



Extended Pedigrees

HGEN619 class 2007



Classic Twin Design

- ACE / ADE
 - heterogeneity
 - multivariate
 - developmental
- Issues
 - generalizability >Additional Siblings

Example Data

- Study: Virginia 30,000: twins, parents, sibs, spouses, children
- Data: church attendance
- Variable: categorical, 6 ordered categories > 5 thresholds
- Analysis: 2 groups, males

ACE Model Results

- Parameter Estimates
a: 0.44 c: 0.59 e: 0.680
- Standardized Estimates + Confidence Intervals
a²: 0.20 c²: 0.34 e²: 0.46
CI 0.01-0.20 0.18-0.49 0.42-0.48
- Fit Statistics
 - Estimated parameters: 23
 - Observed statistics: 2807, 1 constraint
 - -2 times log-likelihood of data: 9364.528
 - Degrees of freedom: 2784

CTD Assumptions

- Random mating
 - Assortment will increase MZ and DZ correlations
 - When fitting ACE model, with assortment present, C will be overestimated
 - When fitting AE model, with assortment present, A will be overestimated
- No Age Moderation
 - When fitting ACE model, with G x age interaction present, C will be overestimated

Correlations

	Mm	Ff	Mf	Fm
MZ	.64	.63	—	—
DZ	.49	.53	.41	—
Sibs	.41	.47	.39	—
P-O	.49	.49	.49	.46
Spouse	—	—	.74	—

Genetic Factors

- Decreasing correlations with a decreasing genetic relatedness: MZ twins > first-degree relatives (DZ twins, siblings, parent-child pairs) > second-degree relatives (grandparents, half-siblings, avuncular pairs) > more distant relatives such as cousins >> **additive genetic factors**
- Sibling and DZ correlations less than half MZ correlations (expectation is $DZ=1/4MZ$) and zero correlations for other pairs of relatives >> **dominance**
- MZ correlations less than 1 >> **specific environmental factors**

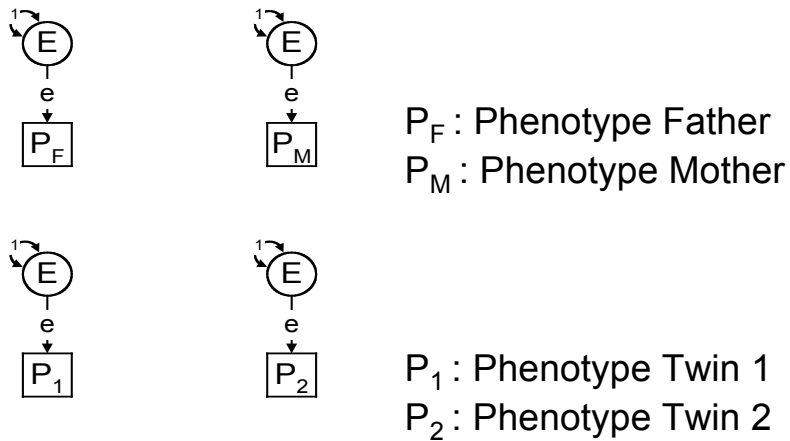
Environmental Factors

- Similar sibling, DZ, parent-offspring correlations >> **shared environmental factors**: increase similarity between people living or having grown up in the same home (first-degree relatives and MZs)
- Sibling > parent-offspring correlations >> **non-parental environmental factors**: in common for siblings, such as school environment, peers, friends
- Twin > sibling correlations >> **special twin environment**: additional similarity due to greater sharing of aspects of the environment
- Siblings = parent-offspring correlations > half MZ twins >> **cultural transmission**

Other Factors

- If cultural transmission based on phenotype of parents for a trait which also has a genetic component >> **GE covariance**
- **Non-random mating**: source of similarity which may have both genetic and environmental implications
 - effects of assortative mating depend on mechanism by which people chose spouses
 - if selection is based on phenotype of partner > correlations between sources of variance in one spouse with those of other spouse induced, genetic and/or environmental covariance between parent-offspring and sibling pairs increased

