Twin and Adoption Designs

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1 The ACE Model

Let P represent a phenotype of interest (e.g. IQ, BMI, height, personality) for a given individual. We assume that the phenotype P can be partitioned into three additive and independent components.

$$P = aA + cC + e\epsilon$$

These components have the following definitions:

1. aA represents the component of the phenotype caused by additive genetic effects.
2. cC represents the component of the phenotype caused by shared environmental effects (i.e. environmental variables which make a given pair of relatives more similar to one another with respect to the phenotype in question).
3. $e\epsilon$ represents the component of the phenotype caused by non-shared environmental effects (i.e. environmental variables that are uncorrelated between a given pair of relatives which impact the phenotype in question).

Note that all capitalized variables (i.e. the $PACE$ variables) are assumed to have a mean of 0 and variance of 1. This model of an individual's phenotype is called the "ACE" model and serves as the basis for the classical twin design and many adoption designs.

2 Heritability

Heritability is defined as the variation in a given phenotype that is driven by variation in genetics. In the ACE model, heritability is calculated like so:

$$\begin{aligned} h^2 &= \frac{Var(aA)}{Var(P)} \\ &= a^2 \cdot \frac{Var(A)}{Var(P)} \\ &= a^2 \cdot \frac{1}{1} \\ &= a^2 \end{aligned}$$

Because the ACE model assumes that all genetic effects are additive, the estimated heritability is described as *narrow-sense* heritability. This type of heritability contrasts with *broad-sense* heritability which encompasses non-additive genetic variation in addition to additive genetic variation.

3 Classical Twin Design

In the classical twin design, heritability is estimated like so:

$$h^2 = 2 \cdot (r_{MZ} - r_{DZ})$$

To understand the intuition behind this formula, I will sketch out a mathematical proof. To simplify the math behind this proof, we will assume that the variance of the phenotype in question is one (i.e. $Var(P) = 1$).

3.0.1 The Monozygotic Twin Correlation

Let P_{MZ1} and P_{MZ2} denote the phenotype values for a given pair of monozygotic twins. Under the ACE model, the covariance between the phenotypes of monozygotic twins can be written like so:

$$Cov(P_{MZ1}, P_{MZ2}) = Cov(aA_{MZ1} + cC_{MZ1} + e\epsilon_{MZ1}, aA_{MZ2} + cC_{MZ2} + e\epsilon_{MZ2})$$

Because the ACE model assumes independence between the phenotype components, we can simplify like so:

$$= Cov(aA_{MZ1}, aA_{MZ2}) + Cov(cC_{MZ1}, cC_{MZ2}) + Cov(e\epsilon_{MZ1}, e\epsilon_{MZ2})$$

Because monozygotic twins ...

- share 100% of their genomes, the additive genetic components of their phenotypes are exactly equal (i.e. $A_{MZ1} = A_{MZ2}$).
- experience uncorrelated non-shared environmental influences, the covariance between the non-shared environment components of their phenotypes is equal to zero (i.e. $Cov(\epsilon_{MZ1}, \epsilon_{MZ2}) = 0$).

Thus, we can simplify the above equation like so:

$$\begin{aligned}
&= Cov(aA_{MZ1}, aA_{MZ1}) + Cov(cC_{MZ1}, cC_{MZ2}) \\
&= a^2 Var(A_{MZ1}) + c^2 Cov(C_{MZ1}, C_{MZ2}) \\
&= a^2 + c^2 Cov(C_{MZ1}, C_{MZ2})
\end{aligned}$$

Note that the correlation in the phenotype between monozygotic twins can be expressed like so:

$$Corr(P_{MZ1}, P_{MZ2}) = \frac{Cov(P_{MZ1}, P_{MZ2})}{Var(P_{MZ1}) \cdot Var(P_{MZ2})}$$

Because we have assumed that the variance in the phenotype is equal to one (i.e. $Var(P_{MZ1}) = Var(P_{MZ2}) = 1$), the monozygotic twin correlation is equal to the monozygotic twin covariance shown above.

3.0.2 The Dizygotic Twin Correlation

Let P_{DZ1} and P_{DZ2} denote the phenotype values for a given pair of dizygotic twins. Under the ACE model, the covariance between the phenotypes of dizygotic twins can be written like so:

$$Cov(P_{DZ1}, P_{DZ2}) = Cov(aA_{DZ1} + cC_{DZ1} + e\epsilon_{DZ1}, aA_{DZ2} + cC_{DZ2} + e\epsilon_{DZ2})$$

Because dizygotic twins ...

