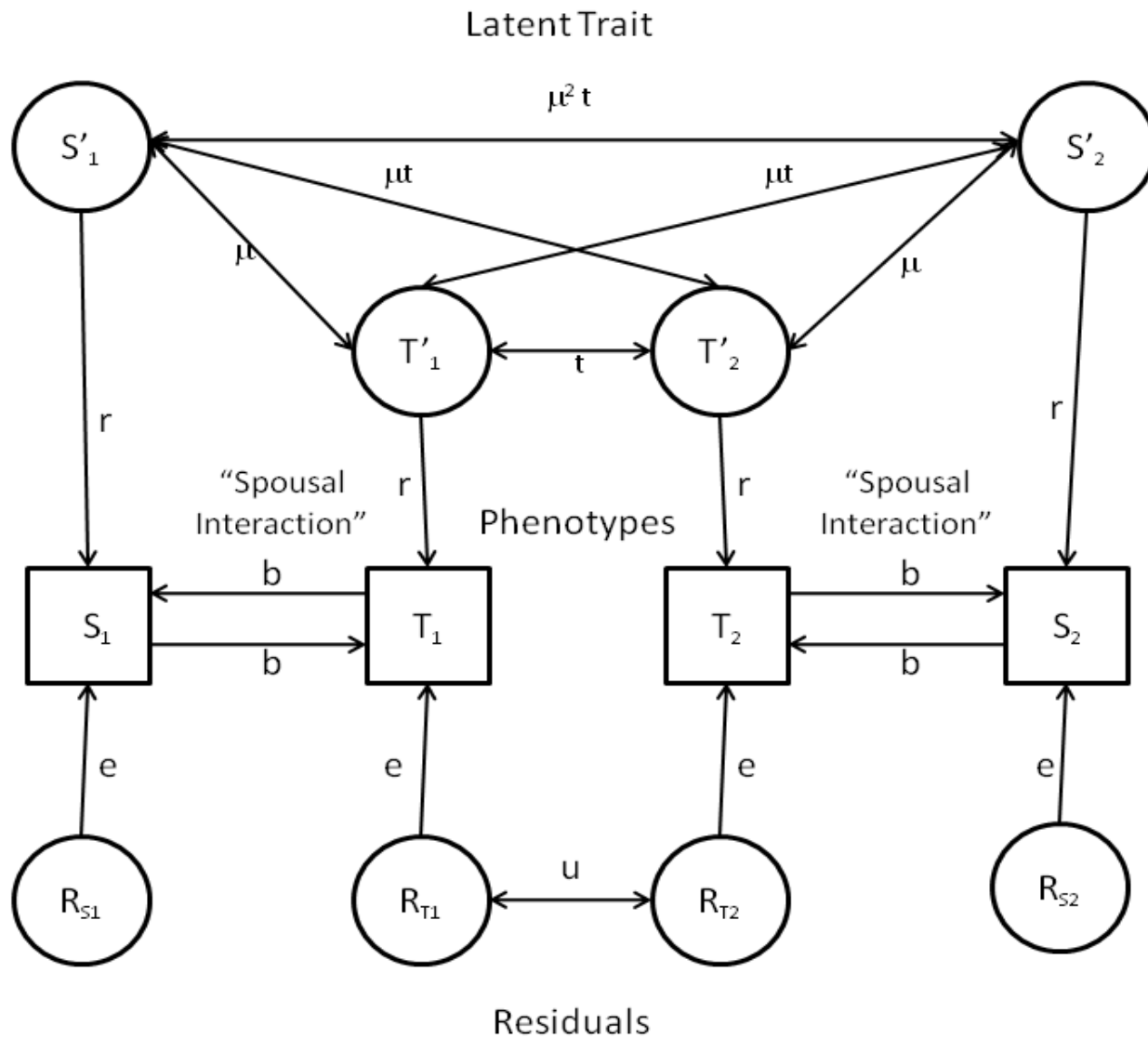


Table 19: Goodness-of-fit statistics (weighted residual sums of squares, S^2) for selected models for assortative mating in the US and Australia

