RELATIVE RISK ASSESSMENTS: The only individuals for whom relative risks can be applied for a simple autosomal recessive trait are affected dogs, or phenotypically normal individuals who are:

Parents of affected = 100% chance of being a carrier.

Offspring of affected (if not affected themselves due to mating to a carrier) = 100% chance of being a carrier.

Full-sibs of carriers = 50% chance of being a carrier.
Full-sib of affected, a) If cannot determine if affected or not (due to late onset disease or variable expressivity) = 75% chance of being a carrier.
b) If not affected = 67% chance of being a carrier. (2 out of 3 phenotypically normal appearing littermates will be carrier).

Offspring of carrier = 50% chance of being a carrier.

If an individual is a parent of a carrier, or a half-sib to a carrier, no objective risk assessment can be made, as it is not known which parent passed on the defective gene. It can only be confirmed that it is the breeding pair (parent of an obligate carrier) that passed on the defective gene. Without a further diagnosis that identifies which parent was the carrier, you can't penalize an individual based on who it was bred to. Objective risk must be based on definitive risk of carrier status.

If an individual has an undetermined risk (no known risk in the background), then the minimum calculable risk is 0%.

If an individual is affected, their risk of carrying the defective gene is 100%

An offspring of an individual will inherit 1/2 risk of the parent.

If there is risk from both parents:

The risk of being affected is the product of the risk from both parents:

S = risk of being carrier from the Sire.
D = risk of being carrier from the Dam.

Risk of being affected = S x D

The risk of being carrier depends on if you have knowledge of the affected or non-affected status of the individual :

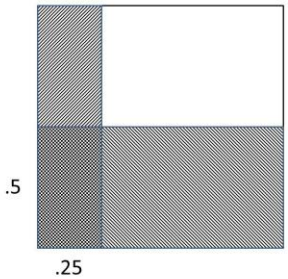
- If you **do not know** if the individual is affected or not, then:

- The risk of being a carrier is the sum of the risk from both parents, minus the risk of being affected.

Carrier Risk = S + D - (S x D)

Some people want to not subtract the affected risk from this calculation, mistakenly thinking that

the risk of being affected is not being taken into account. This is fallacious. The affected risk is being subtracted so that it is not being counted twice in a carrier risk assessment. The below matrix example shows why this is so:



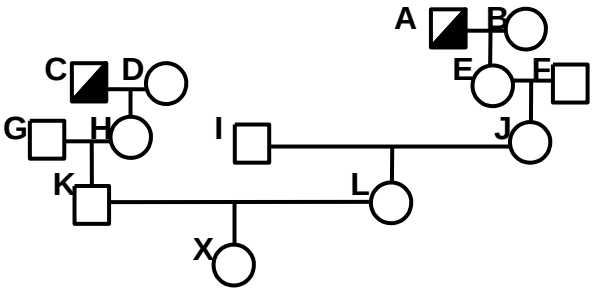
If the carrier risk from one parent is 50%, and the carrier risk from the other parent is 25%, the risk of being affected is 12.5% (in the double cross-hatched area). The risk of carrying the defective gene (including the risk of being affected) is .5 + .25 – (.5 x .25) = 62.5%, and the chance of being homozygous normal is 37.5%. If the risk of being affected is not subtracted in the calculation, the cross-hatched area is counted twice.

- If affected individuals cannot reproduce, or it is **known** that the individual is not affected, then:

$$\text{Carrier Risk} = \frac{S + D - (2\,(S \times D))}{1 - (S \times D)}$$

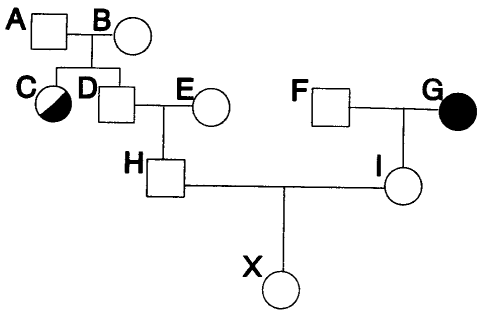
Examples: Assume that it is not known if individual X is affected.

1. Individuals A and C are carriers of simple autosomal recessive gene. What is the risk of individual X of being carrier? Of being affected?



-Individual H has a .50 chance of being a carrier from C.
-Individual K has a .25 chance of being a carrier from H.
-Individual X has a .125 chance of being a carrier from K.
-Individual E has a .50 chance of being a carrier from A.
-Individual J has a .25 chance of being a carrier from E.
-Individual L has a .125 chance of being a carrier from J.
-Individual X has a .063 chance of being a carrier from L.
The chance of individual X being affected = .125 X .063 = .0079 or 0.79%.
The chance of individual X being carrier = .125 + .063 - .0079 = .1801 or 18.01%

2. Individual C is a carrier, and individual G is affected with a simple autosomal recessive disorder. What are the risks of X being affected or a carrier?



-Individual D is a full sib to C, and has a .50 chance of being a carrier.
-Individual H has a .25 chance of being carrier from D.
-Individual X has a .125 chance of being carrier from H.
-Individual I is a carrier, being an offspring of G.
-Individual X has a .50 chance of being a carrier from I.

The chance of individual X being affected = .125 X .5 = .0625 or 6.25%.
The chance of individual X being a carrier = .125 + .5 - .0625 = .5625 or 56.25%.

Note that these relative risk assessments only take into account the known carrier and affected individuals in the pedigree. Therefore, these estimates give the minimum risk assessment based on the information available. Pedigree analysis can never clear an animal of being a carrier unless test matings have been performed (see next section).

At the end of the syllabus, is a page of relative risk analysis problems, and the following page are the answers. Practice these in preparation of your take home (graded) homework assignment.

The clinical use of relative risk pedigree analysis

-Breed a superior quality higher-risk individual to a lower risk individual, resulting in offspring lower than the average risk for the breed.
-Replace the higher-risk parent with a lower-risk offspring that equals or exceeds it in quality in the next generation.
-Pros:
- Allows breeders with higher-risk breeding stock to lower their risk
- Allows breeders to understand their own risk, and that of their proposed matings
- Objectifies risk relative to the population

-Cons:
- Selects against families, based on relatives with risk
- Selects against carrier and normal individuals