



Resemblance Between Relatives (Part 2)

Resemblance of Full-Siblings



- Additive variance components can be estimated using the covariances of the trait values for relatives that do not have dominance effects.
- If we have trait values for half-siblings pairs and full-sibling pairs, we can theoretically obtain an estimate of the dominance variance component under the trait model considered
- Note that $cov_{HS} = \frac{1}{4}\sigma_A^2$ and the genetic covariance for full sibs is $cov_{FS} = \frac{1}{2}\sigma_A^2 + \frac{1}{4}\sigma_D^2$. Show how a dominance variance component can be obtained from these covariances.

Resemblance of Full-Siblings



- Since the genetic covariance for half-sibs is $cov_{HS} = \frac{1}{4}\sigma_A^2$ and the genetic covariance for full sibs is $cov_{FS} = \frac{1}{2}\sigma_A^2 + \frac{1}{4}\sigma_D^2$.
- So $cov_{FS} - 2cov_{HS} = \frac{1}{4}\sigma_D^2$, and we can multiple $cov_{FS} - 2cov_{HS}$ by 4 to obtain an estimate of σ_D^2 .

Shared Environmental Effects



- The resemblance between relatives is not solely due to genetic causes
- There are also environmental factors that tend to make relatives resemble each other
- If members of a family are reared together, they share a common environment
- This common environment contributes to the covariances of related individuals
- The sources of common environmental variance are many and arise from environmental factors such as nutrition, climate, cultural influences, etc.

Model with Shared Environmental Effects



- When analyzing covariances of trait value of relatives, one can also include a family effect in the trait model. Consider the following trait model:

$$Y = A + D + C + E$$

where C is the family effect and E can be viewed in this model as environmental influences that are not shared by family members..

- In this case we would have

$$\text{Cov}(Y_i, Y_j) = 2\theta\sigma_A^2 + k_2\sigma_D^2 + \sigma_C^2$$

where σ_C^2 is the variance of the shared environment/family effect for individuals i and j from the same family.

Model with Shared Environmental Effects



- As previously mentioned, the family effect (C) results from environmental influences shared by family members, such as prenatal environment (e.g., for MZ or DZ twins), home environment, socioeconomic status, and residential area.
- The shared environment component can be present with large effects in some traits, particularly for full-siblings.
- Twin studies comparing variance components of monozygotic (MZ) and dizygotic (DZ) twins are commonly used to estimate heritability and to adjust for shared environments in the heritability estimates.
- Twins share a common environment from conception to birth and over the period during which they are reared together.

Model with Shared Environmental Effects



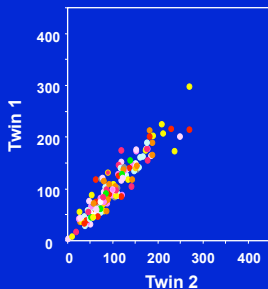
- As a result, the between-pair covariance contains the variance due to common environment, σ_C^2 , is confounded with the genetic covariance.
- DZ twins are full siblings that share a common environment to approximately the same extent as MZ twins.
- To estimate the genetic variance, we essentially need to determine how much less alike are DZ than MZ twins.

MZ TWINS Example (from Peter Visscher)

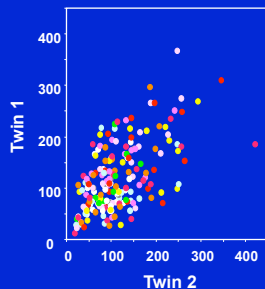


Total mole count for MZ and DZ twins

MZ twins - 153 pairs, $r = 0.94$



DZ twins - 199 pairs, $r = 0.60$



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Model with Shared Environmental Effects



- Assume that the dominance effect is 0, then for MZ twins and DZ twins we have

$$Cov_{MZ} = \sigma_A^2 + \sigma_C^2$$

and

$$Cov_{DZ} = \frac{1}{2}\sigma_A^2 + \sigma_C^2$$

- The mole counts have been standardized, where the mean is 0 and the variance is 1, so the covariances and the correlations are the same.
- Based on the phenotypic correlations for the MZ-twins and DZ-twins, obtain an estimate of the narrow-sense heritability, h^2 .

Model with Shared Environmental Effects



$$2(\hat{r}_{MZ} - \hat{r}_{DZ}) = 2 \left(\frac{\text{Cov}_{MZ}}{\hat{\sigma}_Y^2} - \frac{\text{Cov}_{DZ}}{\hat{\sigma}_Y^2} \right) = \frac{\hat{\sigma}_A^2}{\hat{\sigma}_Y^2} = \hat{h}^2$$

- Since the trait is standardized, i.e., $\sigma_Y^2 = 1$, we have that an estimate for $\sigma_A^2 = h^2$ is $2(.94 - .60) = .68$

Model with Shared Environmental Effects



- Once again, assume that the dominance effect is 0, and for MZ twins and DZ twins we have

$$Cov_{MZ} = \sigma_A^2 + \sigma_C^2$$

and

$$Cov_{DZ} = \frac{1}{2}\sigma_A^2 + \sigma_C^2$$

- The mole counts have been standardized, where the mean is 0 and the variance is 1.
- Based on the phenotypic correlations for the MZ-twins and DZ-twins, now obtain an estimate of the shared common environment variance