Model		Random mating	Phenotypic assortment (P)	P+Error	Spousal Interaction	Social Homogamy
d.f.		16	15	13	14	11
Variable	Sample	S^2	S^2	S^2	S^2	S^2
Stature	US	449.179	31.363	24.423 ¹	78.930	28.786
	AU	239.827	12.947	11.817 ¹	31.694	25.353
Conservatism	US	2535.373	14.845	12.143	118.266	328.491
	AU	2041.407	31.627	29.669	113.276	239.123
Neuroticism	US	63.371	17.811	See note ²	20.226	19.458
	AU	28.337	17.444	See note ²	15.583	22.807
Church attendance	US	3375.872	15.187	12.841	103.042	611.006
	AU	3019.544	22.140	21.548 ¹	76.574	403.950
Political affiliation	US	2213.625	22.254	18.500	87.889	429.819
	AU	2337.500	34.183	32.537	70.696	322.685
Educational attainment	US	2477.957	46.210	28.207	243.100	57.774
	AU	1430.440	44.146	18.624	160.747	82.086

Notes:

¹ Estimated regression of male outcome on latent trait on upper bound (1.000).

² This model is poorly identified for Neuroticism because the correlation between mates is close to zero. Stable parameter estimates are not available.

Published in final edited form as:

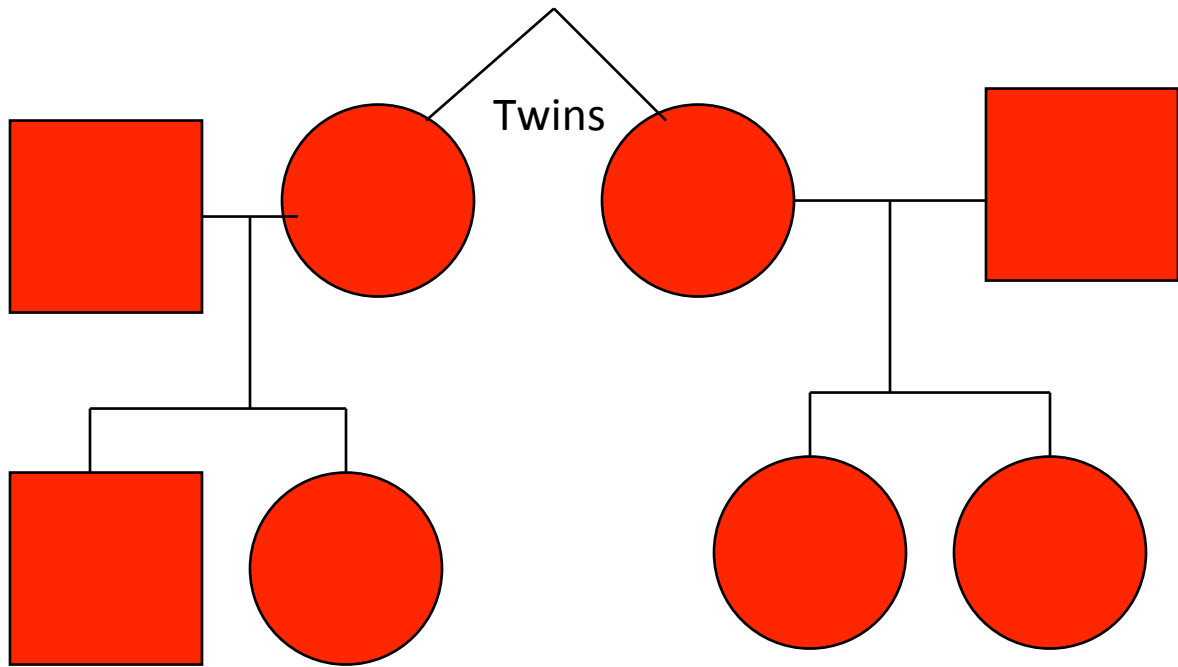
J Child Psychol Psychiatry. 2010 June 1; 51(6): 734–744. doi:10.1111/j.1469-7610.2010.02205.x.