- share 50% of their genomes, the covariance between the additive genetic components of their phenotypes is equal to one-half (i.e. $Cov(A_{DZ1}, A_{DZ2}) = \frac{1}{2}$).
- experience uncorrelated non-shared environmental influences, the covariance between the non-shared environment components of their phenotypes is equal to zero (i.e. $Cov(\epsilon_{DZ1}, \epsilon_{DZ2}) = 0$).

Thus, we can simplify the above equation like so:

$$\begin{aligned}
&= Cov(aA_{DZ1}, aA_{DZ1}) + Cov(cC_{DZ1}, cC_{DZ2}) \\
&= a^2 Cov(A_{DZ1}, A_{DZ2}) + c^2 Cov(C_{DZ1}, C_{DZ2}) \\
&= \frac{1}{2} a^2 + c^2 Cov(C_{DZ1}, C_{DZ2})
\end{aligned}$$

Because we have assumed that the variance in the phenotype is equal to one (i.e. $Var(P_{DZ1}) = Var(P_{DZ2}) = 1$), the dizygotic twin correlation is equal to the dizygotic twin covariance shown above.

3.0.3 Estimating Heritability

With the monozygotic and dizygotic twin correlations specified, we can now estimate heritability like so:

$$\begin{aligned} h^2 &= 2 \cdot (r_{MZ} - r_{DZ}) \\ &= 2 \cdot (a^2 + c^2 Cov(C_{MZ1}, C_{MZ2}) - (\frac{1}{2}a^2 + c^2 Cov(C_{DZ1}, C_{DZ2}))) \\ &= 2 \cdot (\frac{1}{2}a^2 + c^2 Cov(C_{MZ1}, C_{MZ2}) - c^2 Cov(C_{DZ1}, C_{DZ2})) \end{aligned}$$

By the Equal Environments Assumption, the covariance between shared environment components of the phenotype for monozygotic twins is equal to the covariance between the shared environment components of the phenotype for dizygotic twins (i.e. $Cov(C_{MZ1}, C_{MZ2}) = Cov(C_{DZ1}, C_{DZ2})$). Thus, we can simplify the equation to yield heritability like so:

$$\begin{aligned} &= 2 \cdot (\frac{1}{2}a^2) \\ &= a^2 \end{aligned}$$

3.0.4 Genetic Homogamy Bias

The $2 \cdot (r_{MZ} - r_{DZ})$ formula assumes that the covariance between the additive genetic components of the phenotype for dizygotic twins is one-half (i.e. $Cov(A_{DZ1}, A_{DZ2}) = \frac{1}{2}$). However, this assumption is violated in the presence of genetic homogamy.

To understand the impact of genetic homogamy bias, we must first understand what impact genetic homogamy has on the covariance between the additive genetic components of non-identical siblings.

To start, let us suppose that the additive genetic components of the *parent's* phenotypes are correlated at m (i.e. $Corr(A_{MOM}, A_{DAD}) = m$). Then, the covariance between the additive genetic components of the mother's and father's phenotype can be expressed like so:

$$\begin{aligned} Cov(A_{MOM}, A_{DAD}) &= Corr(A_{MOM}, A_{DAD}) \cdot \sqrt{Var(A_{MOM}) \cdot Var(A_{DAD})} \\ &= m \cdot \sqrt{Var(A_{MOM}) \cdot Var(A_{DAD})} \\ &= m \cdot \sqrt{1 \cdot 1} \\ &= m \end{aligned}$$

Next, note that, in the average case, the additive genetic component of the child's phenotype is equal to an average of the mother and father's additive genetic components:

$$A_{CHILD} = \frac{1}{2}(A_{MOM} + A_{DAD})$$

We can now estimate the covariance of the additive genetic component of the phenotype between two non-identical children of the same parents like so:

$$\begin{aligned}
Cov(A_{CHILD1}, A_{CHILD2}) &= Cov(\frac{1}{2}(A_{MOM} + A_{DAD}), \frac{1}{2}(A_{MOM} + A_{DAD})) \\
&= \frac{1}{4}Cov(A_{MOM}, A_{MOM}) + \frac{1}{4}Cov(A_{DAD}, A_{DAD}) + \frac{1}{2}Cov(A_{MOM}, A_{DAD}) \\
&= \frac{1}{4}Var(A_{MOM}) + \frac{1}{4}Var(A_{DAD}) + \frac{1}{2}Cov(A_{MOM}, A_{DAD}) \\
&= \frac{1}{2} + \frac{m}{2} \\
&= \frac{1+m}{2}
\end{aligned}$$

