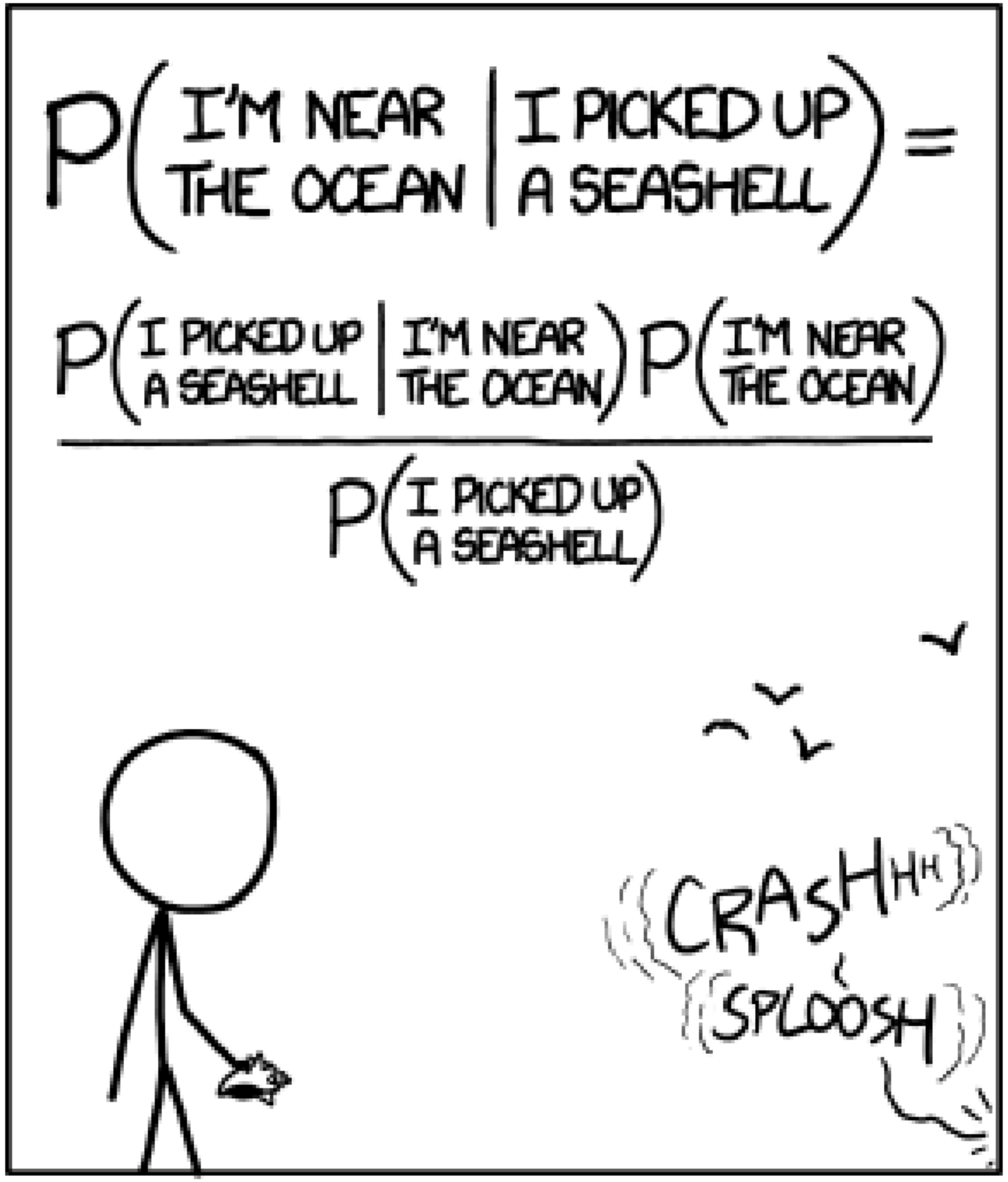


STATISTICALLY SPEAKING, IF YOU PICK UP A SEASHELL AND *DON'T* HOLD IT TO YOUR EAR, YOU CAN PROBABLY HEAR THE OCEAN.

Lecture 03

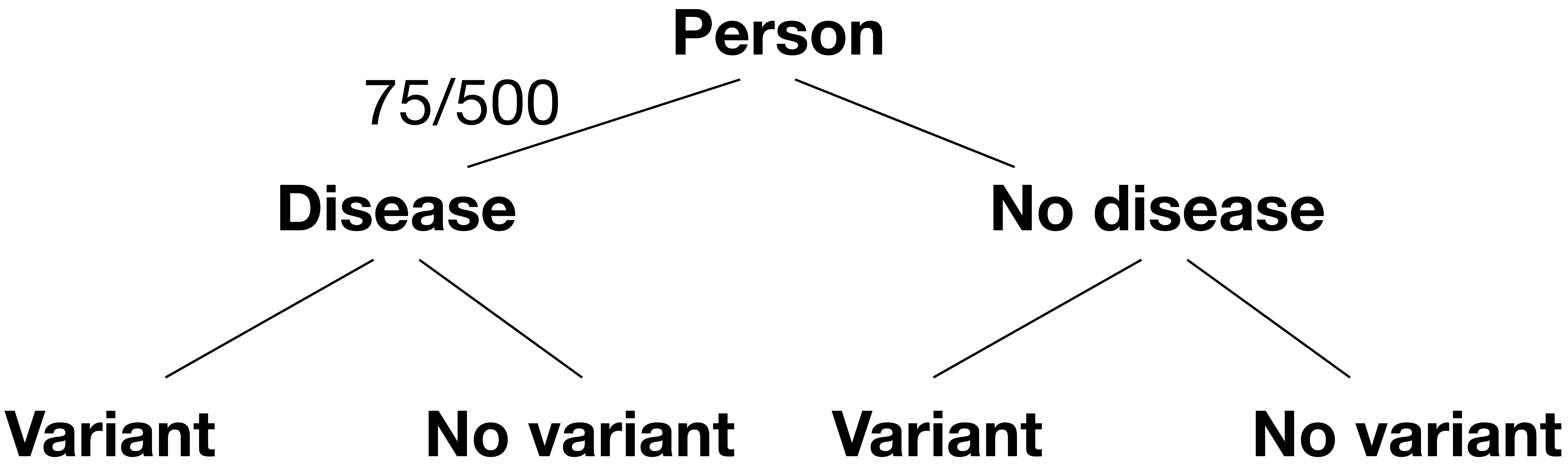
9.28.21

Cr: XKCD

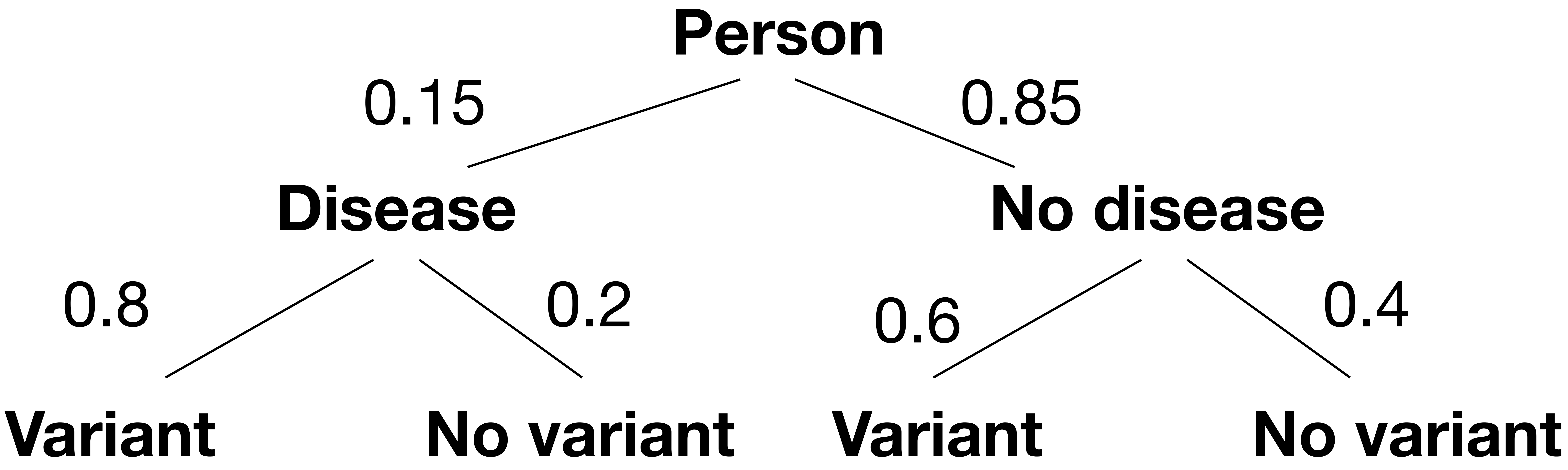
Refresher Quiz

Suppose you have a sample of 500 individuals. 75 of these individuals have a rare genetic disease and you identified a genetic variant that might be associated with this disease. 80% of individuals with the disease and 60% of individuals without the disease have the genetic variant. What is the probability of randomly selecting an individual with the variant?

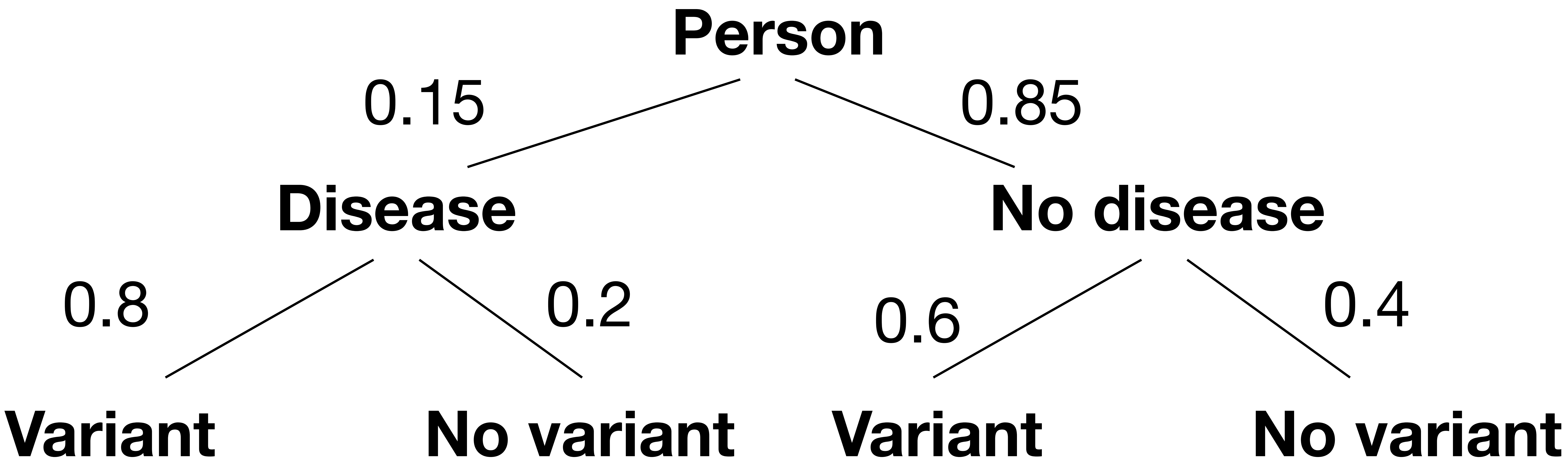
Suppose you have a sample of 500 individuals. 75 of these individuals have a rare genetic disease and you identified a genetic variant that might be associated with this disease. 80% of individuals with the disease and 60% of individuals without the disease have the genetic variant. What is the probability of randomly selecting an individual with the variant?



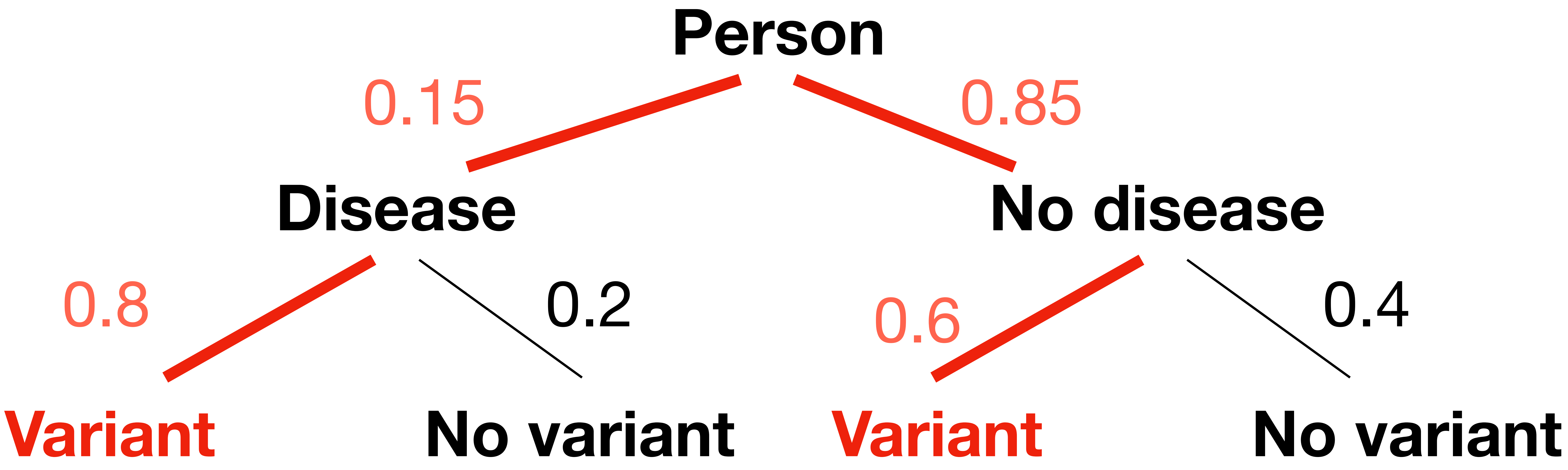
Suppose you have a sample of 500 individuals. 75 of these individuals have a rare genetic disease and you identified a genetic variant that might be associated with this disease. 80% of individuals with the disease and 60% of individuals without the disease have the genetic variant. What is the probability of randomly selecting an individual with the variant?