Genetic and environmental influences on the transmission of parental depression to children's depression and conduct disturbance: An extended Children of Twins study

Judy L. Silberg¹, Hermine Maes¹, and Lindon J. Eaves¹

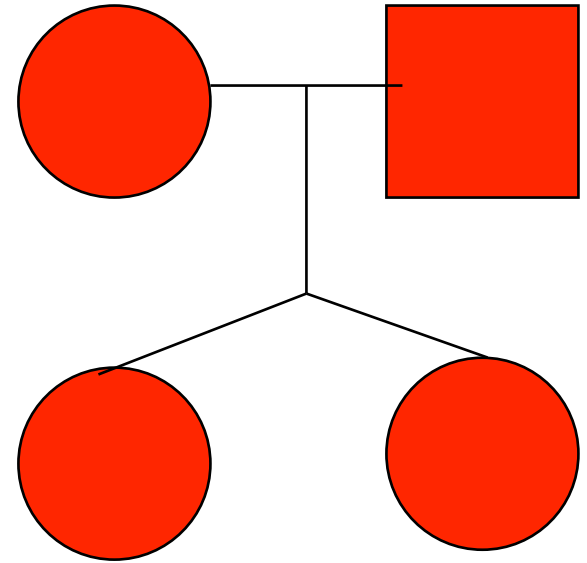
¹ Virginia Institute for Psychiatric and Behavioral Genetics, Department of Human and Molecular Genetics, Virginia Commonwealth University, Richmond, VA USA

E-COT ADULTS



Offspring of Twins

Parents of Twins



Twins

JUVENILES

Twin, parent - child, avuncular – offspring, and cousin correlations for MZ and DZ twins.

Twin correlations	Depression**	Conduct Disturbance***
MZ adult ¹	.32 (n=498)	
DZ adult ¹	.12 (n=545)	
MZ child ²	.34 (n=692)	.73 (n=684)
DZ child ²	.17 (n=645)	.34 (n=627)
Adult - Child correlations ³		
MZ parent	.18 (n=753)	.21 (n=1347)
DZ parent	.20 (n=845)	.23 (n=1508)
MZ avuncular	.07 (n=661)	.11 (n=1141)
DZ avuncular	.01 (n=654)	.06 (n=1129)
Cousin Correlations		
MZ twin pair families	.01 (n=261)	.15 (n=526)
DZ twin pair families	.02 (n=185)	.15 (n=441)

¹Adult twin correlations - Children of Twins Study (COT)

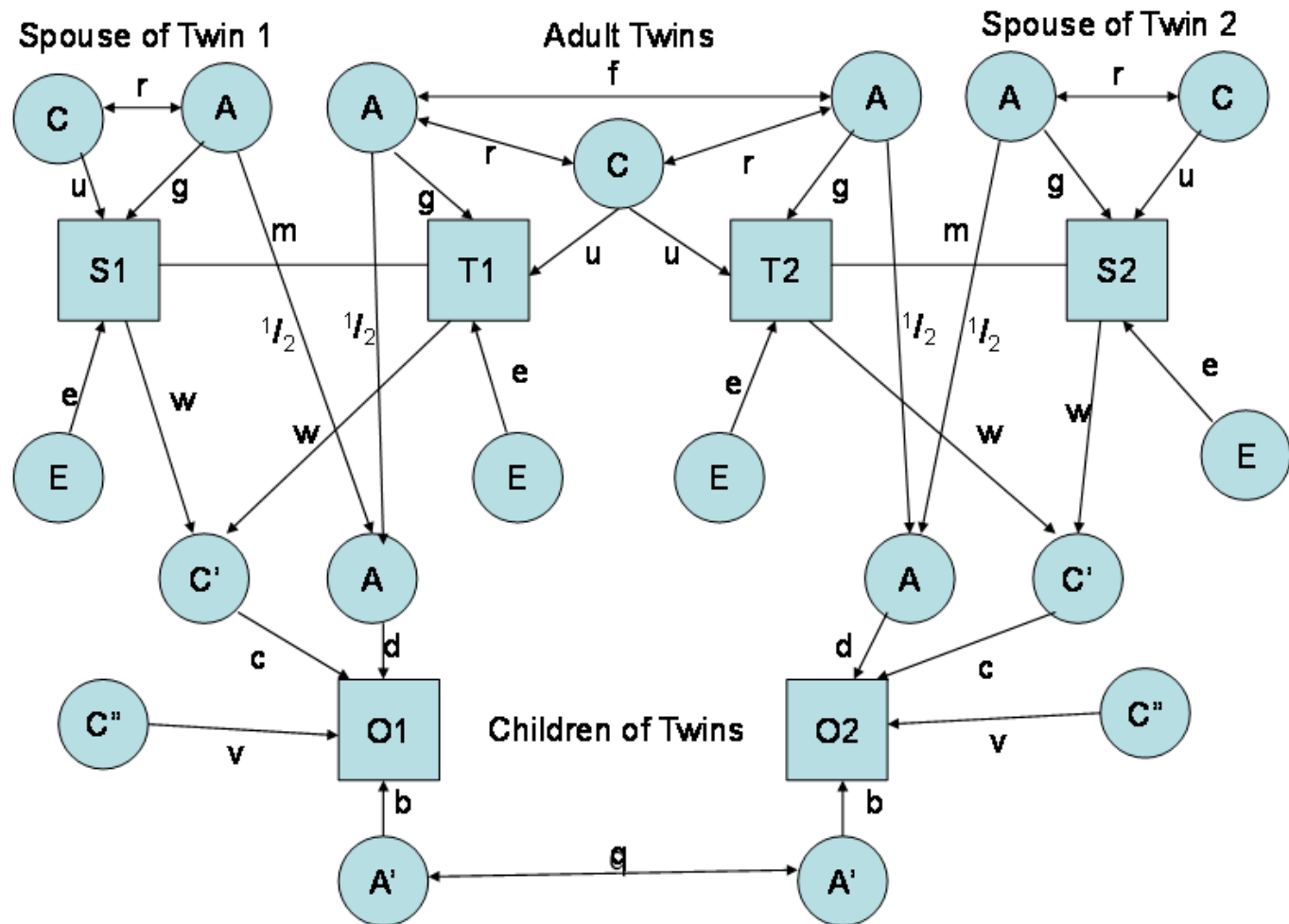
²Juvenile twin correlations - Virginia Twin Study of Adolescent Behavioral Development (VTSABD)