Thus, genetic homogamy of m increases the covariance between the additive genetic components of the phenotype for dizygotic twins from $\frac{1}{2}$ to $\frac{1+m}{2}$. Importantly, this result means that our heritability estimation formula is downwardly biased!

$$\begin{aligned}
h^2 &= 2 \cdot (r_{MZ} - r_{DZ}) \\
&= 2 \cdot (a^2 + c^2 Cov(C_{MZ1}, C_{MZ2}) - (\frac{1+m}{2}a^2 + c^2 Cov(C_{DZ1}, C_{DZ2}))) \\
&= 2 \cdot (\frac{1-m}{2}a^2 + c^2 Cov(C_{MZ1}, C_{MZ2}) - c^2 Cov(C_{DZ1}, C_{DZ2})) \\
&= 2 \cdot (\frac{1-m}{2}a^2) \\
&= (1-m)a^2
\end{aligned}$$

Instead of yielding heritability equal to a^2, the formula yields $(1-m)a^2$. To eliminate this genetic homogamy bias, we can divide the estimated heritability by $1-m$ like so:

$$h^2 = \frac{h^2_{twin}}{1-m}$$

3.0.5 Non-Additivity Bias

The $2 \cdot (r_{MZ} - r_{DZ})$ formula assumes that the phenotype of interest can be additively separated into three independent components: an additive genetic component (A), a shared environmental component (C), and a non-shared environmental component (E). However, this assumption is violated when genetic effects are non-additive. To deal with non-additivity, we must extend the ACE model into include a fourth component D which captures dominance and a fifth component $A \times A$ which captures epistasis (i.e. gene-gene interactions). Please excuse the bastardized notation used to denote epistasis.

$$P = aA + cC + dD + (a \times a)(A \times A) + e\epsilon$$

Because monozygotic twins fully share non-additive genetic effects, the monozygotic twin correlation can be written like so:

$$r_{MZ} = a^2 + c^2 Cov(C_{MZ1}, C_{MZ2}) + d^2 + (a \times a)^2$$

Because dizygotic twins share only *one-fourth* of non-additive genetic effects, the dizygotic twin correlation can be written like so:

$$r_{DZ} = \frac{1}{2}a^2 + c^2 Cov(C_{DZ1}, C_{DZ2}) + \frac{1}{4}d^2 + \frac{1}{4}(a \times a)^2$$

The $2 \cdot (r_{MZ} - r_{DZ})$ formula yields the following heritability estimate:

$$\begin{aligned}
h^2 &= 2 \cdot (r_{MZ} - r_{DZ}) \\
&= 2 \cdot (a^2 + c^2 Cov(C_{MZ1}, C_{MZ2}) + d^2 + (a \times a)^2 - (\frac{1}{2}a^2 + c^2 Cov(C_{DZ1}, C_{DZ2}) + \frac{1}{4}d^2 + \frac{1}{4}(a \times a)^2)) \\
&= 2 \cdot (\frac{1}{2}a^2 + \frac{3}{4}d^2 + \frac{3}{4}(a \times a)^2) \\
&= a^2 + \frac{3}{2}d^2 + \frac{3}{2}(a \times a)^2
\end{aligned}$$

Instead of yielding a *broad-sense* heritability estimate equal to $a^2 + d^2 + (a \times a)^2$, the formula yields $a^2 + \frac{3}{2}d^2 + \frac{3}{2}(a \times a)^2$. In other words, the formula over-estimates non-additive genetic variation by 50%!

4 Adoption Designs

Adoption designs estimate heritability in different ways depending on the relative pairs under consideration. We will consider how genetic homogamy impacts each design separately. All calculations will assume the ACE model and that the variance of the phenotype is one (i.e. $Var(P) = 1$).