Suppose you have a sample of 500 individuals. 75 of these individuals have a rare genetic disease and you identified a genetic variant that might be associated with this disease. 80% of individuals with the disease and 60% of individuals without the disease have the genetic variant. What is the probability of randomly selecting an individual with the variant?

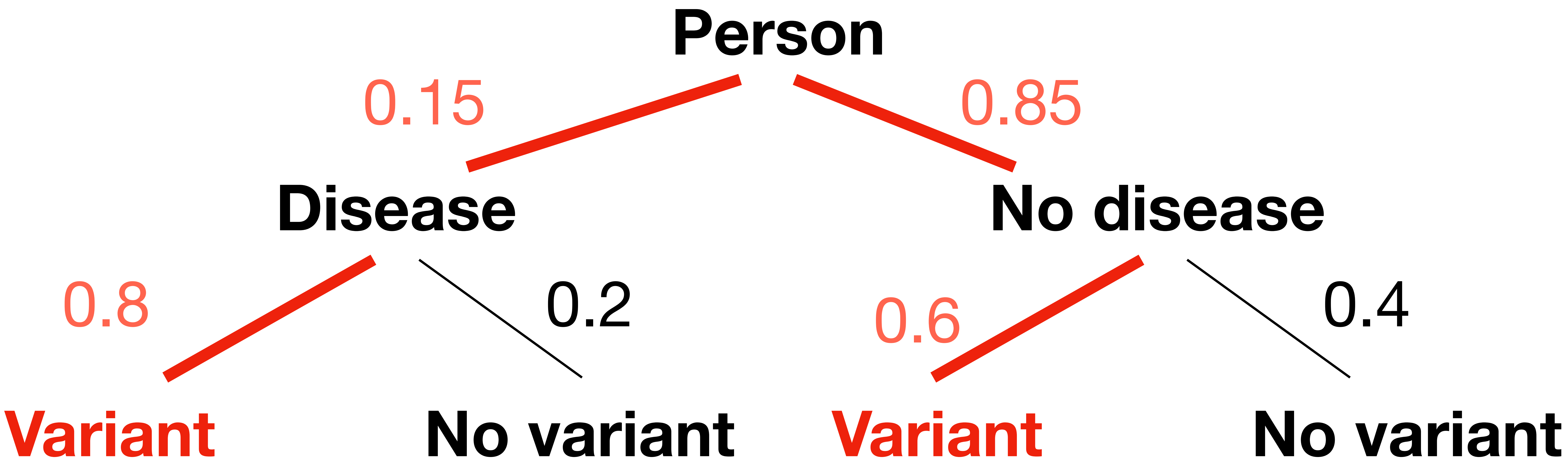


Suppose you have a sample of 500 individuals. 75 of these individuals have a rare genetic disease and you identified a genetic variant that might be associated with this disease. 80% of individuals with the disease and 60% of individuals without the disease have the genetic variant. **What is the probability of randomly selecting an individual with the variant?**



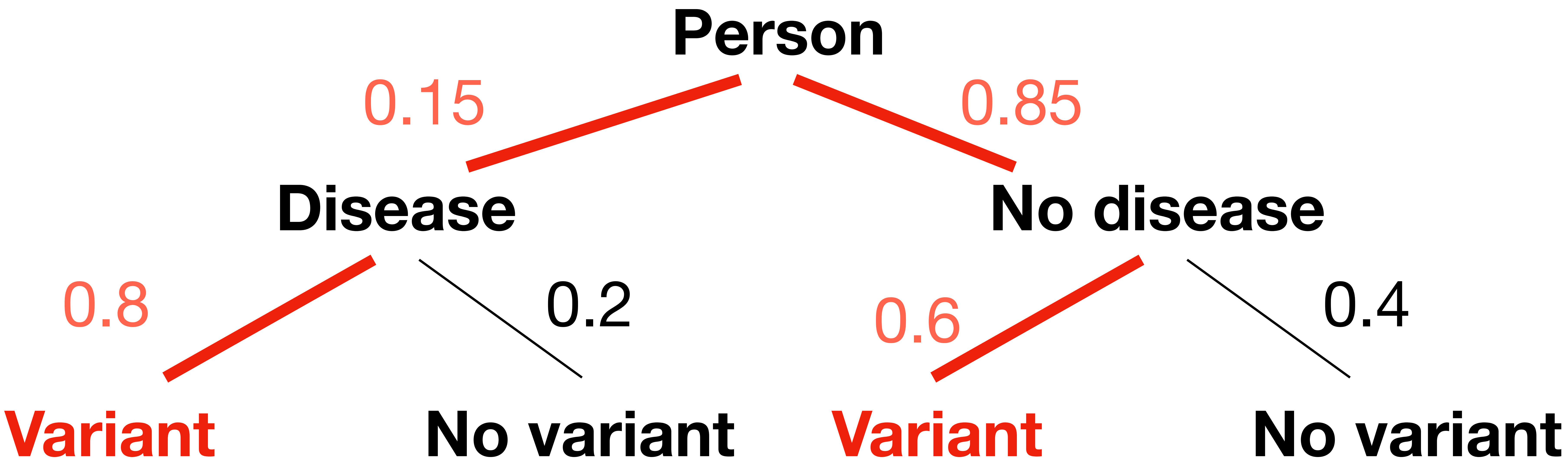
$$\Pr\{\text{variant}\} = \Pr\{\text{variant} \mid \text{disease}\} + \Pr\{\text{variant} \mid \text{no disease}\}$$

Suppose you have a sample of 500 individuals. 75 of these individuals have a rare genetic disease and you identified a genetic variant that might be associated with this disease. 80% of individuals with the disease and 60% of individuals without the disease have the genetic variant. **What is the probability of randomly selecting an individual with the variant?**



$$\Pr\{\text{variant}\} = (0.15)(0.8) + \Pr\{\text{variant} \mid \text{no disease}\}$$

Suppose you have a sample of 500 individuals. 75 of these individuals have a rare genetic disease and you identified a genetic variant that might be associated with this disease. 80% of individuals with the disease and 60% of individuals without the disease have the genetic variant. What is the probability of randomly selecting an individual with the variant?



$$\Pr\{\text{variant}\} = (0.15)(0.8) + (0.85)(0.6) \quad = 0.63$$

	Income			
	Low	Medium	High	Total
Stressed	526	274	216	**1,016**
Not stressed	1,954	1,680	1,899	**5,533**
Total	**2,480**	**1,954**	**2,115**	**6,549**

Given that someone in this study is from the highest income group, what is the probability that the person is stressed?

$$\Pr\{\text{Stressed} \mid \text{High income}\} = \frac{\#\ \text{Stressed (High income)}}{\#\ \text{Total (High income)}} = \frac{216}{2{,}115} = 10.21\%$$

$$\boxed{\mathit{Pr\{B \mid A\} = Pr\{A\ and\ B\} \,/\, Pr\{A\}}}$$

What is the probability of randomly selecting an individual who is male and loves chocolate?

Gender	Vanilla	Chocolate	Strawberry	Total
Male	47	15	29	**91**
Female	48	32	29	**109**
Total	**95**	**47**	**58**	**200**

Disjoint or non-disjoint?

What is the probability of randomly selecting an individual who is male and loves chocolate?

Gender	Vanilla	Chocolate	Strawberry	Total
Male	47	15	29	**91**
Female	48	32	29	**109**
Total	**95**	**47**	**58**	**200**

Disjoint or **non-disjoint**?

Pr{A and B} = Pr{A} x Pr{B | A}

Pr{Male + Chocolate} = Pr{Male} * Pr{Chocolate | Male}

(91/200) **(15/91)** **= 0.075**

What is the probability of randomly selecting an individual who is male and loves chocolate?

Gender	Vanilla	Chocolate	Strawberry	Total
Male	47	15	29	**91**
Female	48	32	29	**109**
Total	**95**	**47**	**58**	**200**

Independent or dependent?

Pr{B | A} = Pr{B} (for independent events)

Pr{Chocolate | Male} ? Pr{Chocolate}

$$\mathbf{(15/91)} \neq \mathbf{(15/47)}$$

What is the probability of randomly selecting an individual who is male and loves chocolate?

Gender	Vanilla	Chocolate	Strawberry	Total
Male	47	15	29	**91**
Female	48	32	29	**109**
Total	**95**	**47**	**58**	**200**

Independent or **dependent**?

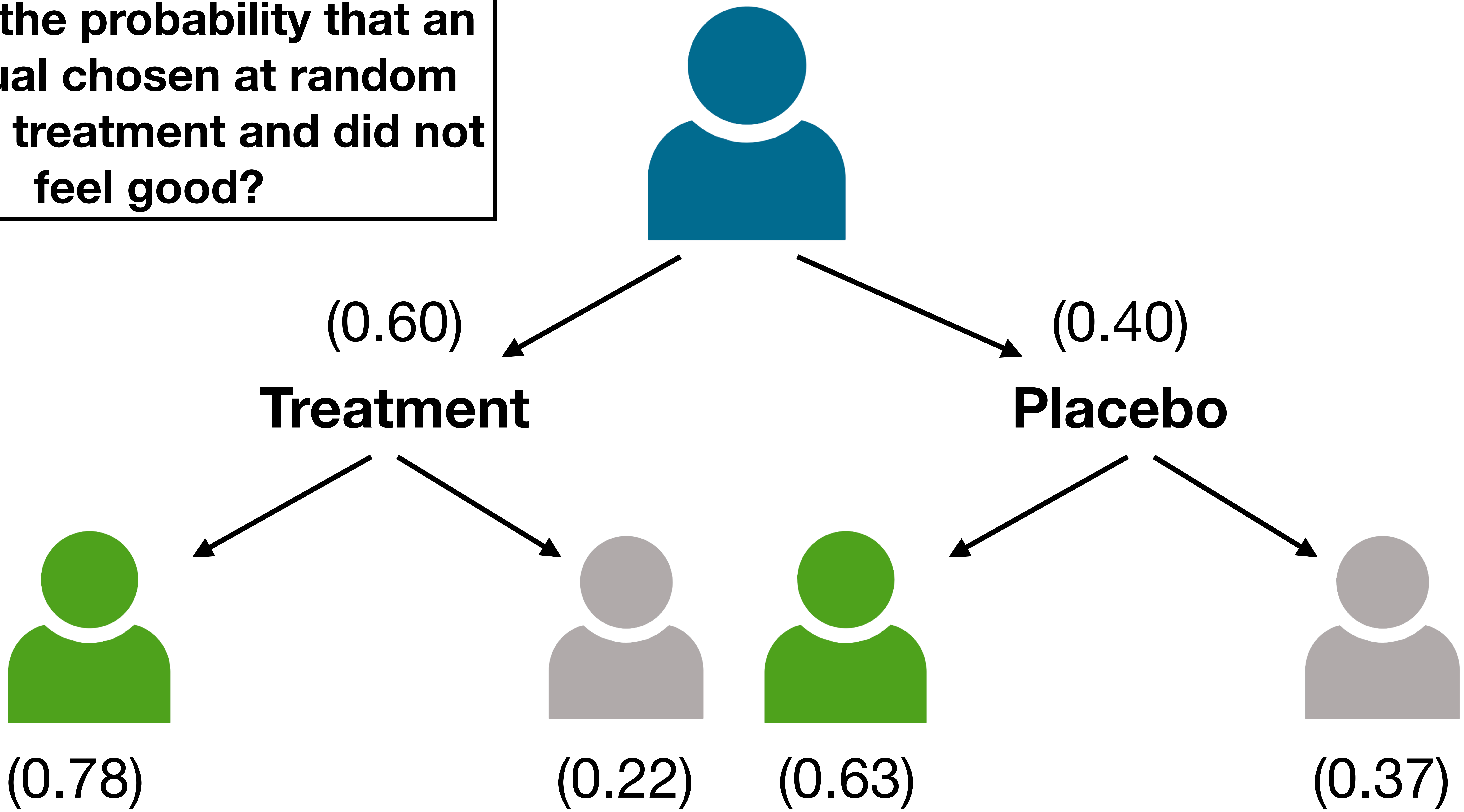
Pr{B | A} = Pr{B} (for independent events)