³Complete and incomplete twin pair families

* Child ratings of depression

** Parental ratings of conduct

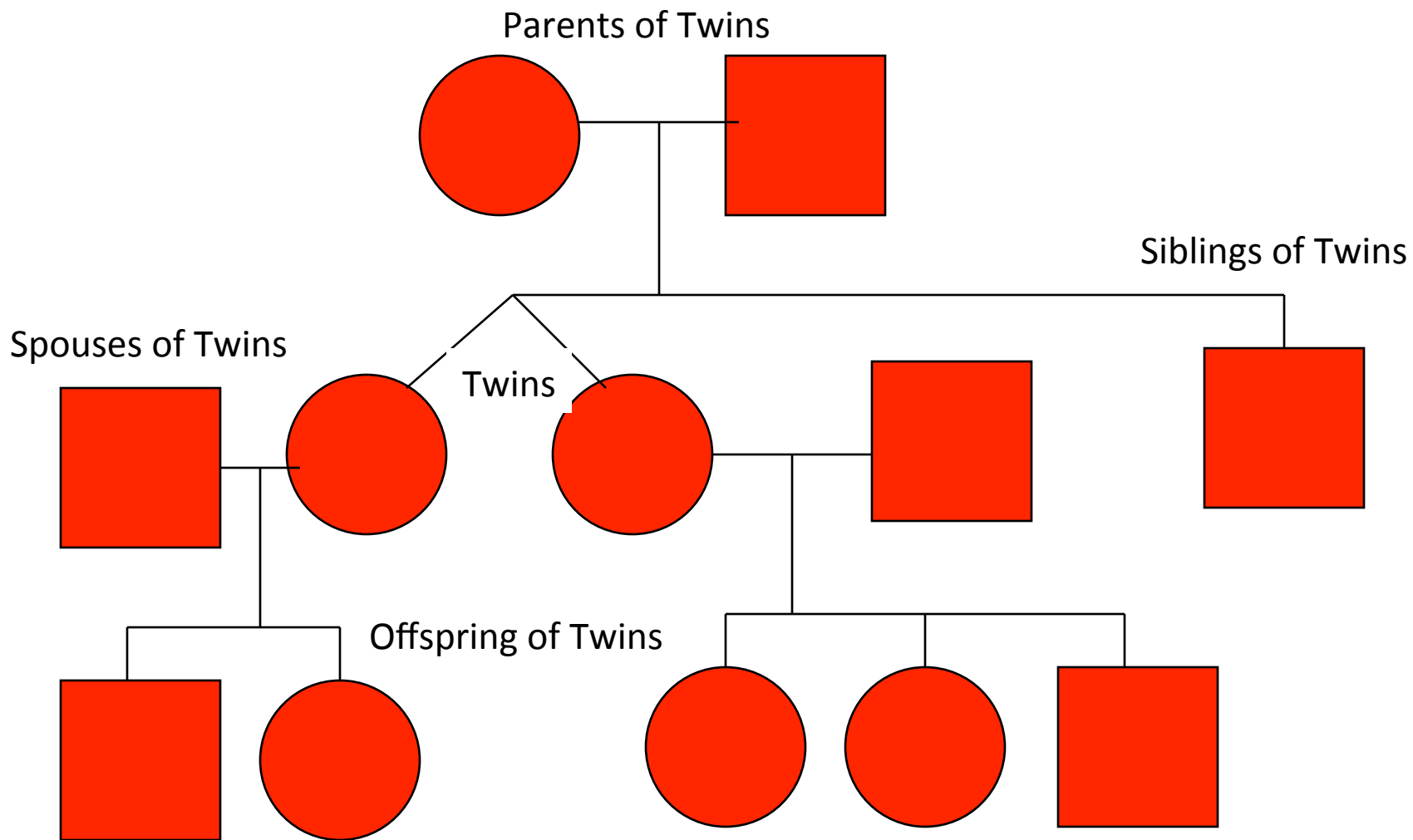
Children of Twins Model (COT)