4.1 Birth Parent - Adoptive Child Formulation

In the Birth Parent-Adoptive Child Formulation, heritability is estimated like so:

$$h^2 = 2 \cdot r_{BP-AC}$$

4.1.1 The Birth Parent - Adoptive Child Correlation

Let P_{BP} and P_{AC} denote the phenotype values for the birth parent and their child who was adopted away, respectively. Under the ACE model, the covariance between the phenotypes of the birth parent and the adoptive child can be written like so:

$$Cov(P_{BP}, P_{AC}) = Cov(aA_{BP} + cC_{BP} + e\epsilon_{BP}, aA_{AC} + cC_{AC} + e\epsilon_{AC})$$

Because birth parents and their adopted-away children:

- share 50% of their genomes, the covariance between the additive genetic components of their phenotypes is equal to one-half (i.e. $Cov(A_{BP}, A_{AC}) = \frac{1}{2}$).
- do not live in the same environment, the covariance between the shared environment components of their phenotype is assumed to be equal to zero (i.e. $Cov(C_{BP}, C_{AC}) = 0$).
- experience uncorrelated non-shared environmental influences, the covariance between the non-shared environment components of their phenotypes is equal to zero (i.e. $Cov(\epsilon_{BP}, \epsilon_{AC}) = 0$).

Thus, we can simplify the above equation like so:

$$\begin{aligned} &= Cov(aA_{BP}, aA_{AC}) \\ &= a^2 Cov(A_{BP}, A_{AC}) \\ &= \frac{1}{2}a^2 \end{aligned}$$

Because we have assumed that the variance in the phenotype is equal to one (i.e $Var(P_{BP}) = Var(P_{AC}) = 1$), the birth parent-adoptive child correlation is equal to the birth parent-adoptive child covariance shown above.

4.1.2 Estimating Heritability

With the birth parent-adoptive child correlation specified, we can now estimate heritability like so:

$$\begin{aligned} h^2 &= 2 \cdot r_{BP-AC} \\ &= 2 \cdot \frac{1}{2}a^2 \\ &= a^2 \end{aligned}$$

4.1.3 Genetic Homogamy Bias

The $2 \cdot r_{BP-AC}$ formula assumes that the covariance between the additive genetic components of the phenotype for birth parents and their adopted-away children is one-half (i.e. $Cov(A_{BP}, A_{AC}) = \frac{1}{2}$. However, this assumption is violated in the presence of genetic homogamy.

Let us suppose that the additive genetic components of the *parent's* phenotypes are correlated at m (i.e. $Corr(A_{MOM}, A_{DAD}) = m$). By the derivation in Section 3.0.4, the covariance is also equal to m (i.e. $Cov(A_{MOM}, A_{DAD}) = m$).

Next, recall that, in the average case, the additive genetic component of the child's phenotype is equal to an average of the mother and father's additive genetic components:

$$A_{CHILD} = \frac{1}{2}(A_{MOM} + A_{DAD})$$

We can now estimate the covariance of the additive genetic component of the phenotype between a parent and their biological offspring. Without loss of generalization, assume that the parent in question is the mother of the child:

$$\begin{aligned} Cov(A_{CHILD}, A_{MOM}) &= Cov(\frac{1}{2}(A_{MOM} + A_{DAD}), A_{MOM}) \\ &= \frac{1}{2}Cov(A_{MOM}, A_{MOM}) + \frac{1}{2}Cov(A_{DAD}, A_{MOM}) \\ &= \frac{1}{2}Var(A_{MOM}) + \frac{1}{2}m \\ &= \frac{1}{2} + \frac{m}{2} \\ &= \frac{1+m}{2} \end{aligned}$$

Thus, genetic homogamy of m increase the covariance between the additive genetic components of the phenotype for birth parents and their adopted-away offspring from $\frac{1}{2}$ to $\frac{1+m}{2}$. Importantly, this result means that our heritability estimation formula is upwardly biased!

$$\begin{aligned} h^2 &= 2 \cdot r_{BP-AC} \\ &= 2 \cdot \frac{1+m}{2}a^2 \\ &= (1+m)a^2 \end{aligned}$$