Pr{Chocolate | Male} ? Pr{Chocolate}

$$(15/91) \neq (15/47)$$

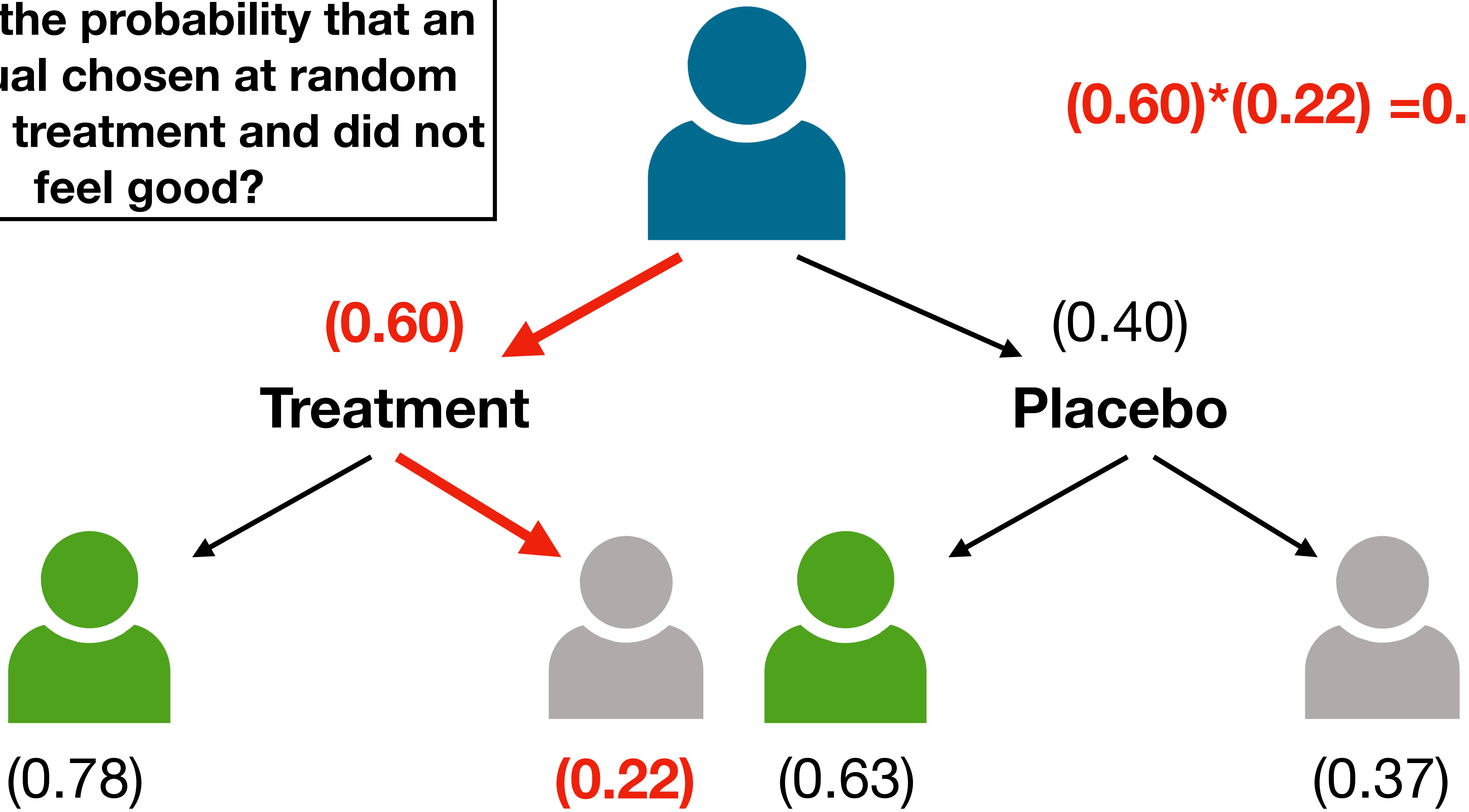
Conditional probability with Bayes' Theorem

What is the probability that an individual chosen at random received treatment and did not feel good?



Conditional probability with Bayes’ Theorem

What is the probability that an individual chosen at random received treatment and did not feel good?

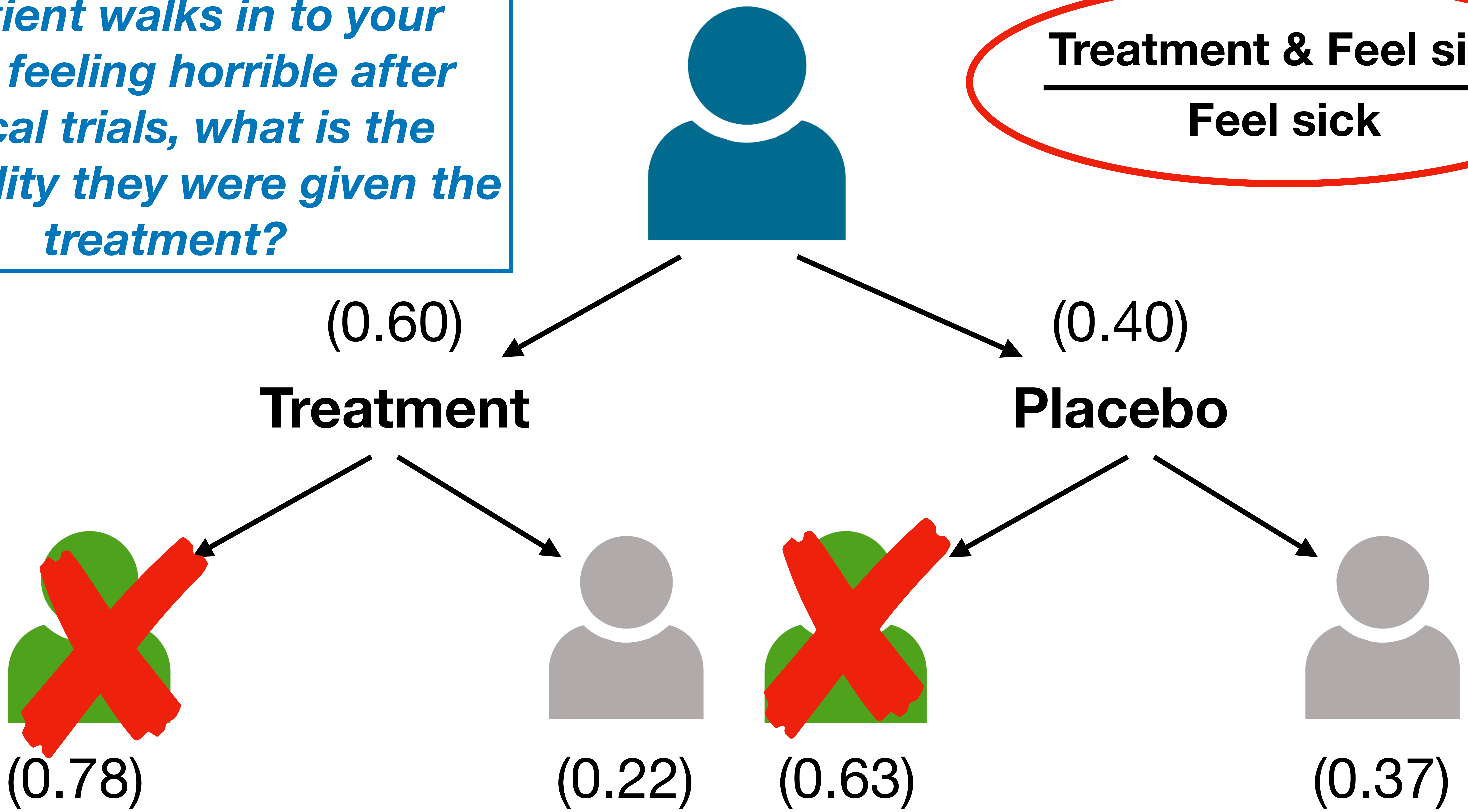


(0.60)*(0.22) =0.132

Conditional probability with Bayes' Theorem

A patient walks in to your office feeling horrible after clinical trials, what is the probability they were given the treatment?

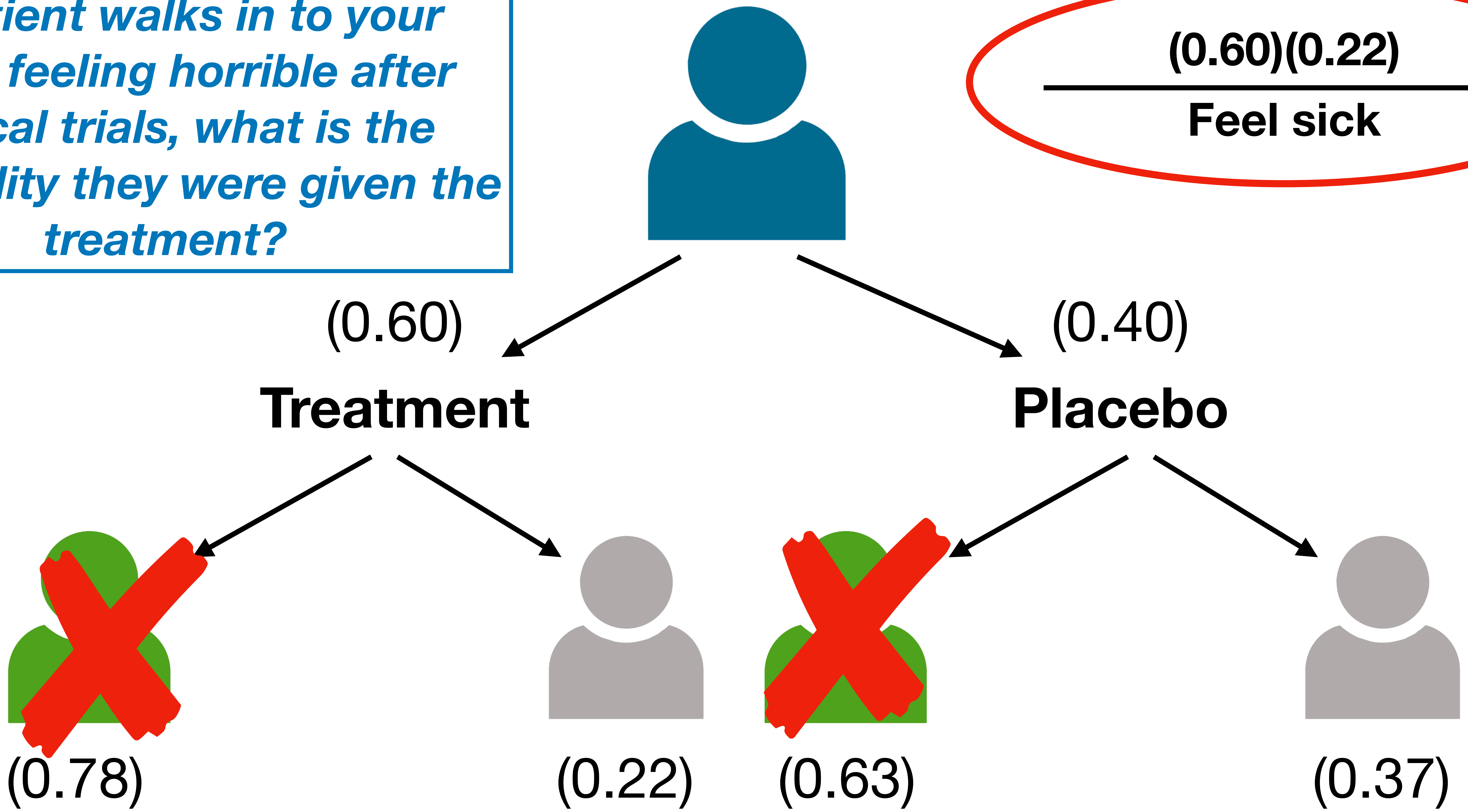
$$\frac{\textbf{Treatment \& Feel sick}}{\textbf{Feel sick}}$$



Conditional probability with Bayes' Theorem

A patient walks in to your office feeling horrible after clinical trials, what is the probability they were given the treatment?