Path Diagram Twins & Parents



Covariance Matrices MZ/DZ

$$\begin{array}{c}
 \text{Fa Mo T1 T2} \\
 \text{Fa} \begin{bmatrix} P & W' & O' & O' \\ W & P & O' & O' \\ O & O & P & U' \\ O & O & U & P \end{bmatrix} \\
 \text{Mo} \\
 \text{T1} \\
 \text{T2}
 \end{array}$$

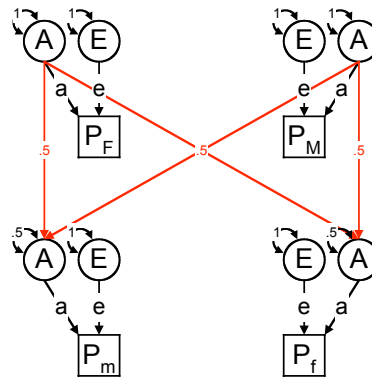
- Variance [P]
- MZ Covariance [U]
- DZ Covariance [V]

$$\begin{array}{c}
 \text{Fa Mo T1 T2} \\
 \text{Fa} \begin{bmatrix} P & W' & O' & O' \\ W & P & O' & O' \\ O & O & P & V' \\ O & O & V & P \end{bmatrix} \\
 \text{Mo} \\
 \text{T1} \\
 \text{T2}
 \end{array}$$

- Spousal Covariance [W]
- Parent-offspring Covariance [O]

Genetic Transmission Model

- Genetic transmission
 - Fixed at .5
- Residual Genetic Variance
 - Fixed at .5
 - Equilibrium of variances across generations

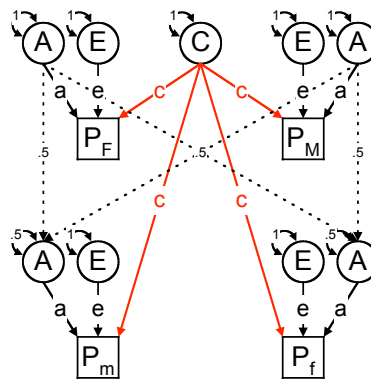


Genetic Transmission Expectations

- $W = 0$; ! covariance spouse
- $O = .5a^2$; ! covariance parent-offspring
- $U = a^2$; ! covariance MZ twins
- $V = .5a^2$; ! covariance DZ twins
- $P = a^2 + e^2$; ! variance twins
- $Q = a^2 + e^2$; ! variance parents

Common Environment Model

- Common environment
 - Same for all family members
- Assortment
 - Function of common environment



Common Environment Expectations

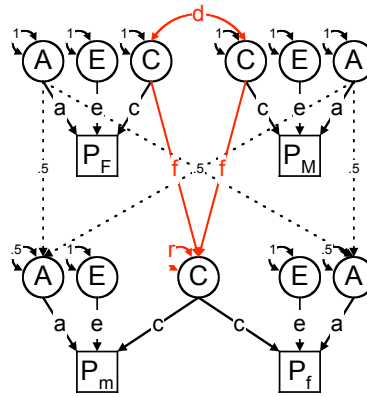
- $W = c^2$; ! covariance spouse
- $O = .5a^2 + c^2$; ! covariance parent-offspring
- $U = a^2 + c^2$; ! covariance MZ twins
- $V = .5a^2 + c^2$; ! covariance DZ twins
- $P = a^2 + c^2 + e^2$; ! variance twins
- $Q = a^2 + c^2 + e^2$; ! variance parents

Common Environment Results

- Parameter Estimates
a: 0.26 c: 0.66 e: 0.700
- Standardized Estimates + Confidence Intervals
a²: 0.07 c²: 0.44 e²: 0.49
CI 0.00-0.18 0.35-0.52 0.44-0.55
- Fit Statistics
 - Estimated parameters: 43
 - Observed statistics: 3351, 1 constraint
 - -2 times log-likelihood of data: 10999.249
 - Degrees of freedom: 3308

Social Homogamy Model

- Assortment
 - Social
- Cultural Transmission
 - From C to C
- Non-parental Shared Environment
 - Residual