Instead of yielding heritability equal to a^2, the formula yields $(1+m)a^2$. To eliminate this genetic homogamy bias, we can divide the estimated heritability by $1+m$ like so:

$$h^2 = \frac{h^2_{adoption}}{1+m}$$

4.2 Biological Child - Adoptive Child Formulation

In the Biological Child - Adoptive Child Formulation, heritability is estimated like so:

$$h^2 = 2 \cdot (r_{RP-BC} - r_{RP-AC})$$

4.2.1 The Rearing Parent-Biological Child Correlation

Let P_{RP} and P_{BC} denote the phenotype values for the rearing parent and their biological child, respectively. Under the ACE model, the covariance between the phenotypes of the rearing parent and the biological child can be written like so:

$$Cov(P_{RP}, P_{BC}) = Cov(aA_{RP} + cC_{RP} + e\epsilon_{RP}, aA_{BC} + cC_{BC} + e\epsilon_{BC})$$

Because rearing parents and their biological children:

- share 50% of their genomes, the covariance between the additive genetic components of their phenotypes is equal to one-half (i.e. $Cov(A_{RP}, A_{BC}) = \frac{1}{2}$).
- live in the same environment, the covariance between the shared environment components of their phenotype is assumed to be equal to one (i.e. $Cov(C_{RP}, C_{BC}) = 1$).
- experience uncorrelated non-shared environmental influences, the covariance between the non-shared environment components of their phenotypes is equal to zero (i.e. $Cov(\epsilon_{RP}, \epsilon_{BC}) = 0$).

Thus, we can simplify the above equation like so:

$$\begin{aligned} &= Cov(aA_{RP}, aA_{BC}) + Cov(cC_{RP}, cC_{BC}) \\ &= a^2 Cov(A_{BP}, A_{AC}) + c^2 Cov(C_{RP}, C_{BC}) \\ &= \frac{1}{2}a^2 + c^2 Cov(C_{RP}, C_{BC}) \end{aligned}$$

Because we have assumed that the variance in the phenotype is equal to one (i.e $Var(P_{RP}) = Var(P_{BC}) = 1$), the rearing parent-biological child correlation is equal to the rearing parent-biological child covariance shown above.

4.2.2 The Rearing Parent-Adoptive Child Correlation

Let P_{RP} and P_{AC} denote the phenotype values for the rearing parent and their adoptive child, respectively. Under the ACE model, the covariance between the phenotypes of the rearing parent and the adoptive child can be written like so:

$$Cov(P_{RP}, P_{AC}) = Cov(aA_{RP} + cC_{RP} + e\epsilon_{RP}, aA_{AC} + cC_{AC} + e\epsilon_{AC})$$

Because rearing parents and their adoptive children:

- are assumed to share 0% of their genomes, the covariance between the additive genetic components of their phenotypes is assumed to be equal to zero (i.e. $Cov(A_{RP}, A_{AC}) = 0$).
- live in the same environment, the covariance between the shared environment components of their phenotype is assumed to be equal to one (i.e. $Cov(C_{RP}, C_{AC}) = 1$).
- experience uncorrelated non-shared environmental influences, the covariance between the non-shared environment components of their phenotypes is equal to zero (i.e. $Cov(\epsilon_{RP}, \epsilon_{AC}) = 0$).

Thus, we can simplify the above equation like so:

$$\begin{aligned} &= Cov(cC_{RP}, cC_{AC}) \\ &= c^2 Cov(C_{RP}, C_{AC}) \end{aligned}$$

Because we have assumed that the variance in the phenotype is equal to one (i.e $Var(P_{RP}) = Var(P_{AC}) = 1$), the rearing parent-adoptive child correlation is equal to the rearing parent-adoptive child covariance shown above.

4.2.3 Estimating Heritability

With the parent-biological child and rearing parent-adoptive child correlations specified, we can now estimate heritability like so:

$$\begin{aligned} h^2 &= 2 \cdot (r_{RP-BC} - r_{RP-AC}) \\ &= 2 \cdot (\frac{1}{2}a^2 + c^2 Cov(C_{RP}, C_{BC}) - (c^2 Cov(C_{RP}, C_{AC}))) \end{aligned}$$