$$\frac{(0.60)(0.22)}{\textbf{Feel sick}}$$

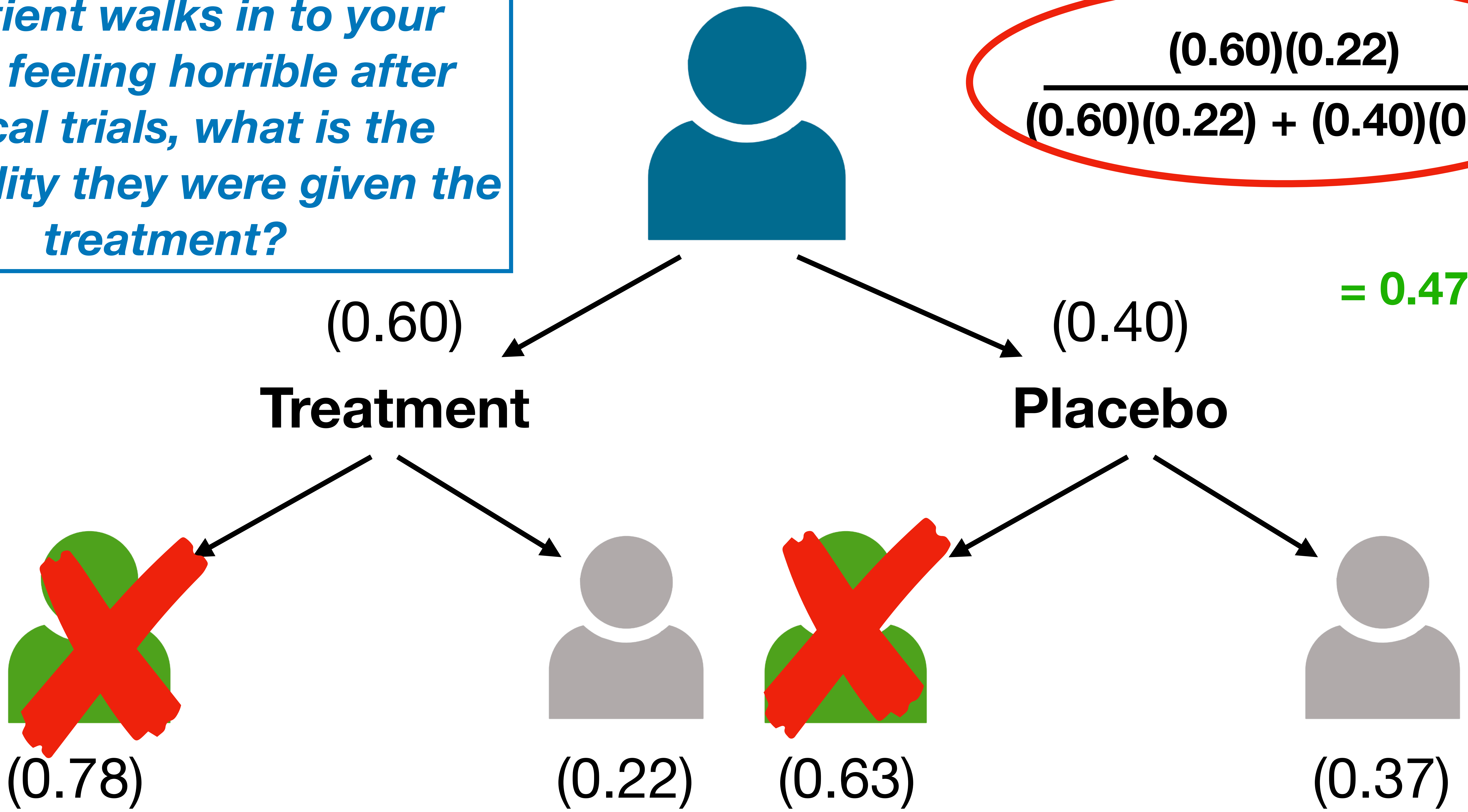


Conditional probability with Bayes' Theorem

A patient walks in to your office feeling horrible after clinical trials, what is the probability they were given the treatment?

$$\frac{(0.60)(0.22)}{(0.60)(0.22) + (0.40)(0.37)}$$

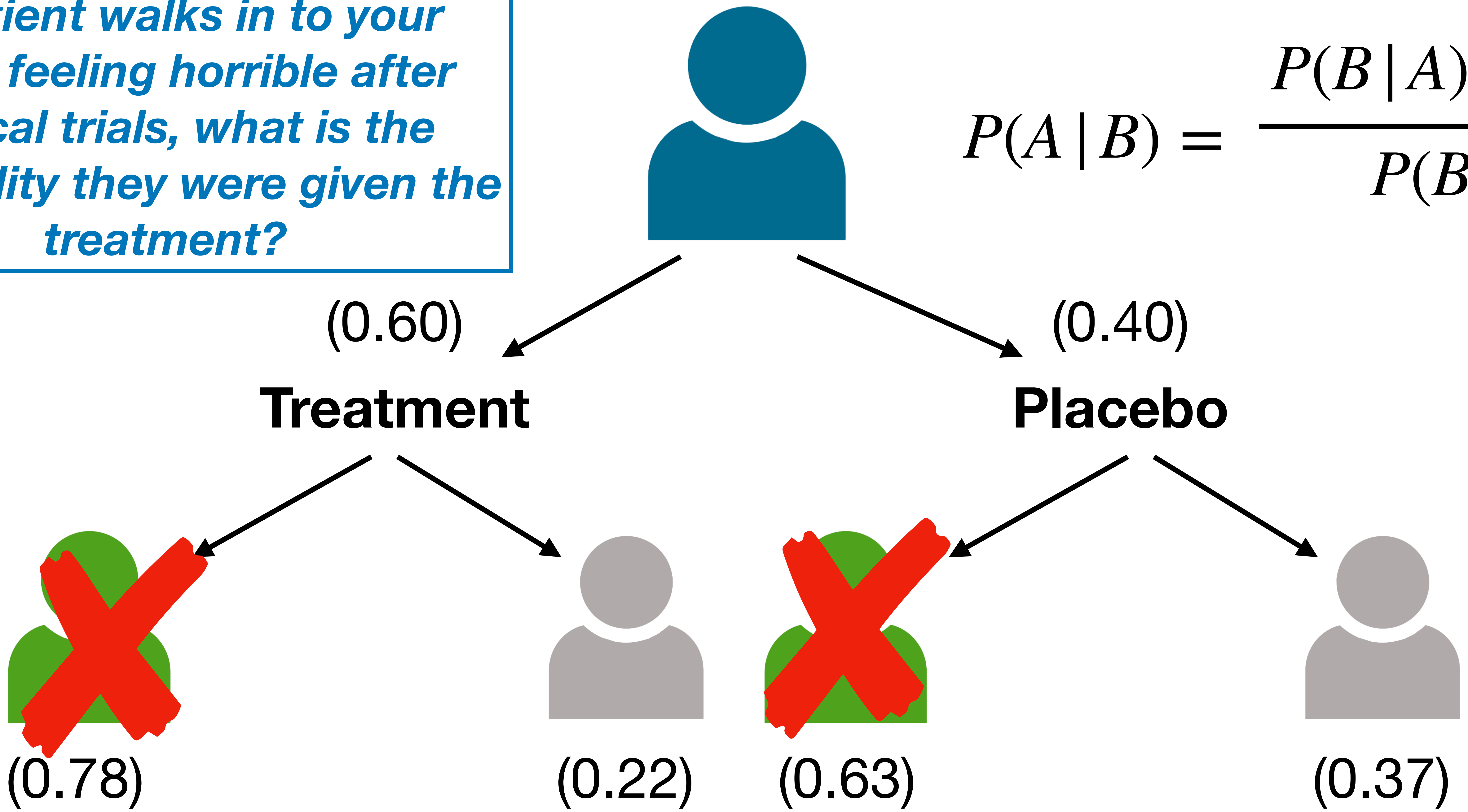
= 0.471



Conditional probability with Bayes' Theorem

A patient walks in to your office feeling horrible after clinical trials, what is the probability they were given the treatment?

$$P(A \mid B) = \frac{P(B \mid A)P(A)}{P(B)}$$



Conditional probability with Bayes' Theorem

"The probability of A given B"

$$P(A|B) = \frac{P(B|A)P(A)}{P(B)}$$

"Posterior"

"Likelihood"

"Prior"

"Evidence"

Conditional probability with Bayes' Theorem

A patient walks in to your office feeling horrible after clinical trials, what is the probability they were given the treatment?

"The probability of A given B"

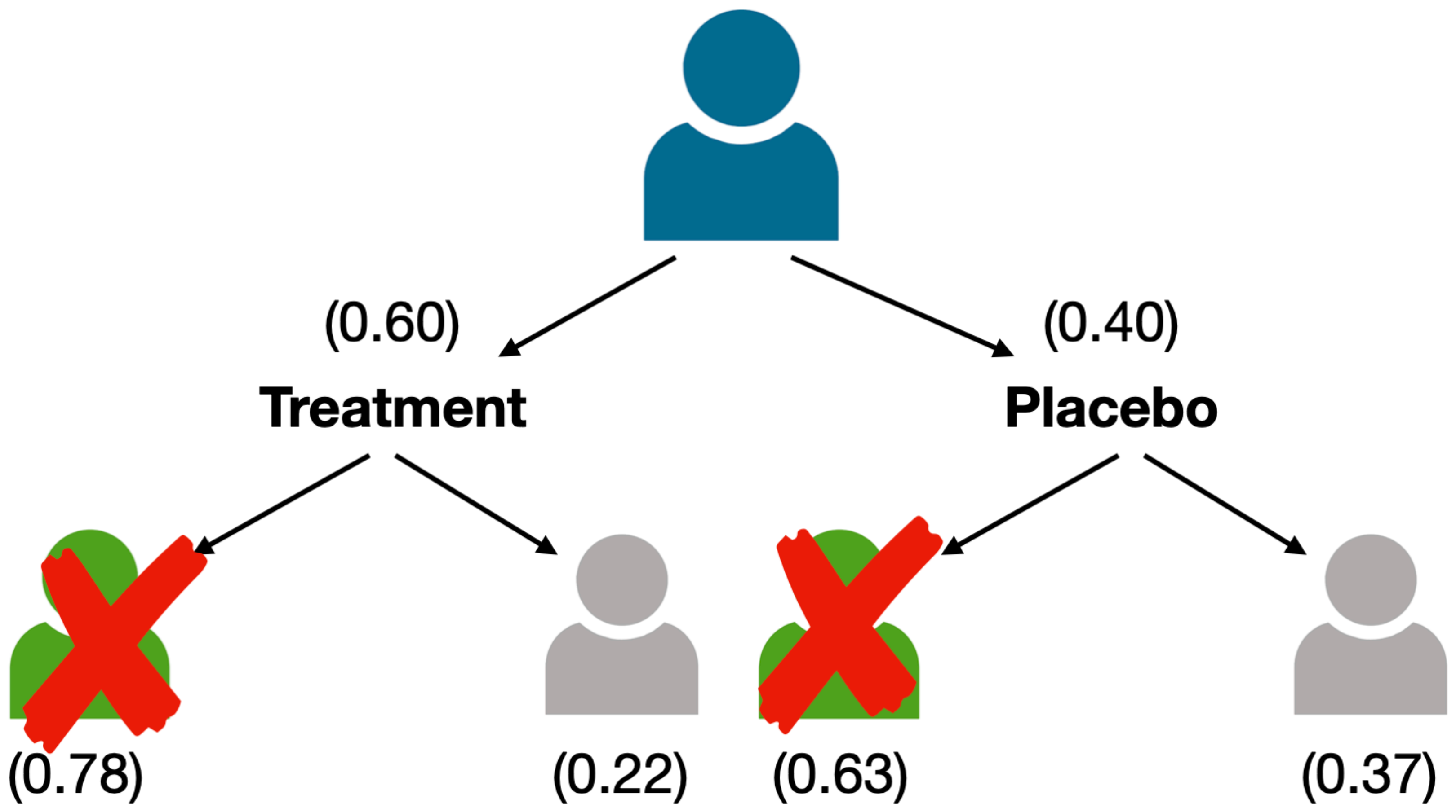
A: treatment;
B: feeling sick

$$P(A\,|\,B) = \frac{P(B\,|\,A)P(A)}{P(B)}$$

0.60

(0.60)(0.22) + (0.40)(0.37)

0.22



$$\mathbf{\frac{(0.60)(0.22)}{(0.60)(0.22) + (0.40)(0.37)}}$$

- Scenario: I always get itchy eyes and runny nose when I am around cats. Let's say I decide to get allergy tested:
  - The test is positive 80% of the time for people with allergies
  - The test is positive 10% of the time for people without allergies
- If 1% of the population has allergies and my test came back positive, what is the probability that I have allergies?