Model with Shared Environmental Effects



- For the shared environmental variance we have

$$2(\hat{r}_{DZ}) - \hat{r}_{MZ} = 2(Cov_{DZ}) - Cov_{MZ} = \sigma_C^2$$

- So, an estimate for σ_C^2 is $2(.60) - .94 = .26$

Model with Shared Environmental Effects



- $2(\hat{r}_{MZ} - \hat{r}_{DZ})$ is generally used for heritability estimation in twin studies. What is the bias in the estimate for \hat{h}^2 if the dominance effect is not 0?
- If the dominance effect is not 0, then for MZ twins and DZ twins we have

$$Cov_{MZ} = \sigma_A^2 + \sigma_D^2 + \sigma_C^2$$

and

$$Cov_{DZ} = \frac{1}{2}\sigma_A^2 + \frac{1}{4}\sigma_D^2 + \sigma_C^2$$

- So

$$2(r_{MZ} - r_{DZ}) = 2(Cov_{MZ} - Cov_{DZ}) = \sigma_A^2 + \frac{3}{2}\sigma_D^2 = h^2 + \frac{3}{2}\sigma_D^2$$

for a standardized trait with variance 1.

Human Birth Weight Example



- Several large and independent studies have been performed on human birth weight
- The estimated correlation between relatives are consistent among studies and below is a table of correlations from various studies

Relationship	Correlation
Full Sibs	0.50, 0.52, 0.47, 0.48, 0.48
Maternal Half Sibs	0.58
Paternal Half Sibs	0.10
Maternal First Cousins	0.14, 0.13
Paternal First Cousins	0.02, 0.06
Monozygotic Twins	0.67
Dizygotic Twins	0.59, 0.66
Cousins by female parent MZ twins	0.31
Cousins by male parent MZ twins	-0.03, 0.12

Human Birth Weight Example



- Is there anything striking about the pattern of the birth weight correlations?
- Are there any plausible shared environmental effects? If so, what are they?
- Which relative pair birth weight correlation appears to be implausible based on other relative pair correlation estimates?

Human Birth Weight Example



- The data make it quite clear that maternal environment has a substantial influence on birth weight.
- We can partition the maternal effect variance into genetic and environmental components

$$\sigma_C^2 = \sigma_{C_G}^2 + \sigma_{C_E}^2$$

- For example, MZ twin sisters provide the same genetic environment for their progeny but different home settings, so it is reasonable that the shared maternal effect for the offspring of one the MZ twins and the offspring of the other MZ twin to be $\sigma_{C_G}^2$
- Similarly, since full sibling sisters share half of the genome IBD, the shared maternal effect for the offspring of one female sibling and the offspring of the other female sibling can be modeled as $\frac{1}{2}\sigma_{C_G}^2$

Human Birth Weight Example



- Assume that there is negligible dominance and negligible gene-environmental interaction for human birth weight.
- Under this assumption (and with a normalized trait) we have that $h^2 = \sigma_A^2$
- Fill in the variance components for the different relative pairs.

Relationship	Avg. Corr	Variance Components
Full Sibs	0.49	$\frac{1}{2}\sigma_A^2 + \sigma_C^2$
Maternal Half Sibs	0.58	
Paternal Half Sibs	0.10	
Maternal First Cousins	0.135	
Paternal First Cousins	0.04	
Monozygotic Twins	0.67	
Dizygotic Twins	0.625	
Cousins by female parent MZ twins	0.31	
Cousins by male parent MZ twins	0.045	

Human Birth Weight Example



- We have the following table with variance components

Relationship	Avg. Corr	variance components
Full Sibs	0.49	$\frac{1}{2}\sigma_A^2 + \sigma_C^2$
Maternal Half Sibs	0.58	$\frac{1}{4}\sigma_A^2 + \sigma_C^2$
Paternal Half Sibs	0.10	$\frac{1}{4}\sigma_A^2$
Maternal First Cousins	0.135	$\frac{1}{8}\sigma_A^2 + \frac{1}{2}\sigma_{CG}^2$
Paternal First Cousins	0.04	$\frac{1}{8}\sigma_A^2$
Monozygotic Twins	0.67	$\sigma_A^2 + \sigma_C^2$
Dizygotic Twins	0.625	$\frac{1}{2}\sigma_A^2 + \sigma_C^2$
Cousins by female parent MZ twins	0.31	$\frac{1}{4}\sigma_A^2 + \sigma_{CG}^2$
Cousins by male parent MZ twins	0.045	$\frac{1}{4}\sigma_A^2$

- Obtain estimates for $h^2 = \sigma_A^2$, σ_C^2 , and σ_{CG}^2 using the birth weight correlations for the relative pairs.

Human Birth Weight Example



- One approach for estimate $h^2 = \sigma_A^2$ is to use only the relative pairs that do not have a dominance component.
 - ▶ For paternal half sibs we have that the correlation of birth weight is 0.10. The expected trait covariance (or correlation for a standardized trait) for this relative pair type is $\frac{1}{4}\sigma_A^2$. So $.10 = \frac{1}{4}\hat{\sigma}_A^2$ and thus our estimate for h^2 is $\hat{\sigma}_A^2 = (.10)4 = .40$
 - ▶ For paternal first cousins we have that the average correlation of birth weight is 0.05 and the expected trait covariance is $\frac{1}{8}\sigma_A^2$, so our estimate for h^2 is $(0.04)8 = .32$
 - ▶ For cousins who have parents that are MZ twin brothers, we have that the average correlation of birth weight is 0.045. The expected trait covariance for this pair is $\frac{1}{4}\sigma_A^2$, and thus our estimate for h^2 is $(0.045)4 = .18$
- Averaging the three independent estimates for h^2 , $\hat{h}^2 \approx .3$
- Using our estimate for $h^2 = \sigma_A^2$, we can now easily obtain estimates for σ_C^2 and σ_{CG}^2 .