By the Equal Environments Assumption, the covariance between shared environment components of the phenotype for rearing parents and their biological children is equal to the covariance between the shared environment components of the phenotype for rearing parents and their adoptive children (i.e. $Cov(C_{RP}, C_{BC}) = Cov(C_{RP}, C_{AC})$). Thus, we can simplify the equation to yield heritability like so:

$$\begin{aligned} &= 2 \cdot (\frac{1}{2}a^2) \\ &= a^2 \end{aligned}$$

4.2.4 Genetic Homogamy Bias

By the derivation in Section 4.1.3, the covariance between the additive genetic components of the phenotype for rearing parents and their biological children is equal to $\frac{1+m}{2}$ in the presence of genetic homogamy. Importantly, this result means that our heritability estimation formula is upwardly biased!

$$\begin{aligned} h^2 &= 2 \cdot r_{RP-BC} - r_{RP-AC} \\ &= 2 \cdot (\frac{1+m}{2}a^2 - c^2 Cov(C_{RP}, C_{BC}) - (c^2 Cov(C_{RP}, C_{AC}))) \\ &= 2 \cdot (\frac{1+m}{2}a^2) \\ &= (1+m)a^2 \end{aligned}$$

Instead of yielding heritability equal to a^2, the formula yields $(1+m)a^2$. To eliminate this genetic homogamy bias, we can divide the estimated heritability by $1+m$ like so:

$$h^2 = \frac{h^2_{adoption}}{1+m}$$

4.3 Biological Sibling - Adoptive Sibling Formulation

In the Biological Sibling - Adoptive Sibling Formulation, heritability is estimated like so:

$$h^2 = 2 \cdot (r_{BS} - r_{AS})$$

4.3.1 The Biological Sibling Correlation

Let P_{BS1} and P_{BS2} denote the phenotype values for a given pair of biological siblings. Under the ACE model, the covariance between the phenotypes of monozygotic twins can be written like so:

$$Cov(P_{BS1}, P_{BS2}) = Cov(aA_{BS1} + cC_{BS1} + e\epsilon_{BS1}, aA_{BS2} + cC_{BS2} + e\epsilon_{BS2})$$

Because biological siblings ...

- share 50% of their genomes, the covariance between the additive genetic components of their phenotypes is one-half (i.e. $Cov(A_{BS1}, A_{BS2}) = \frac{1}{2}$).
- experience uncorrelated non-shared environmental influences, the covariance between the non-shared environment components of their phenotypes is equal to zero (i.e. $Cov(\epsilon_{BS1}, \epsilon_{BS2}) = 0$).

Thus, we can simplify the above equation* like so:

$$\begin{aligned}
&= Cov(aA_{BS1}, aA_{BS1}) + Cov(cC_{BS1}, cC_{BS2}) \\
&= \frac{1}{2}a^2 Var(A_{BS1}) + c^2 Cov(C_{BS1}, C_{BS2}) \\
&= \frac{1}{2}a^2 + c^2 Cov(C_{BS1}, C_{BS2})
\end{aligned}$$

Because we have assumed that the variance in the phenotype is equal to one (i.e. $Var(P_{BS1}) = Var(P_{BS2}) = 1$), the biological sibling correlation is equal to the biological sibling covariance shown above.

4.3.2 The Adoptive Sibling Correlation

Let P_{AS1} and P_{AS2} denote the phenotype values for a given pair of adoptive siblings (i.e. sibling pairs where at least one member is adopted). Under the ACE model, the covariance between the phenotypes of adoptive siblings can be written like so:

$$Cov(P_{AS1}, P_{AS2}) = Cov(aA_{AS1} + cC_{AS1} + e\epsilon_{AS1}, aA_{AS2} + cC_{AS2} + e\epsilon_{AS2})$$

Because adoptive siblings ...

- are assumed to share 0% of their genomes, the covariance between the additive genetic components of their phenotypes is assumed to be equal to zero (i.e. $Cov(A_{AS1}, A_{AS2}) = 0$).
- experience uncorrelated non-shared environmental influences, the covariance between the non-shared environment components of their phenotypes is equal to zero (i.e. $Cov(\epsilon_{AS1}, \epsilon_{AS2}) = 0$).

Thus, we can simplify the above equation* like so:

$$\begin{aligned} &= Cov(aA_{AS1}, aA_{AS1}) + Cov(cC_{AS1}, cC_{AS2}) \\ &= c^2 Cov(C_{AS1}, C_{AS2}) \end{aligned}$$

Because we have assumed that the variance in the phenotype is equal to one (i.e. $Var(P_{AS1}) = Var(P_{AS2}) = 1$), the adoptive sibling correlation is equal to the adoptive sibling covariance shown above.