Contingency Table

Probability Tree

Bayes' Theorem

Probability Tree

- Scenario: I always get itchy eyes and runny nose when I am around cats. Let's say I decide to get allergy tested:
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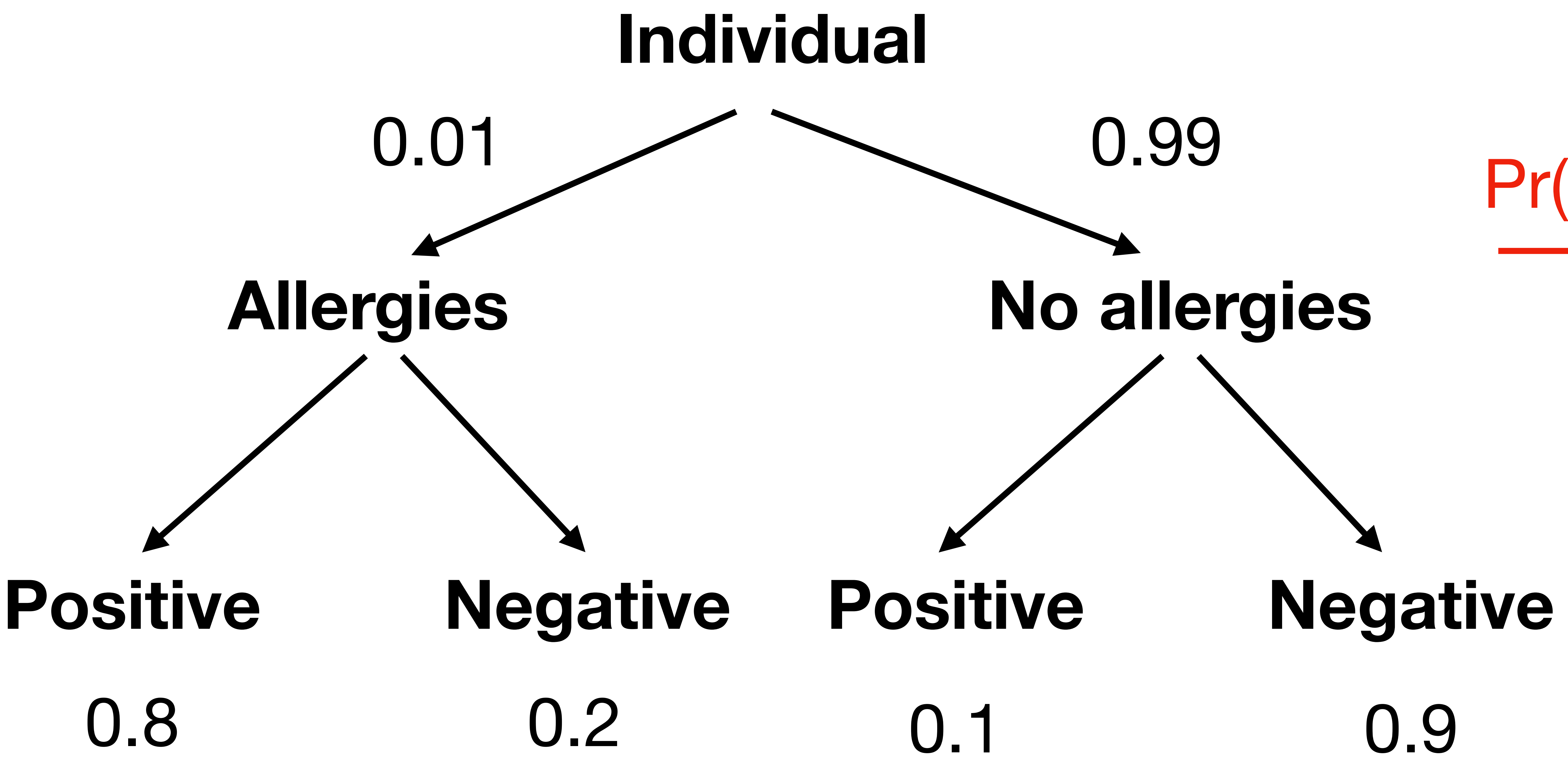

$$\frac{\Pr(\text{allergies + positive})}{\Pr(\text{positive})}$$

- Scenario: I always get itchy eyes and runny nose when I am around cats. Let’s say I decide to get allergy tested:
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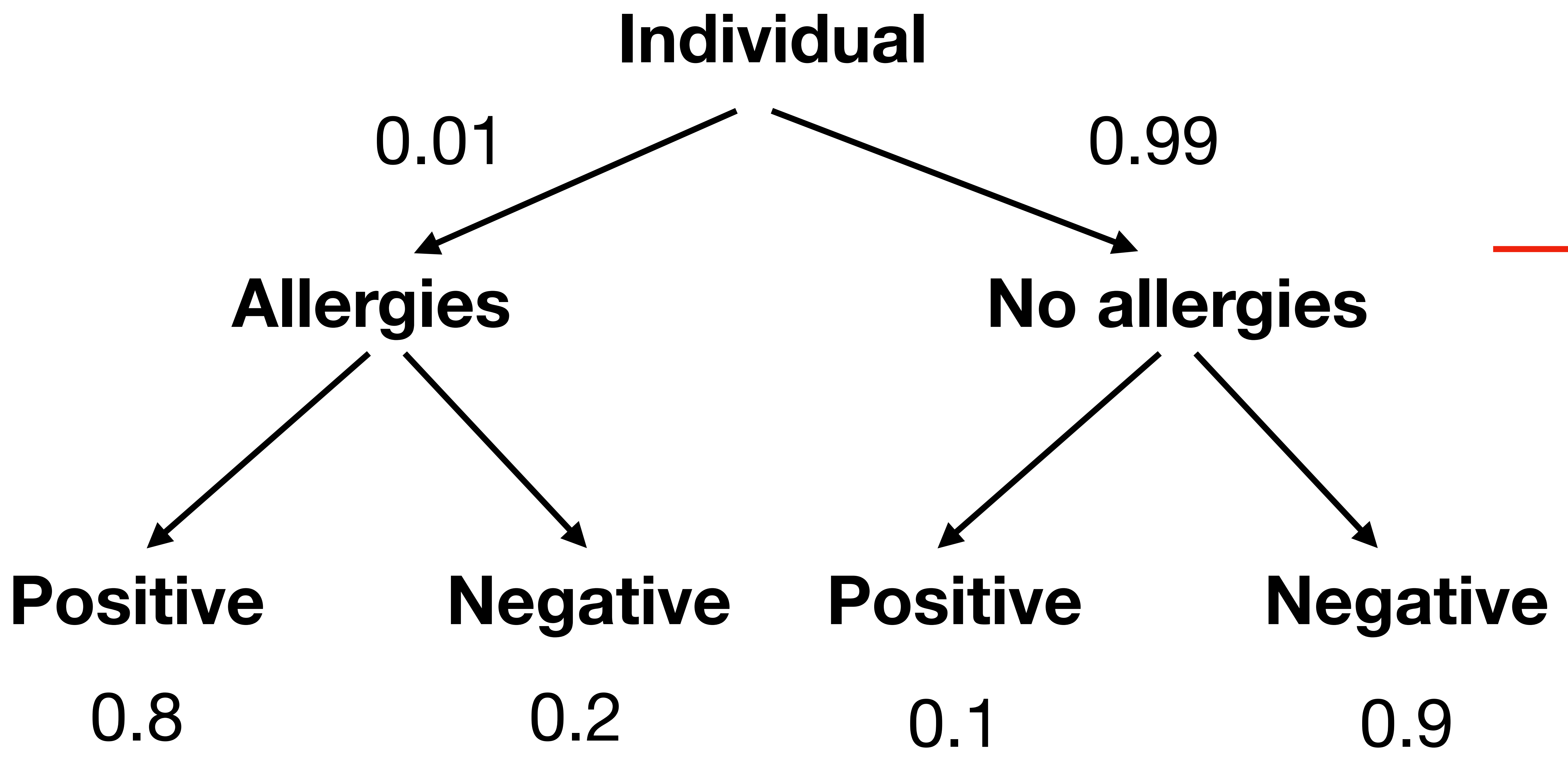
Probability Tree



$$\frac{(0.01)(0.8)}{\Pr(\text{positive})}$$

- Scenario: I always get itchy eyes and runny nose when I am around cats. Let's say I decide to get allergy tested:
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  - The test is positive 10% of the time for people without allergies
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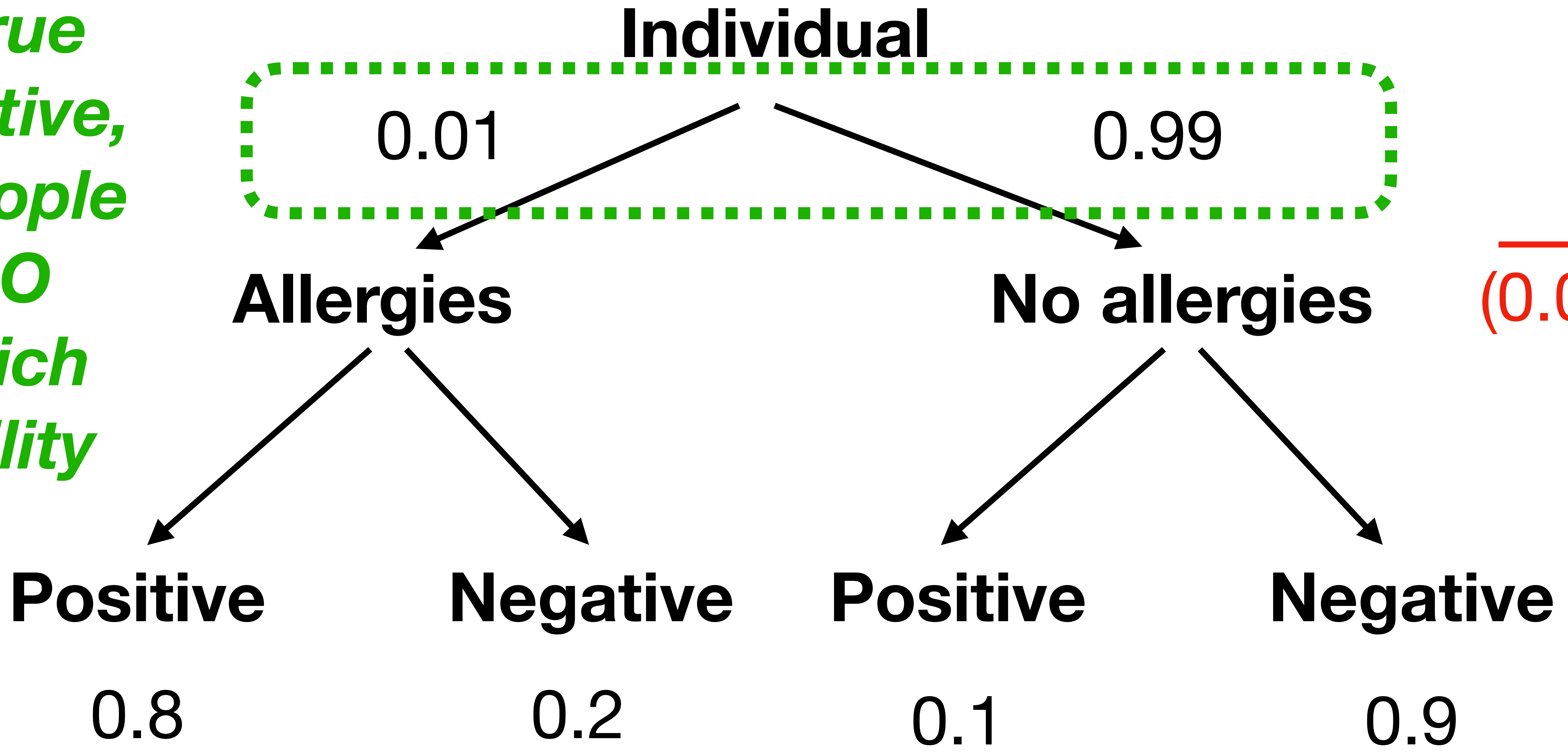
Probability Tree

Even though the true positive > false positive, the initial rate of people with allergies is SO MUCH LOWER which affects the probability



$$\frac{(0.01)(0.8)}{(0.01)(0.8) + (0.99)(0.1)}$$

$$= 7.4\%$$

$\boxed{????}$

- Scenario: I always get itchy eyes and runny nose when I am around cats. Let's say I decide to get allergy tested:
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Contingency Table

Probability Tree

Bayes' Theorem

- Scenario: I always get itchy eyes and runny nose when I am around cats. Let's say I decide to get allergy tested:
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    - The test is positive 10% of the time for people without allergies
- If 1% of the population has allergies and my test came back positive, what is the probability that I have allergies?

Bayes' Theorem

A: allergies;
B: positive test

$$P(A|B) = \frac{P(B|A)P(A)}{P(B)}$$

0.80

0.01

(0.01)(0.80) + (0.99)(0.1)

- Scenario: I always get itchy eyes and runny nose when I am around cats. Let's say I decide to get allergy tested:
    - The test is positive 80% of the time for people with allergies
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Contingency Table

Probability Tree

Bayes' Theorem

Contingency Table

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- If 1% of the population has allergies and my test came back positive, what is the probability that I have allergies?

	People with allergies	People without allergies	TOTAL
Positive test			
Negative test			
TOTAL			

- Scenario: I always get itchy eyes and runny nose when I am around cats. Let's say I decide to get allergy tested:
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- If 1% of the population has allergies and my test came back positive, what is the probability that I have allergies?

Contingency Table

	People with allergies	People without allergies	TOTAL
Positive test			
Negative test			
TOTAL	10	990	1000

- Scenario: I always get itchy eyes and runny nose when I am around cats. Let's say I decide to get allergy tested:
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  - The test is positive 10% of the time for people without allergies
- If 1% of the population has allergies and my test came back positive, what is the probability that I have allergies?

