

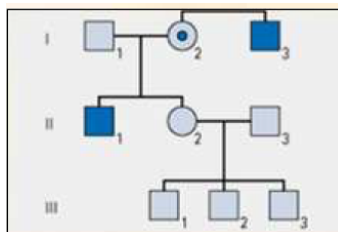
This may be modified by **posterior information**, usually based on number of offspring and/or the results of tests, allowing **conditional probabilities** to be determined.

The resulting probability for each event or outcome is known as its **joint probability**. The final probability for each event = **its posterior or relative probability**

Obtained by dividing the joint probability for the event by the sum of all the joint probabilities.



## Bayesian risk calculation



- XR disorder with two affected males  $I_3$  and  $II_1$
- Sister  $II_2$  of one of the men wishes to know if she is a carrier
- Bayesian calculation reduces her odds from  $1/2$  to  $1/9$

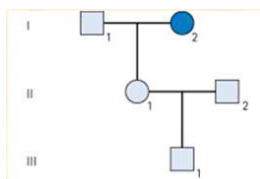
| Probability        | $II_2$ is a carrier | $II_2$ is not a carrier |
|--------------------|---------------------|-------------------------|
| Prior              | $1/2$               | $1/2$                   |
| Conditional        |                     |                         |
| Three healthy sons | $(1/2)^3 = 1/8$     | $(1)^3 = 1$             |
| Joint              | $1/16$              | $1/2 = 8/16$            |
| Expressed as odds  | 1 to                | 8                       |
| Posterior          | $1/9$               | $8/9$                   |

## Autosomal dominant inheritance

### AD disorder with reduced penetrance

Hereditary retinoblastoma has penetrance of  $P = 0.8$

80% of heterozygotes express the condition in some way. The probability that the child of an affected individual ( $II_1$ ) will be affected will be  $\frac{1}{2} \times P = 0.4$



What's the risk reduction for the future child ( $III_1$ ) of such a person?

Can use either a **logical approach** or **Bayes' theorem** to calculate the risk of being affected

("Although it holds true that for many disorders, risk assessment simply involves the provision of a straightforward D or R recurrence risk, and that does still apply in some situations today, but increasing awareness of the complexity and heterogeneity of genetic disease has focused attention on the importance of taking other factors such as reduced penetrance and delayed age of onset, into account. Additionally, the use of linked DNA markers serve to complicate rather than simplify risk calculations that require careful consideration and a relatively high level of numerical competence if the provision of incorrect information is to be avoided – introduction to risk calculation in genetic counselling, **Ian D. Young, 2007**, 3<sup>rd</sup> ed, oxford university press.. (see molc Ecol for right reference)