4.3.3 Estimating Heritability

With the biological and adoptive sibling correlations specified, we can now estimate heritability like so:

$$\begin{aligned} h^2 &= 2 \cdot (r_{BS} - r_{AS}) \\ &= 2 \cdot (\frac{1}{2}a^2 + c^2 Cov(C_{BS1}, C_{BS2}) - c^2 Cov(C_{AS1}, C_{AS2})) \end{aligned}$$

By the Equal Environments Assumption, the covariance between shared environment components of the phenotype for biological siblings is equal to the covariance between the shared environment components of the phenotype for adoptive siblings (i.e. $Cov(C_{BS1}, C_{BS2}) = Cov(C_{AS1}, C_{AS2})$). Thus, we can simplify the equation to yield heritability like so:

$$\begin{aligned} &= 2 \cdot (\frac{1}{2}a^2) \\ &= a^2 \end{aligned}$$

4.3.4 Genetic Homogamy Bias

The $2 \cdot (r_{BS} - r_{AS})$ formula assumes that the covariance between the additive genetic components of the phenotype for biological siblings is one-half (i.e. $Cov(A_{DZ1}, A_{DZ2}) = \frac{1}{2}$). However, this assumption is violated in the presence of genetic homogamy.

By the derivation in Section 3.0.4, the covariance between the additive genetic components of biological siblings is equal to $\frac{1+m}{2}$. Importantly, this result means that our heritability estimation formula is upwardly biased!

$$\begin{aligned} h^2 &= 2 \cdot (r_{BS} - r_{AS}) \\ &= 2 \cdot (\frac{1+m}{2}a^2 + c^2 Cov(C_{BS1}, C_{BS2}) - c^2 Cov(C_{AS1}, C_{AS2})) \\ &= 2 \cdot (\frac{1+m}{2}a^2) \\ &= (1+m)a^2 \end{aligned}$$

Instead of yielding heritability equal to a^2, the formula yields $(1+m)a^2$. To eliminate this genetic homogamy bias, we can divide the estimated heritability by $1+m$ like so:

$$h^2 = \frac{h^2_{adoption}}{1+m}$$

4.4 Monozygotic Twins Reared Apart Formulation

In the Monozygotic Twins Reared Apart Formulation, heritability is estimated like so:

$$h^2 = r_{MZA}$$

4.4.1 The Monozygotic Twins Reared Apart Correlation

Let P_{MZA1} and P_{MZA2} denote the phenotype values for a given pair of monozygotic twins reared apart. Under the ACE model, the covariance between the phenotypes of monozygotic twins reared apart can be written like so:

$$Cov(P_{MZA1}, P_{MZA2}) = Cov(aA_{MZA1}+cC_{MZA1}+e\epsilon_{MZA1}, aA_{MZA2}+cC_{MZA2}+e\epsilon_{MZA2})$$

Because monozygotic twins reared apart...

- share 100% of their genomes, the additive genetic components of their phenotypes are exactly equal (i.e. $A_{MZA1} = A_{MZA2}$).
- do not live in the same environment, the covariance between the shared environment components of their phenotype is assumed to be equal to zero (i.e. $Cov(C_{MZA1}, C_{MZA2}) = 0$).
- experience uncorrelated non-shared environmental influences, the covariance between the non-shared environment components of their phenotypes is equal to zero (i.e. $Cov(\epsilon_{MZA1}, \epsilon_{MZA2}) = 0$.

Thus, we can simplify the above equation like so:

$$\begin{aligned} &= Cov(aA_{MZA1}, aA_{MZA1}) \\ &= a^2 Var(A_{MZA1}) \\ &= a^2 \end{aligned}$$

Because we have assumed that the variance in the phenotype is equal to one (i.e. $Var(P_{MZA1}) = Var(P_{MZA2}) = 1$), the monozygotic twin correlation is equal to the monozygotic twin covariance shown above.

4.4.2 Estimating Heritability

As demonstrated in the previous section, heritability is equal to the correlation between monozygotic twins reared apart.

4.4.3 Genetic Homogamy Bias

Because it is not possible to increase the genetic similarity of monozygotic twins beyond 100%, genetic homogamy has no impact on the resulting heritability estimate.