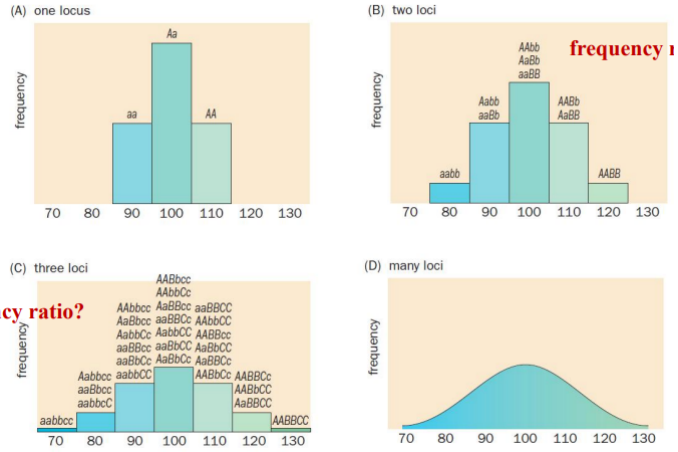
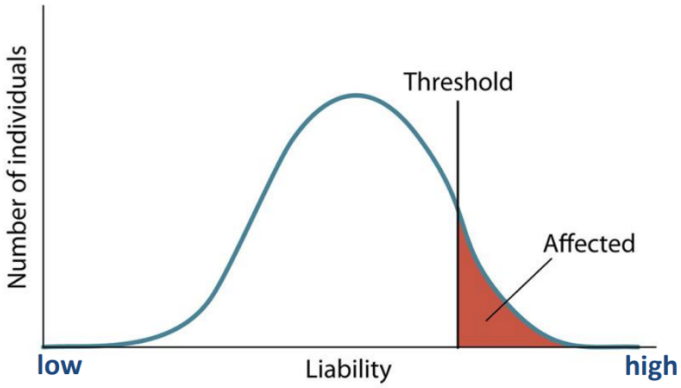
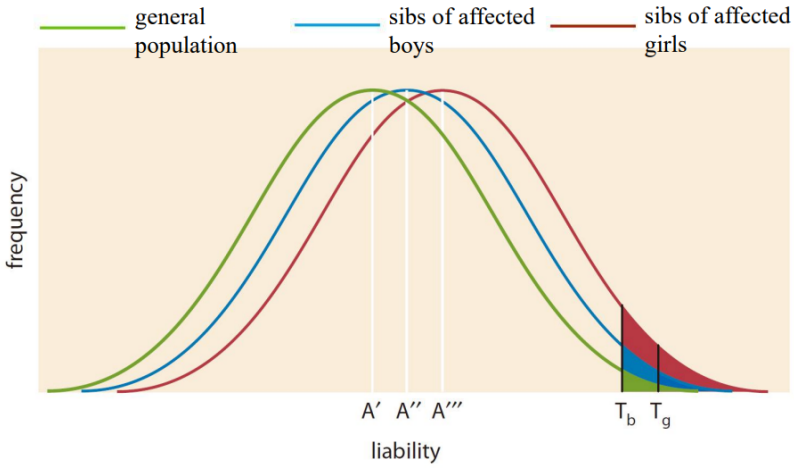
Theory	Explanation
Simple Additive Polygenic Model	Each gene exerts a simple additive effect. No dominance and recessivity. The simple additive model predict a Gaussian distribution as the number of loci increases. 
Liability Threshold Model **= Polygenetic Threshold Model** **= Threshold Theory**	The threshold model extended polygenic theory to cover qualitative characters. To be affected or not depends on a balance between the number and function of good and bad genes and environmental factors  Can nicely explains the major characteristics of MI
Recurrence Risk	The recurrence risk > the incidence in the population, but much < that of a single recessive (25%) or dominant gene (50%). The recurrence risk for first-degree relatives approximates to the sqrt of the general population incidence
MI Characteristics	The incidence of the condition is greatest among relatives of the most severely affect patients The more severe the malformation the greater the recurrence risk. Recurrence risk increases with increasing number of previously affected children, as opposed to single gene trait that the risk to the next child remains unchanged. For multifactorial disorders, bad luck in the past is a predictor of bad luck in the future. The risk is much lower for 2nd degree relatives, but it decreases less

sharply for more remote relative. This characteristic distinguishes MI from AD I, in which the risk drops by 1/2.

If the condition is more common in individuals of one particular sex, recurrence risk varies according to sex of index case. The risk is higher for relatives of patients of the less susceptible sex.

The differential risk to relatives of an affected proband increases as the disease prevalence decreases.

Sex-specific Threshold



The Relative Risk Ratio (λ)

$$\lambda_r = \frac{\text{the frequency of the trait in relatives}}{\text{the frequency in the general population}}$$

A measure for the degree of familial aggregation in qualitative traits.

Heritability (h^2)
= Falconer's Formula

the fraction of the total phenotypic variance of a quantitative trait that is due to allelic variance.

