

Genetics:

Risk Assessment 1

NOTE: when using the term "and" we multiply, & when using the term "or" we add.
 "AND" → ×
 "OR" → +

- What is the probability that if a couple has 4 children that all 4 will be males?

Ans: 1/16

*the probability of each child to be a male is 1/2, since it is an independent event.

$$P(\text{all males}) = \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} = \frac{1}{16}$$

↑ ↑ ↑ ↑
child 1 child 2 ...

- What is the probability that if a couple has 4 children that all 4 will be females?

Ans: 1/16

*the probability of each child to be a female is 1/2, since it is an independent event.

$$P(\text{all females}) = \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} = \frac{1}{16}$$

- What is the probability that if a couple has 4 children that all 4 will be the same gender?

Ans: 2/16

probability all are males + probability all are females

$$= \frac{1}{16} + \frac{1}{16} = \frac{2}{16}$$

↳ all of them are females
 OR
 all 4 are males.

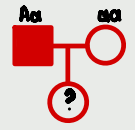
- A woman has a father who died from Huntington's disease. What is the probability that she will develop the symptoms of the disease? (hint: draw or think of a pedigree for those types of questions)

Ans: 1/2

*Remember: Huntington's disease is autosomal dominant therefore any affected individual is assumed to be heterozygous unless indicated otherwise.

* If not mentioned, we assume the individual is unaffected (woman's mother in this case).

In other words, the individual is normal unless indicated otherwise.



* We can draw a Punnett square to predict the outcomes.

	A	a
a	Aa	aa
a	Aa	aa

⇒ 50% odds that the daughter will be affected (Huntington's is a late-onset disease, so even though the woman is unaffected at this point, she might still develop the disease later)

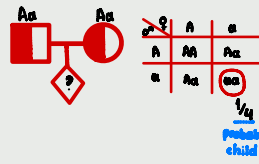
- A couple were both tested and found to be carriers of the Cystic Fibrosis gene. If they have 2 children:

this means that they underwent genetic testing

- What is the chance that both will be affected by Cystic Fibrosis?

Ans: 1/16

• mode of inheritance for CF is autosomal recessive.
 • we can approach this Q by solving for the probability of 1 child at first.



• Ans = probability of 1st child affected * 2nd child affected = $\frac{1}{4} * \frac{1}{4} = \frac{1}{16}$

• another way into Punnett square:
 odds of the father to pass "a" = $\frac{1}{2}$
 odds of the mother to pass "a" = $\frac{1}{2}$
 therefore the odds of passing both mutant alleles "aa" to 1 child is $\frac{1}{4}$
 $\frac{1}{2} * \frac{1}{2}$

• odds for 2 children affected is $\frac{1}{16} \rightarrow \frac{1}{4} * \frac{1}{4}$ child 1 child 2

- What is the chance that both will be carriers?

Ans: 1/4

• genotype of a carrier is Aa.
 • probability of 1 child to be a carrier = $\frac{1}{2}$

probability of both children to be carriers = $\frac{1}{2} * \frac{1}{2} = \frac{1}{4}$

child 1 child 2

- what is the chance that they will have 2 girls that are both affected by Cystic Fibrosis?

Ans: 1/64

• Ans = probability of a girl * probability she is affected * probability of another girl * probability she is affected

child #1 child #2

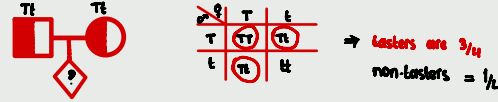
= $\frac{1}{2} * \frac{1}{4} * \frac{1}{2} * \frac{1}{4}$

= $\frac{1}{64}$

- The ability to taste the chemical PTC is determined by a single gene in humans with the ability to taste given by the dominant allele “T” and the inability to taste by the recessive allele “t”. Suppose two heterozygous tasters (Tt) have a large family:

- Predict the proportion of their children who will be tasters & non-tasters. Use a Punnett square to illustrate how you make these predictions.

Ans: 3/4



- What is the likelihood that their first child will be a taster?

Ans: 3/4

- What is the likelihood that their fourth child will be a taster?

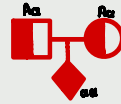
Ans: 3/4 → same probability as 1st child (independent event)

- For a Caucasian couple with no family history, what is the chance they will have a child with Cystic Fibrosis? Knowing that Caucasian population carrier frequency is 1/25.

Ans: 1/2500

- in this Q, there's NO information mentioning that the parents underwent genetic testing nor mentioning someone is affected.
- carrier frequency = 1/25 means that out of 25 people from the Caucasian population 1 of them will be a carrier.

- we assume both parents are unaffected.
- to have an affected child "aa", at least both parents should be carriers "Aa".



