SIGS- Module 10 Quantitative Genetics of Disease

Practical 1.

Heritability of Liability.

1. **Polygenic models generate a normal distribution of genetic values.**

a) Simulate a population of N=10,000 for 10 loci of frequency p

Binomial distribution of genotypes

G1, G2..G10=rbinom(N,2,p), set p =0.5

Make a count of risk alleles across 1,2,..10 loci

R1=G1, R2=G1+G2, …R10 = G1+G2…+G10

Plot histogram of R1…R10

b) repeat for p = 0.1

c) set p randomly eg uniform c(runif(10,0,1))

d) a-c demonstrate normal distribution of risk allele count.

If the effect size for the risk locus at SNP i is ai then what is the distribution of variance of risk allele. Draw the ai from different distributions

 2. **Using simulation to explore the liability threshold model.**

Section 2a-2e. Already programmed.

2a. Run the section – generates sliders (make plot window as big as possible)

2b-2e Run line by line

2b. Simulates phenotypic liability and disease status of parents and children

2c. Some graphs and calculates risks to relatives

2d. Compare simulated values with normal distribution theory

2e. Estimate heritability from recurrence risks to relatives

2f. Complete table to feel sampling variation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Estimatedh2l | K=0.15, h2=0.4 | K=0.15, h2=0.8 | K=0.01, h2=0.4 | K=0.01, h2=0.8 |
| N=e7 |  |  |  |  |
| N=1000 |  |  |  |  |
| N=100 |  |  |  |  |

2g. Extend the simulation to include different types of relatives

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Add to the simulation a Monozygotic twin of the child

Add to the simulation a full-sibling of the child

Add to the simulation a paternal half-sibling of the child

Calculate lambdaMZ, lambdaFS, and lambdaHS

Estimate heritability of liability from lambdaMZ, lambdaFS, and lambdaHS