Contingency Table

	People with allergies	People without allergies	TOTAL
Positive test	8		
Negative test	2		
TOTAL	10	990	1000

- Scenario: I always get itchy eyes and runny nose when I am around cats. Let's say I decide to get allergy tested:
    - The test is positive 80% of the time for people with allergies
    - The test is positive 10% of the time for people without allergies
- If 1% of the population has allergies and my test came back positive, what is the probability that I have allergies?

Contingency Table

	People with allergies	People without allergies	TOTAL
Positive test	8	99	107
Negative test	2	891	893
TOTAL	10	990	1000

- Scenario: I always get itchy eyes and runny nose when I am around cats. Let's say I decide to get allergy tested:
    - The test is positive 80% of the time for people with allergies
    - The test is positive 10% of the time for people without allergies
- If 1% of the population has allergies and my test came back positive, what is the probability that I have allergies?

Contingency Table

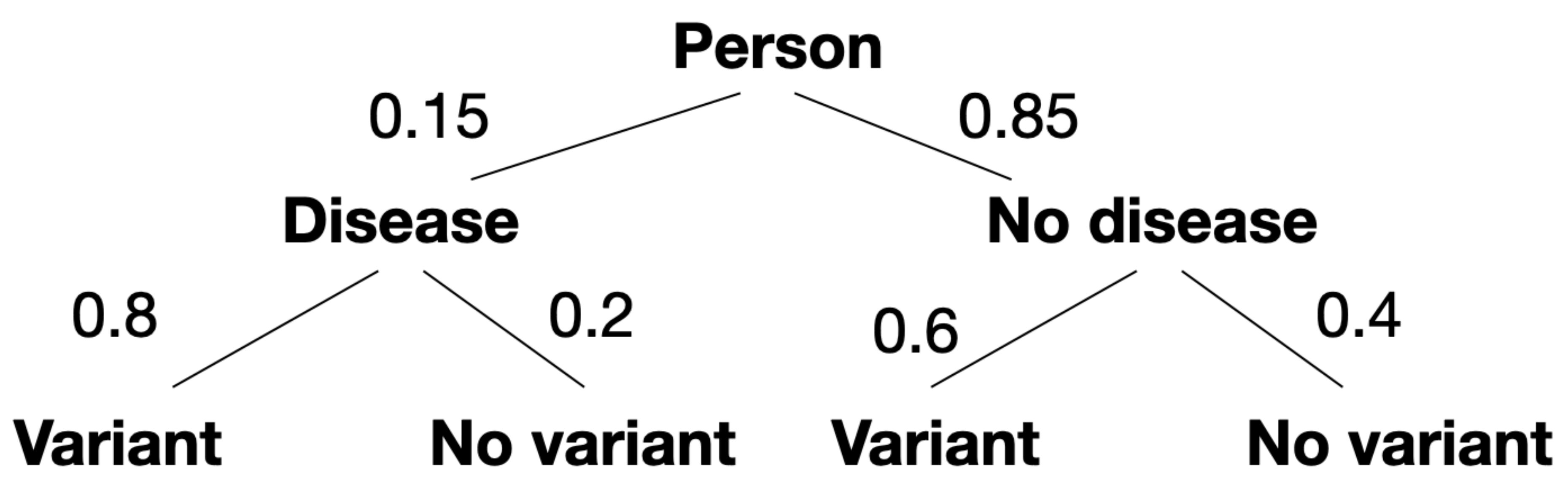
	People with allergies	People without allergies	TOTAL
Positive test	8	99	107
Negative test	2	891	893
TOTAL	10	990	1000

8/107 = 7.47%

Suppose you have a sample of 500 individuals. 75 of these individuals have a rare genetic disease and you identified a genetic variant that might be associated with this disease. 80% of individuals with the disease and 60% of individuals without the disease have the genetic variant. If an individual has the variant, what is the probability that they also have the disease?

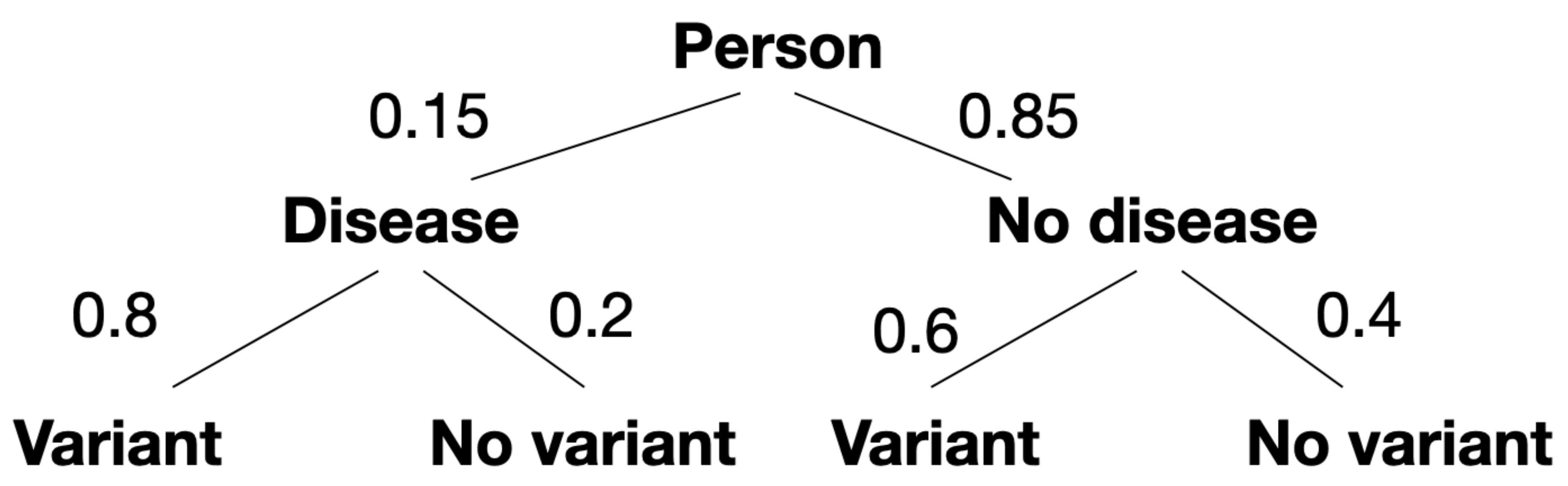
Suppose you have a sample of 500 individuals. 75 of these individuals have a rare genetic disease and you identified a genetic variant that might be associated with this disease. 80% of individuals with the disease and 60% of individuals without the disease have the genetic variant. If an individual has the variant, what is the probability that they also have the disease?

$$P(D|V) = \frac{P(V|D)P(D)}{P(V)}$$



Suppose you have a sample of 500 individuals. 75 of these individuals have a rare genetic disease and you identified a genetic variant that might be associated with this disease. 80% of individuals with the disease and 60% of individuals without the disease have the genetic variant. If an individual has the variant, what is the probability that they also have the disease?

$$P(D|V) = \frac{P(V|D)(0.15)}{P(V)}$$



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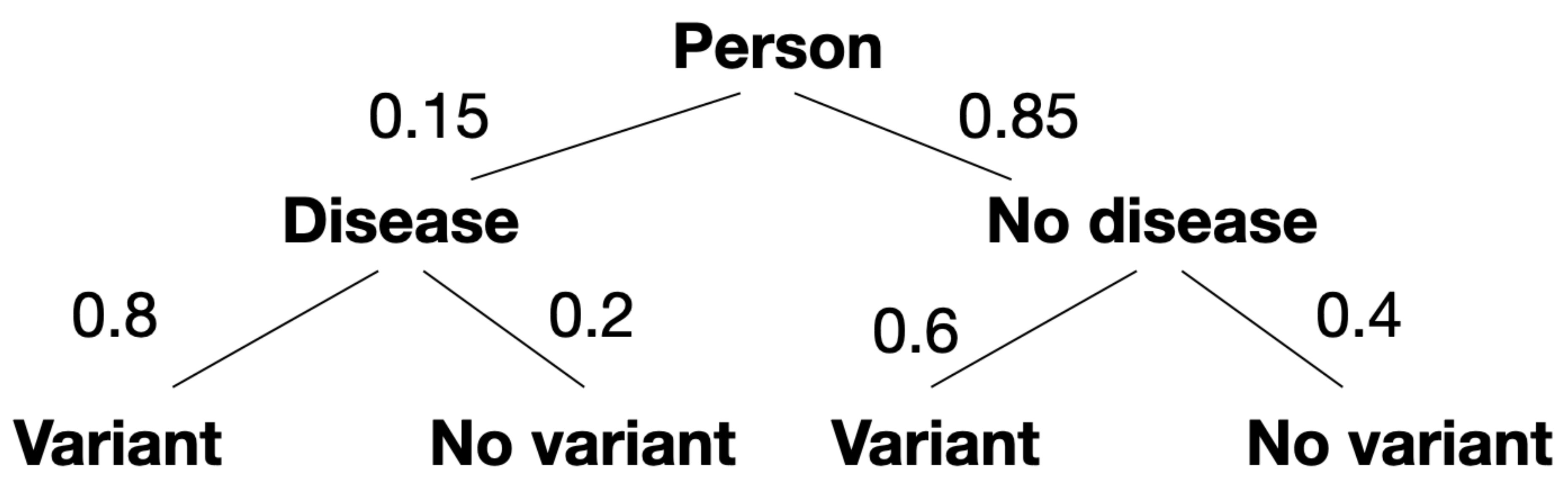
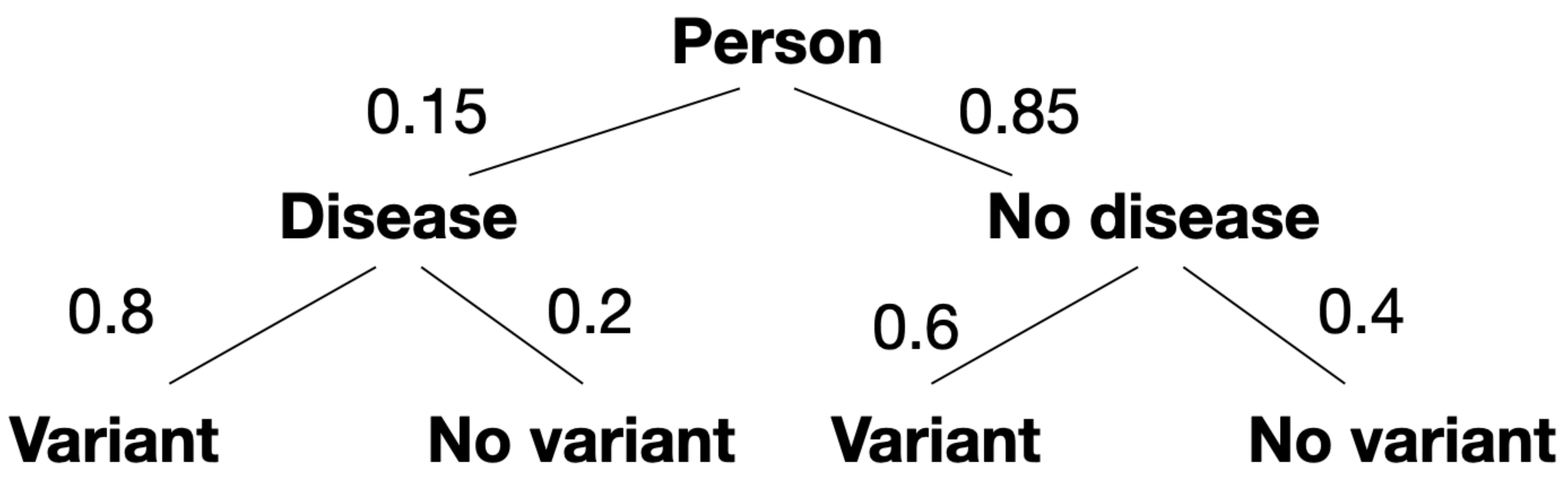
$$P(D \mid V) = \frac{(0.8)(0.15)}{P(V)}$$



Suppose you have a sample of 500 individuals. 75 of these individuals have a rare genetic disease and you identified a genetic variant that might be associated with this disease. 80% of individuals with the disease and 60% of individuals without the disease have the genetic variant. If an individual has the variant, what is the probability that they also have the disease?

$$P(D \mid V) = \frac{(0.8)(0.15)}{(0.8)(0.15) + (0.85)(0.6)} = 0.19$$



Conditional probability with Bayes' Theorem

- Tenant of **Bayes' Theorem** is that you can **modify the existing probably** of an event happening **based on observations**
- Helps address flaw of "**frequentists**" view of statistics that the **result of an experiment depends on the number of times** it is repeated
- <u>Applications of Bayes' theorem:</u>
    - Naive Bayes classifiers (machine learning)
    - Discriminant functions (similar to PCA/SVM grouping)
    - Bayesian parameter estimation (i.e. maximum likelihood estimate)

Review | Open Access | Published: 07 February 2019

Bayesian statistical learning for big data biology

Christopher Yau & Kieran Campbell

Biophysical Reviews **11**, 95–102 (2019) | Cite this article

Abstract

Bayesian statistical learning provides a coherent probabilistic f
uncertainty in systems. This review describes the theoretical fo
statistics and outlines the computational frameworks for imple
practice. We then describe the use of Bayesian learning in sing
high-dimensional, large data sets.