$0 < h^2 < 1$ (for most cases)

$h^2 = V_G / V_P$ $\quad h^2 = 2 \times (C_{MZ} - C_{DZ})$

If $C_{MZ} >> C_{DZ}$ then h^2 is high (approaches 1)
If $C_{MZ} = C_{DZ}$ then h^2 is low (approaches 0)
Sometimes $h^2 > 1$ does happen

Odds Ratio

	Cases	Controls
Risk genotype present	*a*	*c*
Risk genotype absent	*b*	*d*

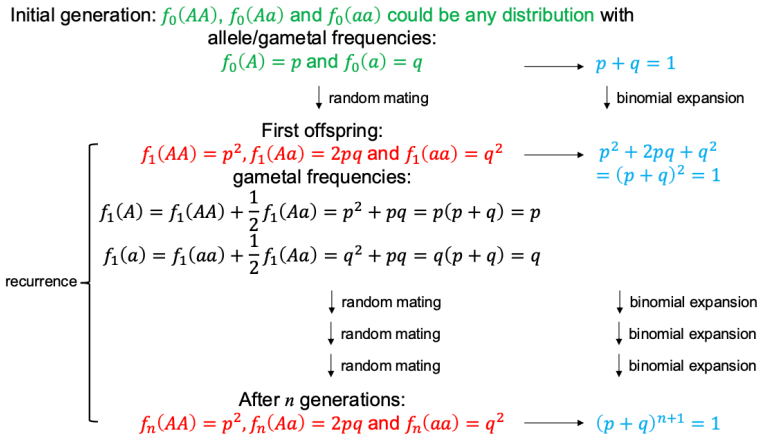
$$\frac{(a/c)}{(b/d)} = ad/bc.$$

The odds ratio is the "measure of association" for a case-control study.
odds ratio > 1: the genetic variant is positively associated with the disorder;
odds ratio < 1: a protective association.

Logarithm of the Odds Score

To answer: are these two loci linked?

(LOD Score)	***Aim:*** to evaluate the significance of linkage results. Calculation $LOD=\log_{10}\frac{\text{likelihood of data if loci linked at a particular } \theta}{\text{likelihood of data if loci unlinked } (\theta=0.5)}=\log_{10}\frac{(1-\theta)^n\theta^r}{(1/2)^{n+r}}$ (Odds ratio) **θ = recombination fraction** n = Number of nonrecombinant offspring r = Number of recombinant offspring n+r = Total number of offspring Interpretation: "LOD score = 3" means the odds are 1000:1 in favour of (supports) genetic linkage. so… LOD score > 3 → linked LOD score < -2 → unlinked
Genotype Frequency → Allele Frequency	$f(A)=f(AA)+\frac{1}{2}f(Aa)$ $f(a)=f(aa)+\frac{1}{2}f(Aa)$
Gene Pool	= potential gametes
Transition Probability = Meiotic Transition Frequency	Aa 到胚子 A 和配子 a 的衔接概率都是 1/2
Genotype Frequency + Meiotic Transition Frequency → Gamete Frequency	Note: maybe transition frequency, in some cases, is not the default 0.5! $g_i=\sum_{j=1}^{n}G_j t_{j\to i}$ $p=f(AA)+\frac{1}{2}f(Aa)$ $q=f(aa)+\frac{1}{2}f(Aa)$
Hardy-Weinberg Equilibrium (HWE)	**Assumptions:** *1. Allele frequencies remain constant over time (after the initial generation).* • No mutations. • No significant immigration from a population with different allele frequencies. • No selection against any genotype. *2. Mating is random with respect to the locus of focus.* • The population under study is large. So, sexes are evenly distributed, and that all are equally fertile. **Violations:** 1. Changes in allele frequencies • Mutation: subtly affects allele frequencies due to the low mutation rate which is a typical case. • Migration: leads to gene flow between populations • Selection: rapidly causes allele frequencies to change • Small population: randomly changes allele frequencies due to sampling effect, i.e., genetic drift 2. Non-random mating like inbreeding



"Under the assumption of HWE" + p > 0.05 → The HWE-predicted genotype frequency not exist in the given population.

Rare AR Allele Frequency

Because the recessive disease-causing allele frequency a is very low, the normal allele frequency A ≈ 1.

Carrier frequency = 2Aa ≈ 2a
Aa (carriers):aa (patients) ≈ $2q/q^2 = 2/q$

➢For an AR gene, the affected alleles are both copies from the recessive homozygotes. So the loss of the relevant alleles at each generation is $2sq^2$.

At equilibrium mutation rate = loss rate due to selection
For a recessive trait,
$2\mu = 2sq^2$.

Rare AD Allele Frequency

$A^2 + 2Aa = A^2 + 2A\ (1 - A) = 2A - A^2$
→ $2A - A^2 \approx 2A$
都是公式的变形

➢For an AD gene, the affected frequency = $p^2 + 2pq \approx 2p$, where $p^2 \to 0$ and $q \to 1$. The proportion of loss alleles at each generation is $2sp$.

At equilibrium mutation rate = loss rate due to selection
For a dominant trait,
$2\mu = 2sp$.

Selective Coefficient (s) → Allele frequency

Allele A: s1 | Allele a: s2

A = $\frac{s_2}{s_1+s_2}$ a = $\frac{s_1}{s_1+s_2}$

allele frequencies at equilibrium are determined by the relative strength of natural selection against each form.

➢For an AR gene, the affected alleles are both copies from the recessive homozygotes. So the loss of the relevant alleles at each generation is $2sq^2$.

➢For an AD gene, the affected frequency = $p^2 + 2pq \approx 2p$, where $p^2 \to 0$ and $q \to 1$. The proportion of loss alleles at each generation is $2sp$.