Q1 Color-blindness (Feller, Ch.5, Ex. 7)
Let us assume that the frequencies of color-blindness are 5% and 0.25% of in men and women, respectively.
Question: What is the chance that a given color-blind person is a man?

Answer
0.05 / (0.05 + 0.0025) = 95%

Q2 Testing HWE
Consider a SNP with variants, A and T. In an association analysis experiment, the following data were obtained: 9 subjects had genotype AA, 136 subjects had genotype AT and 392 subjects had genotype TT.
Question: what is the frequency of A allele? Do the genotypic frequencies follow Hardy-Weinberg distribution?

Answer
The frequency of A allele may be estimated using exoression
P(A) = [2 N(AA) + N(AT)]/[2 N] = [2 9 + 136]/[2 537] = 0.14338919925512
Then, if Hardy-Weinberg equilibrium is true, expected frequencies
of genotypes are
P(AA) = P(A) P(A) = 0.020560462463025
P(AT) = 2 P(A) P(T) = 2 P(A) (1-P(A)) = 0.24565747358419
P(TT) = P(T) P(T) = (1-P(A)) (1-P(A)) = 0.73378206395278
and the expected number of people with these genotypes are
11.040968342644, 131.91806331471, 394.04096834264
in AA, AT and TT groups, respectively
The chi-square statistics is calculated to test is actual data fit
HWE expectation:
CHI2 = SUM (OBS-EXP)^2/EXP =
(9 - 11.040968342644)^2/11.040968342644 +
(136 - 131.91806331471)^2/131.91806331471 +
(392 - 394.04096834264)^2/394.04096834264 =
0.51415999216947
This CHI2 has one degree of freedom, consequently, if CHI2>3.84,
the null hypothesis of HWE is to be rejected.
In this case 0.51415999216947 < 3.84 and, consequently, the null hypothesis holds.

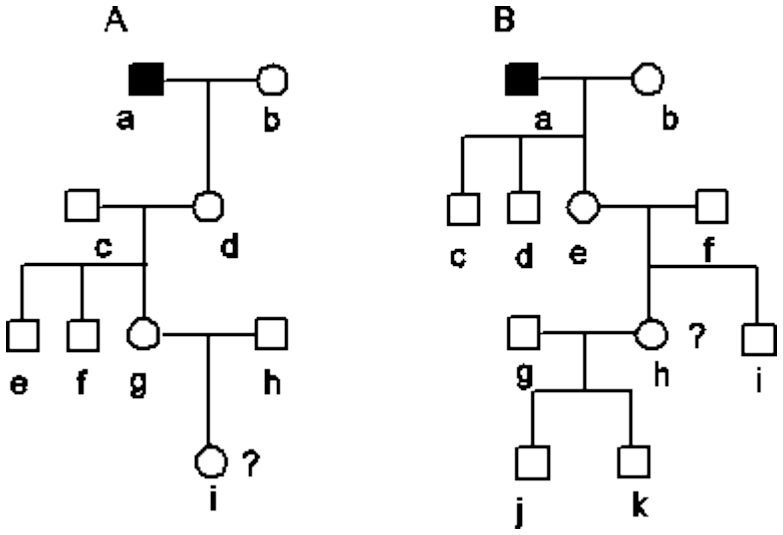
Q3 HWE with multiple alleles
Consider a locus with 3 alleles (named from A_1 to A_3). The frequency of allele A_1 ... A_2 are 0.6713, 0.1861, respectively.
Question: What are the frequencies of A_1/A_1, A_1/A_2, ... A_3/A_3 genotypes under Hardy-Weinberg equilibrium?

Answer
The frequencies of alleles are
Pr(A_1)=0.6713
Pr(A_2)=0.1861
Pr(A_3)=0.1426
According to Hardy-Weinberg principle,
Pr(A_1/A_1) = Pr(A_1) * Pr(A_1) = 0.6713 * 0.6713 = 0.45064369
Pr(A_1/A_2) = 2 * Pr(A_1) * Pr(A_2) = 2 * 0.6713 * 0.1861 = 0.24985786
Pr(A_1/A_3) = 2 * Pr(A_1) * Pr(A_3) = 2 * 0.6713 * 0.1426 = 0.19145476
Pr(A_2/A_2) = Pr(A_2) * Pr(A_2) = 0.1861 * 0.1861 = 0.03463321
Pr(A_2/A_3) = 2 * Pr(A_2) * Pr(A_3) = 2 * 0.1861 * 0.1426 = 0.05307572
Pr(A_3/A_3) = Pr(A_3) * Pr(A_3) = 0.1426 * 0.1426 = 0.02033476