Parental Depression and Childhood Outcomes: Results

Parameter	Depression	Conduct	Parameter Description	Free?
m	0.1761	0.2064	Correlation between spouses	F
g	0.5410	0.5426	Path from persistent additive genetic effect to adult phenotype	F
d	0.0000!	0.3898	Path from persistent additive genetic effect to juvenile phenotype	F
b	0.5339	0.6775	Path from juvenile limited genetic effect to juvenile phenotype	F
u	0.0000!	0.0000!	Path from adult shared environment to adult phenotype	F
w	0.6520	0.6438	Path from parental phenotype to juvenile shared environment	D
c	0.2101	0.1304	Path from juvenile shared environment to juvenile phenotype	F
v	0.0000!	0.0000!	Path from juvenile-specific shared environment to phenotype	F
r	0.4149	0.4215	Correlation between persistent genetic and shared environmental effects	D
wc	0.1369	0.0839	Path from parental phenotype to juvenile shared environment	D
a	0.5410	0.5246	Correlation between genes of parents and phenotype of parents	D
f	0.5226	0.5303	Correlation between additive genetic effects of siblings/twins	D
χ^2	0.325	1.218		
d.f.	3	2		
P	0.9552	0.5438		

The Full Monty



Genetic and Environmental Factors in Relative Body Weight and Human Adiposity

Hermine H. M. Maes, Michael C. Neale and Lindon J. Eaves.

Behavior Genetics, Vol. 27. No. 4, 1997

Table VI. Observed Correlations of BMI for Biological Relationships in the Virginia 30,000 (Eaves, Unpublished Data)^a

