

Determining the Genetic Component of a Trait

$$\sigma_T^2 = \sigma_G^2 + \sigma_E^2 = \sigma_A^2 + \sigma_D^2 + \sigma_E^2$$

total variability = genetic + environmental = additive + dominance + environmental

σ_T^2 = observed phenotypic variability of a trait

σ_G^2 = variability due to genetic effects

σ_E^2 = variability due to environmental effects

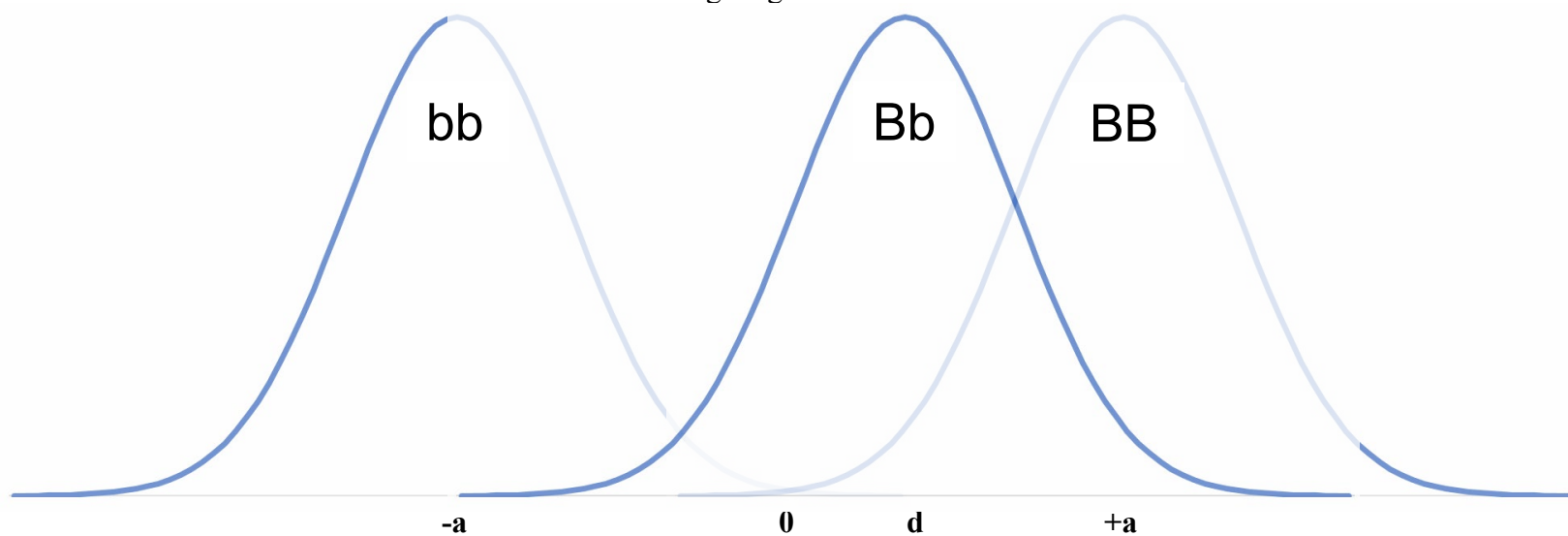
σ_A^2 = additive genetic variance

σ_D^2 = dominance genetic variance

Additive and Dominance Components

polymorphism influences a continuous quantitative trait under genetic control

individuals with an A allele have an average higher level of the trait



shift distributions so midpoint between mean of BB and bb groups is 0

a = mean of BB group

$-a$ = mean of bb group

d = mean of Bb group

$\frac{d}{a}$ = degree of dominance

Genetic Models for Quantitative Trait

Additive Model $d = 0$ no dominance, dominance variance = 0

Recessive Model $d = -a$ only need to have one b allele to show the phenotype

Dominance Model $d = a$ only need to have one B allele to show the phenotype

Heritability

proportion of total phenotypic variance that is due to genetic effects

$$h^2 = \frac{\sigma_G^2}{\sigma_G^2 + \sigma_E^2} = \frac{\sigma_G^2}{\sigma_T^2}$$

broad sense heritability $h_b^2 = \frac{\sigma_A^2 + \sigma_D^2}{\sigma_G^2 + \sigma_E^2} = \frac{\sigma_G^2}{\sigma_T^2}$

narrow sense heritability $h_n^2 = \frac{\sigma_A^2}{\sigma_G^2 + \sigma_E^2} = \frac{\sigma_A^2}{\sigma_T^2}$