VIRUS EVOLUTION

Virus Evolution, 2018, 4(1): vey016

doi: 10.1093/ve/vey016
Resources

Bayesian phylogenetic and phylodynamic da integration using BEAST 1.10

Marc A. Suchard,[1,2,3,*,†] Philippe Lemey,[4,‡] Guy Baele,[4,§] Daniel
Alexei J. Drummond,[6,7,*] and Andrew Rambaut[8,*,**]

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omputer
tional Ev
utionary

Article | Open Access | Published: 20 April 2021

Genomic architecture and prediction of censored time-to-event phenotypes with a Bayesian genome-wide analysis

Sven E. Ojavee, Athanasios Kousathanas, Daniel Trejo Banos, Etienne J. Orliac, Marion Patxot, Kristi Läll, Reedik Mägi, Krista Fischer, Zoltan Kutalik & Matthew R. Robinson

Nature Communications **12**, Article number: 2337 (2021) | Cite this article

Abstract

While recent advancements in computation and modelling have improved the analysis of complex traits, our understanding of the genetic basis of the time at symptom onset remains limited. Here, we develop a Bayesian approach (BayesW) that provides probabilistic inference of the genetic architecture of age-at-onset phenotypes in a sampling scheme that
nsive simulation work the

ELSEVIER

Physics of Life Reviews
Volume 33, July 2020, Pages 88-108

Review

Morphogenesis as Bayesian inference: A variational approach to pattern formation and control in complex biological systems

Franz Kuchling [a], Karl Friston [b], Georgi Georgiev [c], Michael Levin [a, d] [1]

Article | Open Access | Published: 15 July 2021

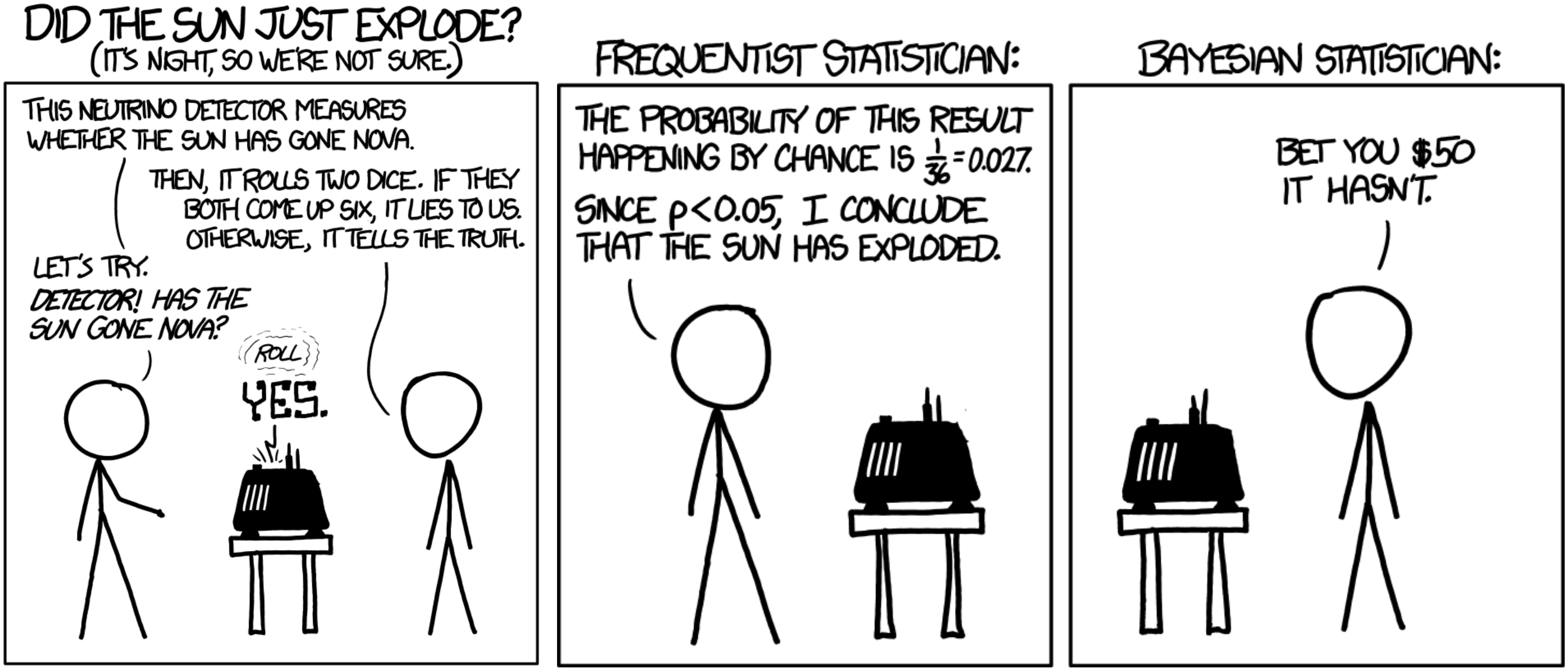
Bayesian analysis of home advantage in North American professional sports before and during COVID-19

Nico Higgs & Ian Stavness

Scientific Reports **11**, Article number: 14521 (2021) | Cite this article

Abstract

Home advantage in professional sports is a widely accepted phenomenon despite the lack of any controlled experiments at the professional level. The return to play of professional sports during the COVID-19 pandemic presents a unique opportunity to analyze the hypothesized effect of home advantage in neutral settings. While recent work has examined the effect of


DID THE SUN JUST EXPLODE?
(IT'S NIGHT, SO WE'RE NOT SURE.)
THIS NEUTRINO DETECTOR MEASURES WHETHER THE SUN HAS GONE NOVA.
THEN, IT ROLLS TWO DICE. IF THEY BOTH COME UP SIX, IT LIES TO US. OTHERWISE, IT TELLS THE TRUTH.
LET'S TRY.
DETECTOR! HAS THE SUN GONE NOVA?
ROLL
YES.
FREQUENTIST STATISTICIAN:
THE PROBABILITY OF THIS RESULT HAPPENING BY CHANCE IS $\frac{1}{36}$ = 0.027.
SINCE $p < 0.05$, I CONCLUDE THAT THE SUN HAS EXPLODED.
BAYESIAN STATISTICIAN:
BET YOU $50 IT HASN'T.

An introduction to **random variables**

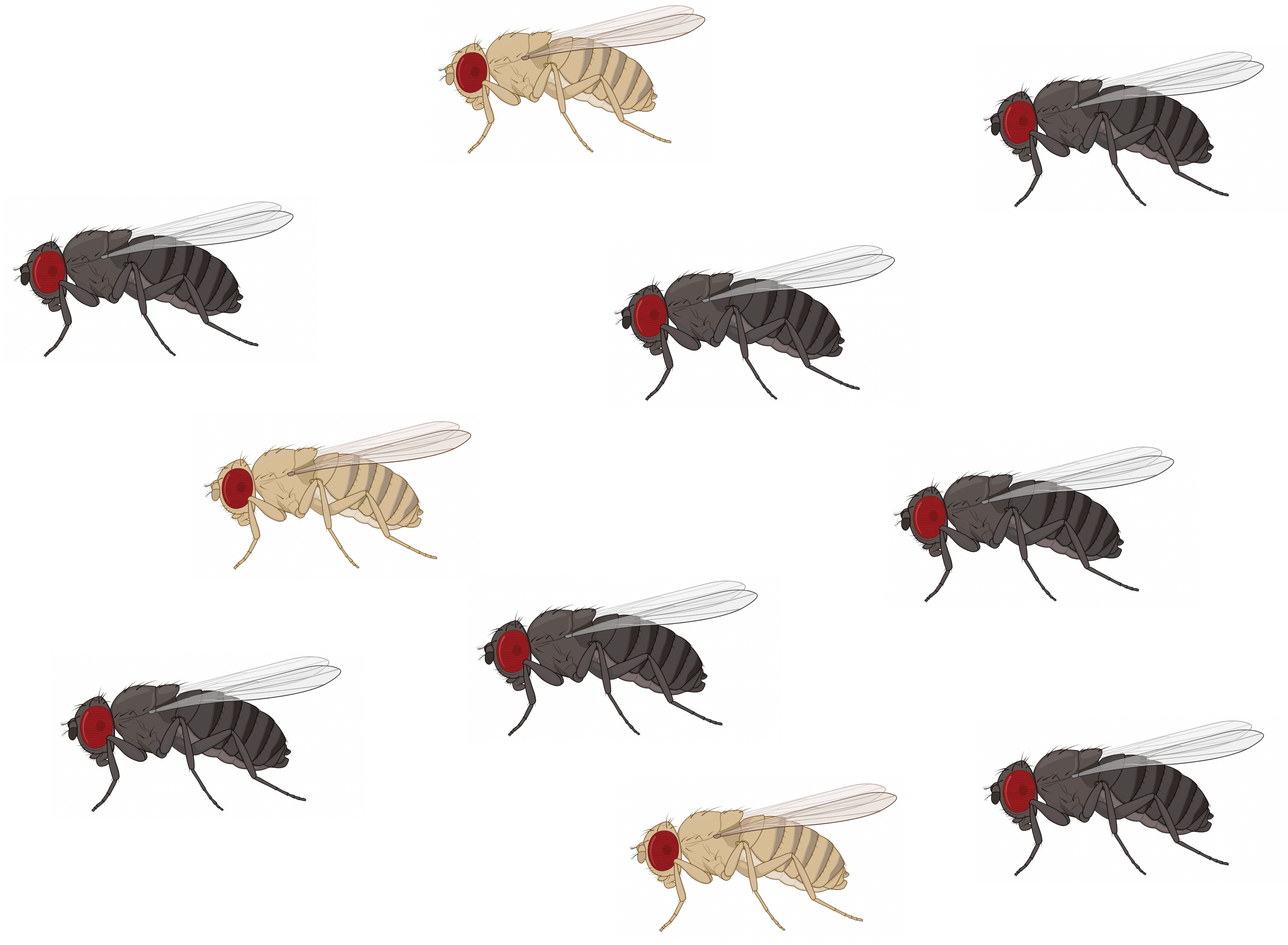
Random variable: variable that takes on a numerical value that depends on the outcome of a chance operation

Pr{Selecting a black fly} = ?

Pr{*Y* = black} = ?

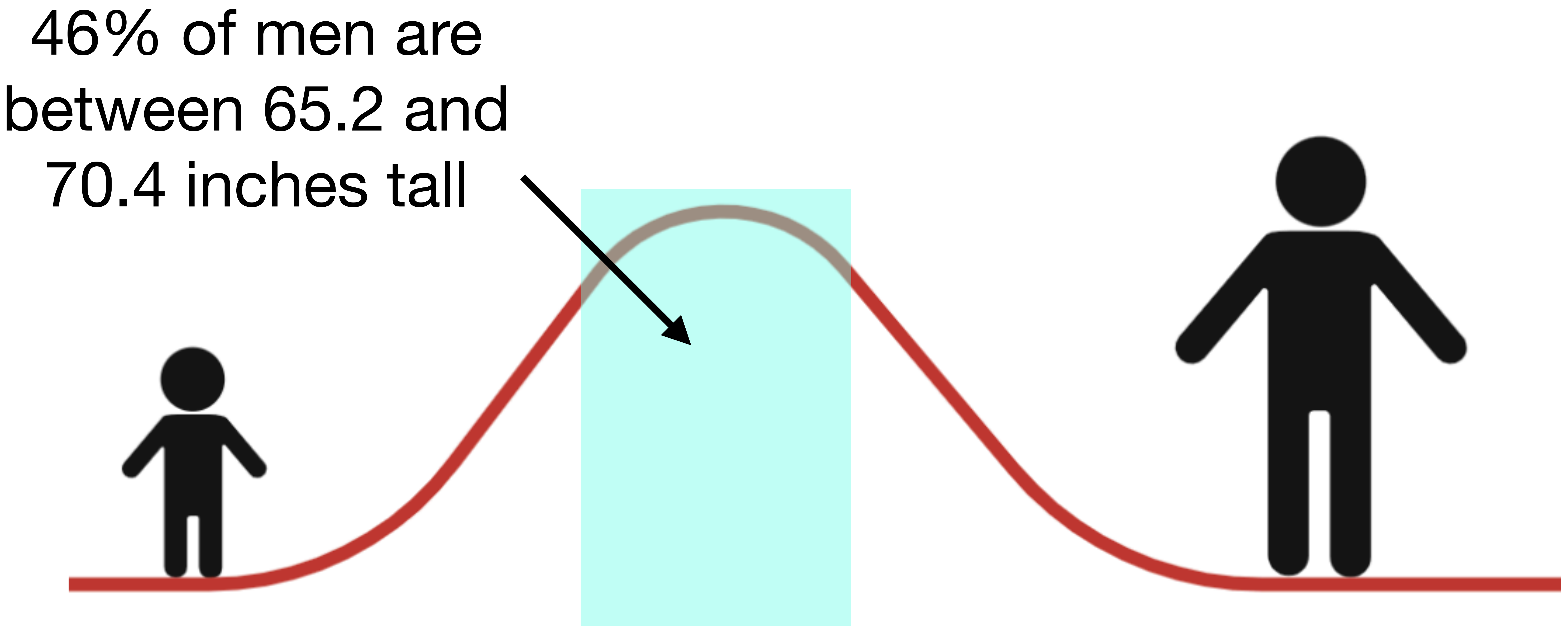
Random variable, *Y*

Y = {black, white}



An introduction to **random variables**

Random variable, *Y* = height of individual chosen at random from population



$$Pr[65.2 \leq Y \leq 70.4] = 0.46$$

Mean of a discrete random variable

$$\mu_Y = \sum y_i Pr(Y = y_i)$$

(Sum of all: possible value for Y * probability of that value for Y)