Family	<i>N</i>	<i>r</i>	Avuncular	<i>N</i>	<i>r</i>	Cousins	<i>N</i>	<i>r</i>	In-laws	<i>N</i>	<i>r</i>		<i>N</i>	<i>r</i>
S	4751	.144	PSib ♂ ♂	92	-.026	Mzm ♂ ♂	39	.094	Sibl ♂ ♀	337	-.075	SPDz ♀ ♂	54	-.223
			PSib ♂ ♀	155	.004	Mzm ♀ ♀	92	.223	Sibl ♀ ♂	728	-.007	SPDz ♀ ♀	80	-.177
Sib ♂ ♂	1493	.234	NSib ♀ ♂	402	.185	Mzm ♂ ♀	107	.185	Sibl ♂ ♂	422	.077	SNDz ♂ ♂	126	.114
Sib ♀ ♀	3524	.317	NSib ♀ ♀	536	.083	Mzf ♂ ♂	153	.040	Sibl ♀ ♀	447	.075	SND ♂ ♀	169	-.043
Sib ♂ ♀	4255	.224	PSib ♀ ♂	131	-.007	Mzf ♀ ♀	340	.191				SPDz ♂ ♂	36	-.255
			PSib ♀ ♀	196	.065	Mzf ♂ ♀	449	.064	Dzl ♂ ♀	387	.047	SPDz ♂ ♀	68	.146
DZ ♂ ♂	573	.292	NSib ♂ ♂	236	.105				Dzl ♀ ♂	603	.126	SNDz ♀ ♂	64	.090
Dz ♀ ♀	1164	.360	NSib ♂ ♀	284	.059	Dzm ♂ ♂	19	-.375	Dzl ♂ ♂	353	.038	SNDz ♀ ♀	95	.106
Dz ♂ ♀	1307	.264				Dzm ♀ ♀	41	.070	Dzl ♀ ♀	458	-.028			
Mz ♂ ♂	775	.692	PDz ♂ ♂	105	.292	Dzm ♂ ♀	52	-.072	Mzl ♂ ♀	589	.048	SPMz ♀ ♂	129	.014
Mz ♀ ♀	1847	.730	PDz ♂ ♀	137	.016	Dzf ♂ ♂	52	.260	Mzl ♀ ♂	1139	.109	SPMz ♀ ♀	213	.062
			NDz ♀ ♂	345	.152	Dzf ♀ ♀	138	.095				SNMz ♂ ♂	342	-.107
Fa-So	2160	.190	NDz ♀ ♀	525	.176	Dzf ♂ ♀	159	-.025	Fa-DaI	205	-.068	SNMz ♂ ♀	502	.040
Fa-Da	2971	.194	PDz ♀ ♂	118	.393	Dzo ♂ ♂	38	.176	Fa-SoI	188	.044			
Mo-So	3035	.227	PDz ♀ ♀	188	-.001	Dzo ♀ ♀	71	.118	Mo-DaI	293	.024	SDzm	100	.126
Mo-Da	4476	.257	NDz ♂ ♂	150	.185	Dzo ♂ ♀	51	-.118	Mo-SoI	338	.102	SDzf	120	-.065
			NDz ♂ ♀	202	.098	Dzo ♀ ♂	72	.141				SDzmf	167	-.057
												SMzm	172	.025
			PMz ♂ ♂	217	.141							SMzf	300	.132
			PMz ♂ ♀	337	.264									
			NMz ♀ ♂	673	.124									
			NMz ♀ ♀	1040	.255									

^a S, spouse; Sib, sibling; Dz, DZ twin; Mz, MZ twin; Fa, father; Mo, mother; So, son; Da, daughter; P, paternal; N, maternal; I, in-laws; m, male; f, female; o, opposite sex; ♂ ♂, male-male pair; ♀ ♀, female-female pair; ♂ ♀, male-female pair; ♀ ♂, female-male pair.