Degree of Relationship	Relative Pair	Expected Probability of # IBD Alleles			Additive Coefficient of Relationship	Kinship Coefficient	Dominance Coefficient
		0	1	2			
Zero Degree	monozygotic twins	0	0	1	$\frac{0 \times 0}{2} + \frac{1 \times 0}{2} + \frac{2 \times 1}{2} = 1$	$\frac{1}{2}$	1
First Degree	dizygotic twins	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{1}{4}$	$\frac{0 \times \frac{1}{4}}{2} + \frac{1 \times \frac{1}{2}}{2} + \frac{2 \times \frac{1}{4}}{2} = \frac{1}{2}$	$\frac{1}{4}$	$\frac{1}{4}$
	siblings	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{1}{4}$	$\frac{0 \times \frac{1}{4}}{2} + \frac{1 \times \frac{1}{2}}{2} + \frac{2 \times \frac{1}{4}}{2} = \frac{1}{2}$	$\frac{1}{4}$	$\frac{1}{4}$
	parent, child	0	1	0	$\frac{0 \times 0}{2} + \frac{1 \times 1}{2} + \frac{2 \times 0}{2} = \frac{1}{2}$	$\frac{1}{4}$	0
Second Degree	half-siblings	$\frac{1}{2}$	$\frac{1}{2}$	0	$\frac{0 \times \frac{1}{2}}{2} + \frac{1 \times \frac{1}{2}}{2} + \frac{2 \times 0}{2} = \frac{1}{4}$	$\frac{1}{8}$	0
	aunt/uncle, niece/nephew	$\frac{1}{2}$	$\frac{1}{2}$	0	$\frac{0 \times \frac{1}{2}}{2} + \frac{1 \times \frac{1}{2}}{2} + \frac{2 \times 0}{2} = \frac{1}{4}$	$\frac{1}{8}$	0
	grandparent, grandchild	$\frac{1}{2}$	$\frac{1}{2}$	0	$\frac{0 \times \frac{1}{2}}{2} + \frac{1 \times \frac{1}{2}}{2} + \frac{2 \times 0}{2} = \frac{1}{4}$	$\frac{1}{8}$	0
	double first cousins	$\frac{9}{16}$	$\frac{6}{16}$	$\frac{1}{16}$	$\frac{0 \times \frac{9}{16}}{2} + \frac{1 \times \frac{6}{16}}{2} + \frac{2 \times \frac{1}{16}}{2} = \frac{1}{4}$	$\frac{1}{8}$	$\frac{1}{16}$
Third Degree	first cousins	$\frac{3}{4}$	$\frac{1}{4}$	0	$\frac{0 \times \frac{3}{4}}{2} + \frac{1 \times \frac{1}{4}}{2} + \frac{2 \times 0}{2} = \frac{1}{8}$	$\frac{1}{16}$	0
	great-grandparent, great-grandchild	$\frac{3}{4}$	$\frac{1}{4}$	0	$\frac{0 \times \frac{3}{4}}{2} + \frac{1 \times \frac{1}{4}}{2} + \frac{2 \times 0}{2} = \frac{1}{8}$	$\frac{1}{16}$	0

additive coefficient = expected proportion of shared IBD alleles by a relative pair

$$C = 2^{-R}$$

R = degree of relationship

dominance coefficient = probability that the genotype of two randomly drawn individuals of that relationship is IBD

kinship coefficient = $\frac{1}{2}$ coefficient of relationship

probability that a randomly selected pair of alleles, one from each individual, is IBD

Estimating Heritability from Continuous Trait

heritability is a function of covariance between relatives, additive coefficient of relationship, and dominance coefficient

if a trait is influenced by genetics, will see greater positive covariance for relatives that are more closely related

if a trait isn't heritable, close relatives will not be more correlated than distant relatives

heritability estimates using close and distant relatives should be similar, unless there is a dominance component

Model Assumptions

$$T = A + D + E = G + E$$

A, D, and E are independent

genetic and environmental factors are uncorrelated

standard deviation of trait is the same for all individuals

Parent, Offspring Pairs

$$h_n^2 = 2\hat{\beta}$$

narrow sense heritability is 2 times the regression coefficient from linear regression on parental value

Both Parent, Offspring Trios

$$h_n^2 = \hat{\beta}$$

narrow sense heritability is the regression coefficient from linear regression on mean parental value

Sibships

$$h^2 = 2 \times ICC = 2 \times \frac{\sum (x_{1i} - \bar{x}) - (x_{2i} - \bar{x})}{(N - 1) \times stdv(x)}$$

x is computed from combining data on all siblings

if $\sigma_D^2 \neq 0$, estimate is between h_n^2 and h_b^2

Twins

$$h^2 = 2(ICC_{MZ} - ICC_{DZ})$$

heritability is 2 times the difference of intraclass correlation between monozygotic and dizygotic twins
by using the difference, any shared environmental variance between twins cancels out
if $\sigma_D^2 \neq 0$, estimate is greater than h_n^2 and h_b^2

Variability

sibling and twin estimates incorporate a dominance variance, parent-offspring estimates do not
when sibling and twin estimates are higher than parent-offspring estimates, it indicates a
dominance component

siblings and twins may also have shared environmental/exposure factors

heritability is a ratio of variances, not an average, so a larger sample size won't fix normality
problems

Estimating Heritability from Dichotomous Trait

recurrence risk ratio $\lambda_R = \frac{K_R}{K}$

K_R = proportion of relatives of affected probands who are also affected

K = proportion of affected individuals in the general population

R = degree of relationship

if a trait is genetic, λ_R should decrease as R increases

if trait doesn't have a genetic component, may see $\lambda_R > 1$ due to shared environment among
siblings of similar age