Q4 X-linked recessive disease

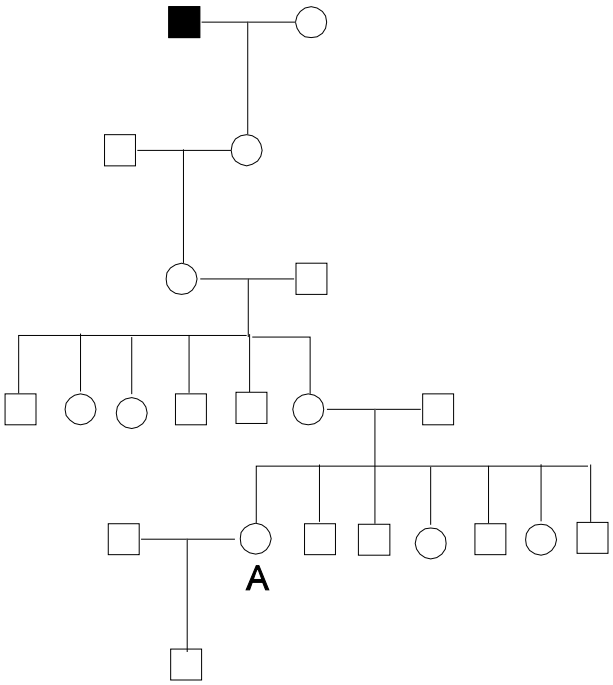
For pedigree **A**: what is the probability that "i" is a carrier? What is the risk for her next boy-child?

For pedigree **B**: what is the probability that "h" is a carrier? What is the risk for her next boy-child?



Answer:
A: the chance g is carrier is ½. The chance i is carrier is ¼.
B: the a priori chance for h to be carrier is ½. To incorporate information on j and k, use Bayes. The posterior probability is 1/5. The risk for next boy-child is 1/10.

The same question for the following pedigree, person A



ANSWER Q4 V. 1

Q4.1.1 You have to take step-wise approach to this problem. First, the posterior probability that grandmother is carrier is to be calculated using information that (1) the prior probability for her to be a carrier is ½ and (2) information that she has 3 healthy boy-children. Next, half of the posterior makes prior for MOTHER of A to be carrier. Based on this information + information that A has 4 healthy brothers, posterior probability that mother of A is to be calculated. Half of this is used as prior for A to be carrier. After incorporation of the information that A already has one healthy boy-child, the answer is ready.

For grandmother of A:

Hypothesis	Carrier	Non-carrier	
Prior	½	½	
Conditional	$½^3$	1	
Joint	$½^4$	½	9/16
Posterior	1/9	8/9	

For mother of A

Hypothesis	Carrier	Non-carrier	
Prior	1/18	17/18	
Conditional	$½^4$	1	
Joint	1/288	17/18	273/288
Posterior	1/273	272/273	

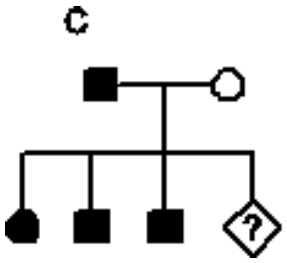
For A

Hypothesis	Carrier	Non-carrier	
Prior	1/546	545/546	
Conditional	½	1	
Joint	1/1092	545/546	1091/1092
Posterior	1/1091	1090/1091	

Thus the probability that A is carrier is 1/1091 = 0.00092

Q5 DOMINANT DISEASE

Given a dominant disease with allele frequency of 0.03, what is the risk for next child?



ANSWER:

Probability given parent's phenotype, P(MN|affected):

0,0300	DN	DD	
prior	0,0582	0,0009	
cond	1,0000	1,0000	Total
joint	0,0582	0,0009	0,0591
post	0,9848	0,0152	

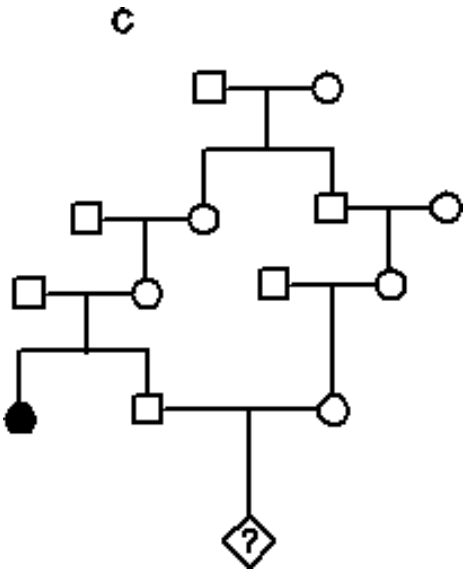
Probability given 3 affected offspring, P(MN|3 x D, also parent =D)

	DN	DD	
prior	0,9848	0,0152	
cond	0,1250	1,0000 Total	
joint	0,1231	0,0152	0,1383
post	0,8899	0,1101	

Risk for a next child = ½ P(MN|3 x D, also parent =D) + P(MM|3 x D, also parent =D) = 0.555

Q5 Receswsive disease, more information

Considered pedigree with a recessive condition. Assume that the frequency of mutation in the population is very low, 0.2%. What is the risk for the "?" child? How it compares with populational risk of the disease (compute RR)? If both parents test negatively at the test with 70% sensivity, how this modifies the risk prediction and RR?



Answer:

Based on phenotype only,
for father P(MN|data)=2/3
for mother P(MN|data) = 1/4

Use these posterior as prior utilizing the test information and consider hypotheses "both are MN" and "NOT"

	both MN	NO	
prior	0,1667	0,8333	
cond	0,1500	1,0000 Total	
joint	0,0250	0,8333	0,8583
post	0,0291	0,9709	

Risk for the child is 0.0291 x 1/4 = 0.0073