The "Stealth" Model

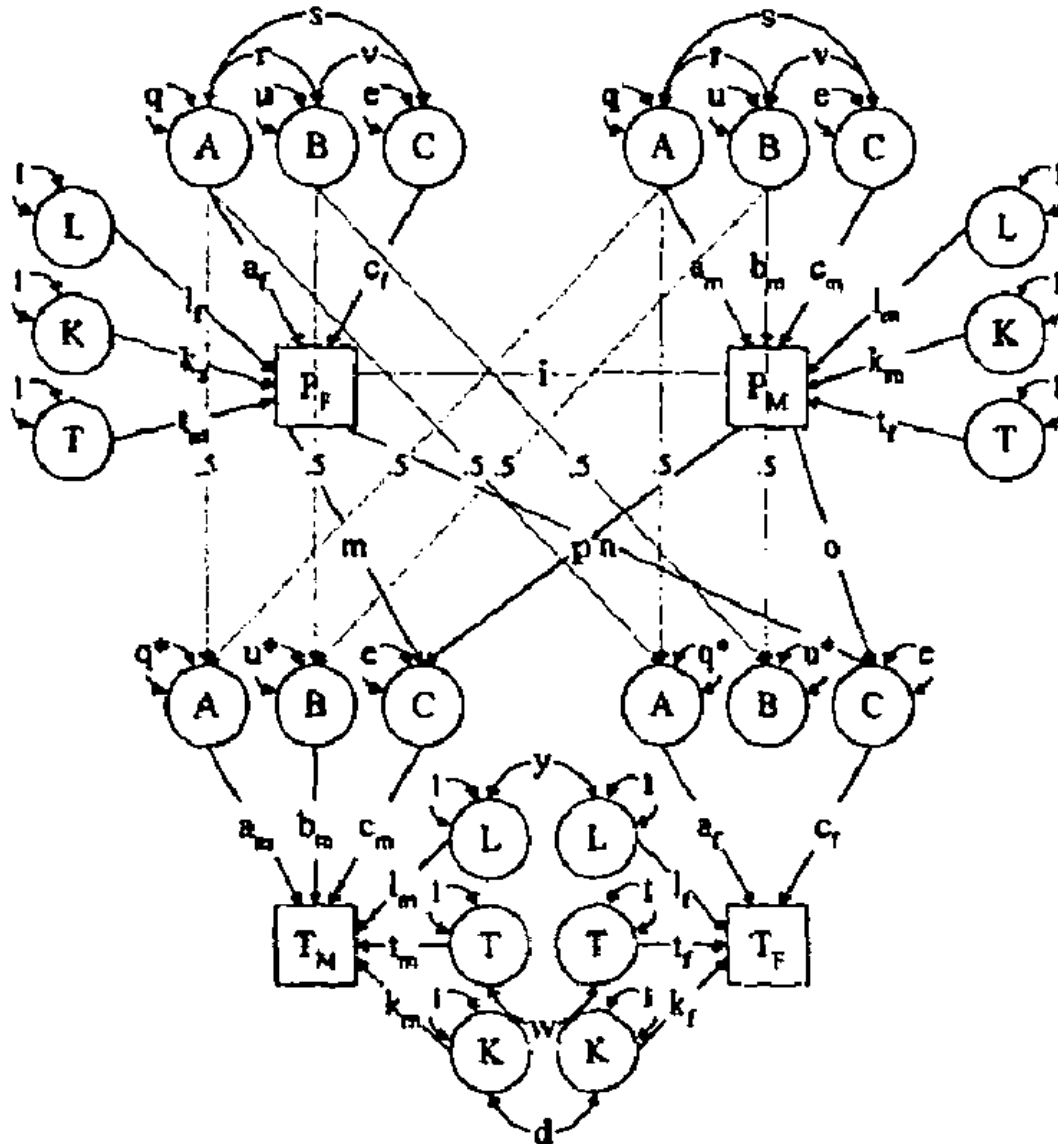


Table V. Statistics, Parameter Estimates, Proportion of Variance, and Confidence Intervals of the Best-Fitting Model for BMI in the Virginia 30,000^a

Full model with special MZ twin environment		Parameter estimate of Full model without special MZ twin environment		Best-fitting model		Proportion of variance of best-fitting model		Confidence intervals
A^2_m	.28+.16	A^2_m	.19+.20	A_m	.521	A^2_m	.351	.290-.415
(asm)	.01	(asm)	.01	A_f	.637	(asm)	(.020)	
D^2_m	.00	D^2_m	.27	E_m	.474	D^2_m	.307	.211-.395
E^2_m	.23	E^2_m	.27	E_f	.543	E^2_m	.274	.247-.304
CT^2_m	.00	CT^2_m	.00	D_m	.501	T^2_m	.068	.023-.134
S^2_m	-.01	S^2_m	.01	D_f	.532			
C^2_m	.02	C^2_m	.00	T_m	-.236	A^2_f	.394	.350-.437
T^2_m	.03	T^2_m	.03	T_f	.292	(asm)	(.022)	
Tmz^2_m	.24	Tmz^2_m		P_m	1.094	D^2_f	.259	.192-.324
A^2_f	.26	A^2_f	.28	P_f	.819	E^2_f	.269	.252-.288
(asm)	.01	(asm)	.01	I	.159	T^2_f	.078	.033-.128
D^2_f	.00	D^2_f	.32					
E^2_f	.21	E^2_f	.27					
CT^2_f	.00	CT^2_f	.01					
S^2_f	.03	S^2_f	.03					
C^2_f	.10	C^2_f	.01					
T^2_f	.06	T^2_f	.06					
Tmz^2_f	.31	Tmz^2_f						

^a Goodness-of-fit statistics of best-fitting model: observed statistics, 24,230; estimated parameters, 72; constraints, 12; active constraints, 7; -2 times log-likelihood of data, 64,988.057; degrees of freedom, 24,158. A^2 , additive genetic factors; asm, assortment; D^2 , dominance factors; E^2 , unique environmental factors; CT^2 , cultural transmission; S^2 , genotype-environment covariance; C^2 , nonparental shared environment; T^2 , special twin environment; Tmz^2 , special twin environment; f and m subscripts, males and females.