Ans = father carrier \times pass "a" to child \times mother carrier \times pass "a" to child

$$= \frac{1}{25} \times \frac{1}{2} \times \frac{1}{25} \times \frac{1}{2}$$

$$= \frac{1}{2500}$$

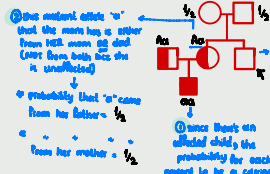
- probability of affected child = $\frac{1}{2} \times \frac{1}{2} = \frac{1}{4}$
- odds of the father being a carrier = $\frac{1}{25}$
- odds of the mother being a carrier = $\frac{1}{25}$

- For a Caucasian couple with diagnosis of CF in the mother's nephew. What is the risk for the fetus? (carrier frequency is 1/25)

Ans: 1/200

(best explanation for this Q is in "Risk assessment 2" lecture, minutes 6:50)

before answering the Q, there's a point to discuss: assume an individual who didn't perform genetic testing BUT his sibling (i.e. sister) has an affected child. What is the probability for this individual to be a carrier? (assume the disease is autosomal recessive)



if the individual is a carrier \rightarrow probability for this individual to be a carrier: 1/2 (How?)

either take "a" from the mom: mom to be a carrier AND pass "a" to the son = $\frac{1}{2} \times \frac{1}{2} = \frac{1}{4}$

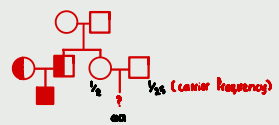
OR take "a" from his dad: dad to be a carrier AND pass "a" to his son = $\frac{1}{2} \times \frac{1}{2} = \frac{1}{4}$

\rightarrow Ans = $\frac{1}{4} + \frac{1}{4} = \frac{1}{2}$

from the mother + from the father

Conclusion: if any niece/nephew is affected with a recessive disease, the odds that I will be a carrier is 1/2

Now back to the Q, based on the conclusion of the discussion, the mother of the fetus has a 50% chance to be a carrier since her nephew is affected.



Ans = mom is a carrier \times pass "a" to fetus \times father is a carrier \times pass "a" to fetus

$$= \frac{1}{2} \times \frac{1}{2} \times \frac{1}{25} \times \frac{1}{2}$$

$$= \frac{1}{2000}$$

Note that the risk increased when there's a family history compared to the population

Additional Q: What is the risk for the same couple to have an affected female? (this Q is in slide # 8)

Ans = $\frac{1}{2000} \times \frac{1}{2} = \frac{1}{4000}$

2 affected females? \rightarrow Ans = $(\frac{1}{2000})^2$

Genetics:

Risk Assessment 2

- A father from a Caucasian couple was tested and found to be a carrier of the CF gene:

(carrier frequency 1/25)

- What is the probability that they will have an affected child?

Ans: 1/100

* In order to have an affected child, the child would

have 2 mutant alleles (1 from each parent)

→ odds for the father to be a carrier = 1, if he is a carrier → odds to pass mutant allele = $\frac{1}{2}$
 → odds that the mom is a carrier = $\frac{1}{25}$, if she is a carrier → odds to pass mutant allele = $\frac{1}{2}$

$$\text{Ans} = 1 * \frac{1}{2} * \frac{1}{25} * \frac{1}{2} = \frac{1}{100}$$

↳ the father is 100% a carrier
his probability of being a carrier is 1.

* the mother wasn't genetically tested, her probability to be a carrier is like any other individual from the population (carrier frequency)

- What is the probability that they will have 2 affected children?

Ans: $(1/100)^2$

Ans = probability of an affected child * probability of another affected child

$$= \frac{1}{100} * \frac{1}{100}$$

↳ from the answer above

$$= \left(\frac{1}{100}\right)^2$$

- What is the probability that they will have an affected girl?

Ans: 1/200

Ans = probability of an affected child * probability of having a girl

$$= \frac{1}{100} * \frac{1}{2}$$

$$= \frac{1}{200}$$

- For a Caucasian couple with diagnosis of CF in the mother's nephew:

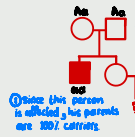
- What is the probability that the fetus is a female and is affected? (carrier frequency is 1/25)
Ans: 1/400

check the additional Q in slide #5 (same)

- What is the probability that they will have 2 affected females? (carrier frequency is 1/25)
Ans: $(1/400)^2$

- For a couple with the diagnosis of CF in the father's brother. What is the risk for the fetus?

Ans: 1/150



	A	a
A	AA	Aa
a	Aa	aa

Based on the pedigree, the father is NOT affected, therefore we exclude "aa" as a possibility from our calculations.

The probability that the father of the fetus is a carrier = $\frac{2}{3}$

Note that the father's probability increased when his brother was affected, which is also higher than the probability if his niece/nephew was affected.

Example: if an unaffected father came to your clinic & informed you that his parents are carriers for an AR disease, you will NOT tell him that his chance to be affected is $\frac{1}{4}$ since he is already unaffected. (symptoms would have appeared earlier in life)

① Ans = Father is a carrier * pass "a" to fetus * mother is a carrier * pass "a" to fetus

$$= \frac{2}{3} * \frac{1}{2} * \frac{1}{25} * \frac{1}{2}$$

$$= \frac{1}{150}$$

(Carrier frequency)

$\frac{1}{150} > \frac{1}{200}$ compared to Q2 in slide #6 the chance here is higher since the uncle is relatively closer to the fetus than his cousin.

Take home message: If my brother is affected, the odds for me to be a carrier: $\frac{2}{3}$. If my niece/nephew is affected, the odds for me to be a carrier: $\frac{1}{2}$.