Social Homogamy Expectations

- $W = dc^2$; ! covariance spouse
- $O = (f+df)c^2 + .5a^2$; ! covariance parent-child
- $x = 2f^2 + 2df^2 + r$; ! common environment variance twins
- $U = a^2 + xc^2$; ! covariance MZ twins
- $V = .5a^2 + xc^2$; ! covariance DZ twins
- $P = a^2 + xc^2 + e^2$; ! variance twins
- $Q = a^2 + c^2 + e^2$; ! variance parents
 - Constrain $x=1$

Social Homogamy Results

- Parameter Estimates

a: 0.20 c: 0.69 e: 0.69 d: 1.00 f: 0.43
 r: 0.26 p: 1.00 q: 1.00 x: 1.00

- Standardized Estimates + Confidence Intervals

a²: 0.04 r²: 0.13 t²: 0.38 e²: 0.48
 CI 0.04-0.05 0.12-0.14 0.23-0.47 0.44-0.49
 r²: non-parental shared environment, t²: cultural transmission
 t² + r² = c²

- Fit Statistics

- Estimated parameters: 46, Obs statistics: 3352, 2 constraints
- -2 times log-likelihood of data: 10994.427, df: 3306

Phenotypic Assortment Model

- Assortment

- Phenotypic

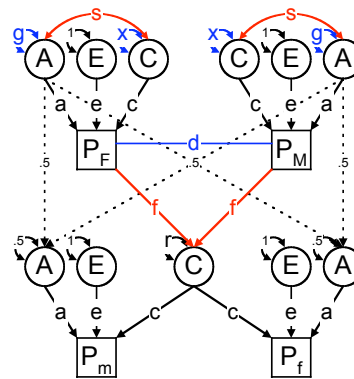
- Cultural Transmission

- From P to C

- Non-parental Shared Environment

- Residual

- Genotype-Environment Covariance



Phenotypic Assortment Expectations

- $W = pdp;$! covariance spouse
- $T = ga + sc;$! covariance G-phenotype
- $O = (pf + wf)c + .5a(1 + pd)t;$! covariance parent-child
- $J = asc + csa;$! covariance GE
- $U = ga^2 + xc^2 + j;$! covariance MZ twin
- $Y = g + .5(t(d+d)t);$! assortment
- $V = .5ya^2 + xc^2 + j;$! covariance DZ twin

Constraints

- $K = .5(g + .5(t(d+d)t') + 1);$
 - ! genetic variance constraint
- $L = .5t(2f + 2dpf);$
 - ! A-C constraint
- $M = 2fpf + 2fwf + r;$
 - ! common environment variance constraint
- $Z = ga^2 + xc^2 + e^2 + 2asc;$
 - ! phenotypic variance constraint

Phenotypic Assortment Results

- Parameter Estimates

a: 0.46 c: 0.31 e: 0.67 d: 0.58 f: 0.36
 g: 1.32 p: 1.00 s: 0.42 x: 1.41

- Standardized Estimates + Confidence Intervals

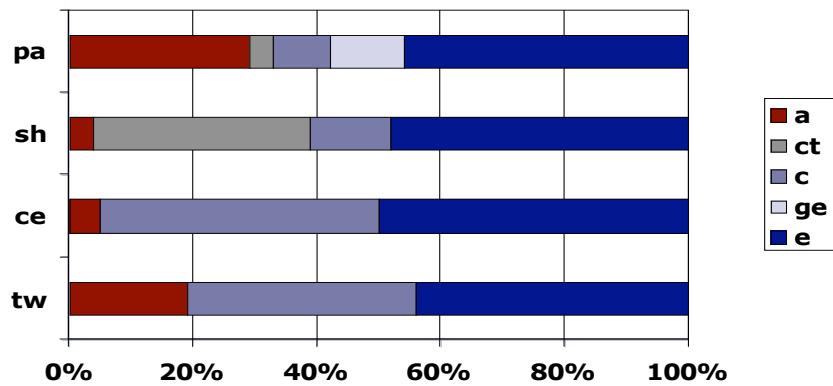
a ² : 0.28	c ² : 0.14	e ² : 0.46	s ² : 0.12
CI 0.04-0.60	0.00-0.41	0.41-0.51	-0.02-0.16
g ² : 0.21	d ² : 0.00	t ² : 0.04	r ² : 0.10
CI 0.04-0.39	0.00-0.21	0.00-0.20	0.00-0.23

s²: genotype-environment covariance, g²: genetic variance, d²: genetic variance through assortment, d² + g² = a²

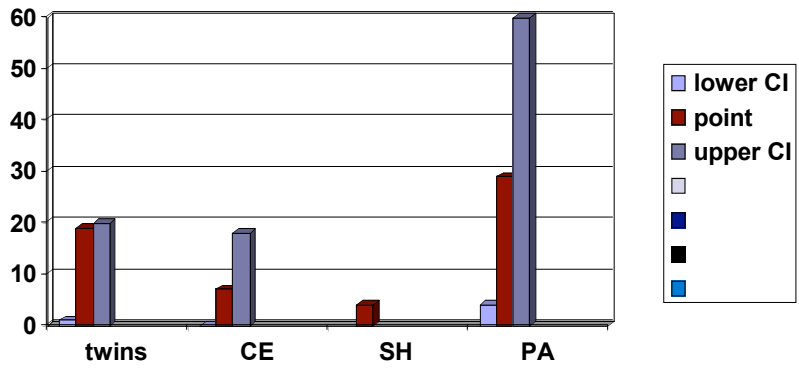
- Fit Statistics

- Estimated parameters: 48, Obs statistics: 3354, 4 constraints
- 2 times log-likelihood of data: 10987.365, df: 3306

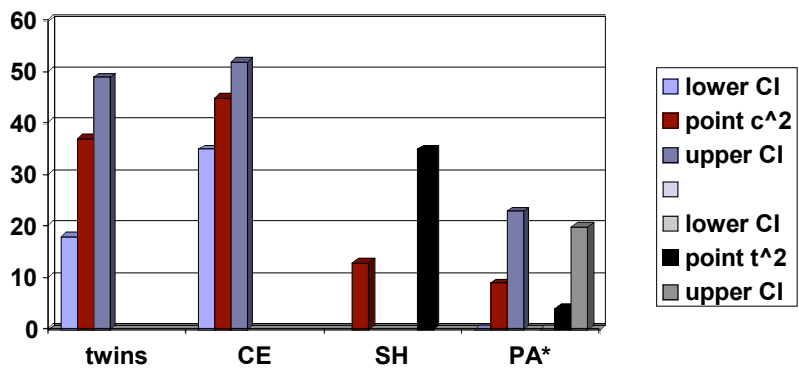
Model Comparisons



Heritability



Shared Environment

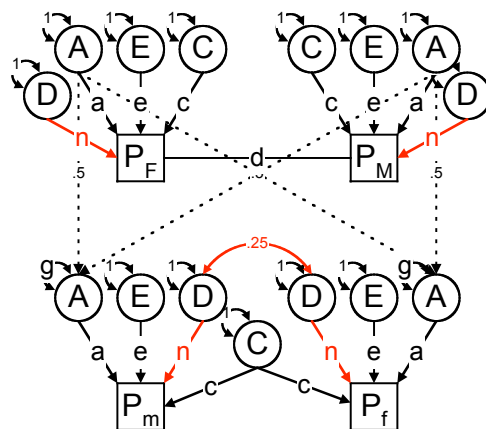


*GE Covariance: lower CI:-2; point:12; upper CI:16

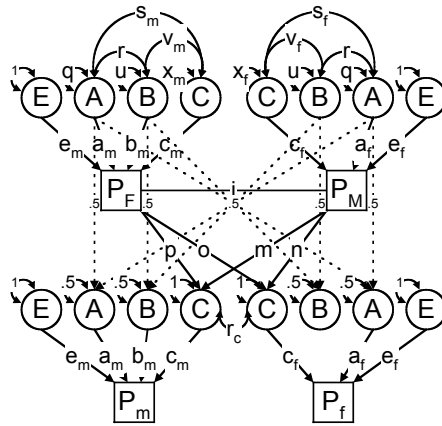
Limitations

- Cultural Transmission versus Dominance versus Reduced Genetic Transmission
- Sex Differences in magnitude or nature of effects
- Age Regression and Moderation

Dominance



Sex Differences



Summary

- Common Environment
 - Assortment function of C
- Social Homogamy
 - Social Assortment
 - Cultural Transmission C->C
- Phenotypic Assortment
 - Phenotypic Assortment
 - Cultural Transmission P->C