This is also called the **expected value, E(Y)**

Mean of a discrete random variable

$$E(Y) = \mu_Y = \sum y_i Pr(Y = y_i)$$

(Sum of all: possible value for Y * probability of that value for Y)

Number of markers	Percent of cells
1	40
2	28
3	19
5	9
8	4

Mean of a discrete random variable

$$E(Y) = \mu_Y = \sum y_i Pr(Y = y_i)$$

(Sum of all: possible value for Y * probability of that value for Y)

Number of markers	Percent of cells	(Y)(Pr(Y))
1	40	(1)(40/100)
2	28	(2)(28/100)
3	19	(3)(19/100)
5	9	(5)(9/100)
8	4	(8)(4/100)

(Sum)

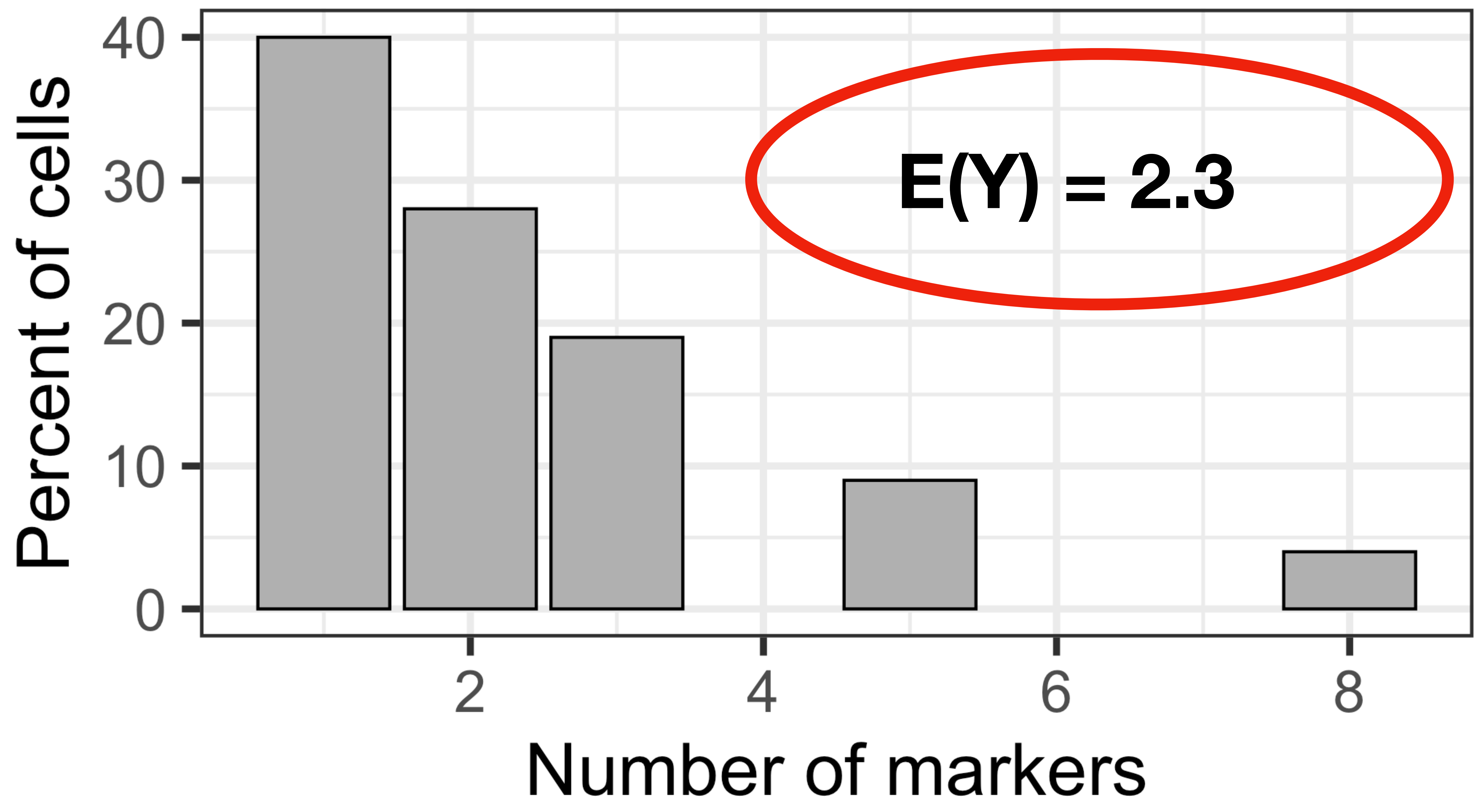
E(Y) = 2.3

Mean of a discrete random variable

$$E(Y) = \mu_Y = \sum y_i Pr(Y = y_i)$$

<u>(Sum of all: possible value for Y * probability of that value for Y)</u>

Number of markers	Percent of cells
1	40
2	28
3	19
5	9
8	4

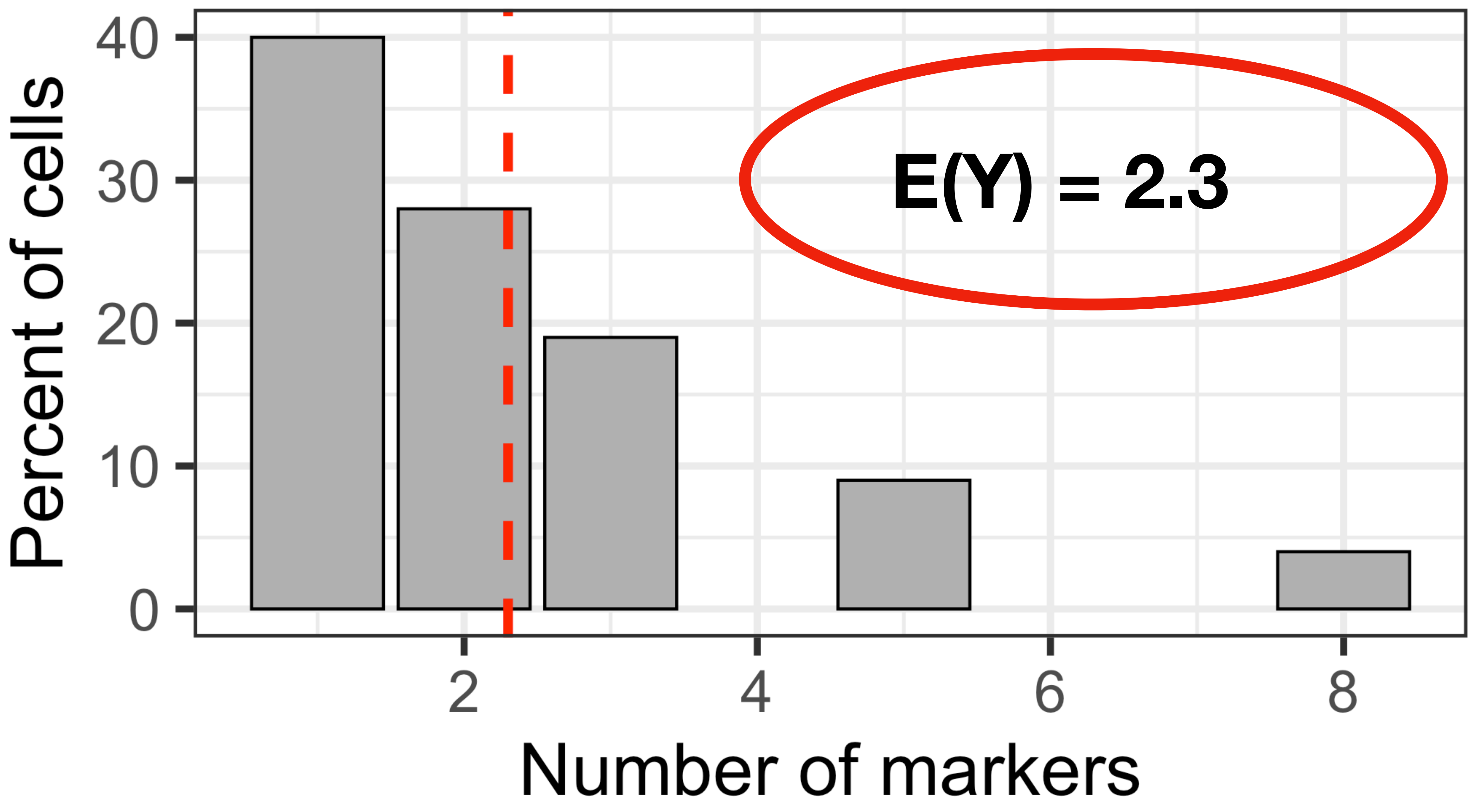


Mean of a discrete random variable

$$E(Y) = \mu_Y = \sum y_i Pr(Y = y_i)$$

(Sum of all: possible value for Y * probability of that value for Y)

Number of markers	Percent of cells
1	40
2	28
3	19
5	9
8	4



Mean of a discrete random variable

<u>This is a theoretical mean value</u>

i.e. if we were to create a sample with this distribution, the mean of that sample would be the expected value

Number of markers	Percent of cells	Total (sample)
1	40	400
2	28	280
3	19	190
5	9	90
8	4	40

Total: 1000

Sample = 1, 1, 1, …, 2, 2, …, 3, …, 5, …, 8

mean(sample) = 2.3

E(Y) = 2.3

Variance of a discrete random variable

(Variance) $$\sigma_Y^2 = \sum (y_i - \mu_Y)^2 Pr(Y = y_i)$$

(Sum of all: squared deviations for each value of Y * probability of that value for Y)

(Standard deviation) $$\sigma = \sqrt{(\sigma_Y^2)}$$

Variance of a discrete random variable

(Variance) $$\sigma_Y^2 = \sum (y_i - \mu_Y)^2 Pr(Y = y_i)$$

E(Y) = 2.3

(Sum of all: squared deviations for each value of Y * probability of that value for Y)

Number of markers	Percent of cells	
1	40	$(1 - 2.3)^2(0.40)$
2	28	$(2 - 2.3)^2(0.28)$
3	19	$(3 - 2.3)^2(0.19)$
5	9	$(5 - 2.3)^2(0.09)$
8	4	$(8 - 2.3)^2(0.04)$

(Sum)

VAR(Y) = 2.75

SD(Y) = 1.65

Sample = 1, 1, 1, …, 2, 2, …, 3, …, 5, …

sd(sample) = 1.65

Summary: discrete random variables

$$E(Y) = \mu_Y = \sum y_i Pr(Y = y_i)$$

(Sum of all: possible value for Y * probability of that value for Y)

(Variance) $$\sigma_Y^2 = \sum (y_i - \mu_Y)^2 Pr(Y = y_i)$$

(Sum of all: squared deviations for each value of Y * probability of that value for Y)

(Similar definitions for continuous random variables, but involve integral calculus…)

Consider a population of *Drosophila* in which 30% of the individuals are black because of a mutation and 70% have the normal gray body color. Suppose three flies are chosen at random from the population, let Y denote the number of black flies out of the three.

Find $Pr[Y \geq 2]$

Y (No. Black)	Probability
0	0.343
1	0.441
2	0.189
3	0.027

0.189 + 0.027 = 0.216

Consider a population of *Drosophila* in which 30% of the individuals are black because of a mutation and 70% have the normal gray body color. Suppose three flies are chosen at random from the population, let Y denote the number of black flies out of the three.

Calculate the mean and standard deviation of the random variable

Y (No. Black)	Probability
0	0.343
1	0.441
2	0.189
3	0.027

$$0(0.343) + 1(0.441) + 2(0.189) + 3(0.027)$$

$$E(Y) = 0.9$$

Consider a population of *Drosophila* in which 30% of the individuals are black because of a mutation and 70% have the normal gray body color. Suppose three flies are chosen at random from the population, let Y denote the number of black flies out of the three.

Calculate the mean and standard deviation of the random variable

Y (No. Black)	Probability
0	0.343
1	0.441
2	0.189
3	0.027

$$\sigma_Y^2 = \sum (y_i - \mu_Y)^2 Pr(Y = y_i)$$

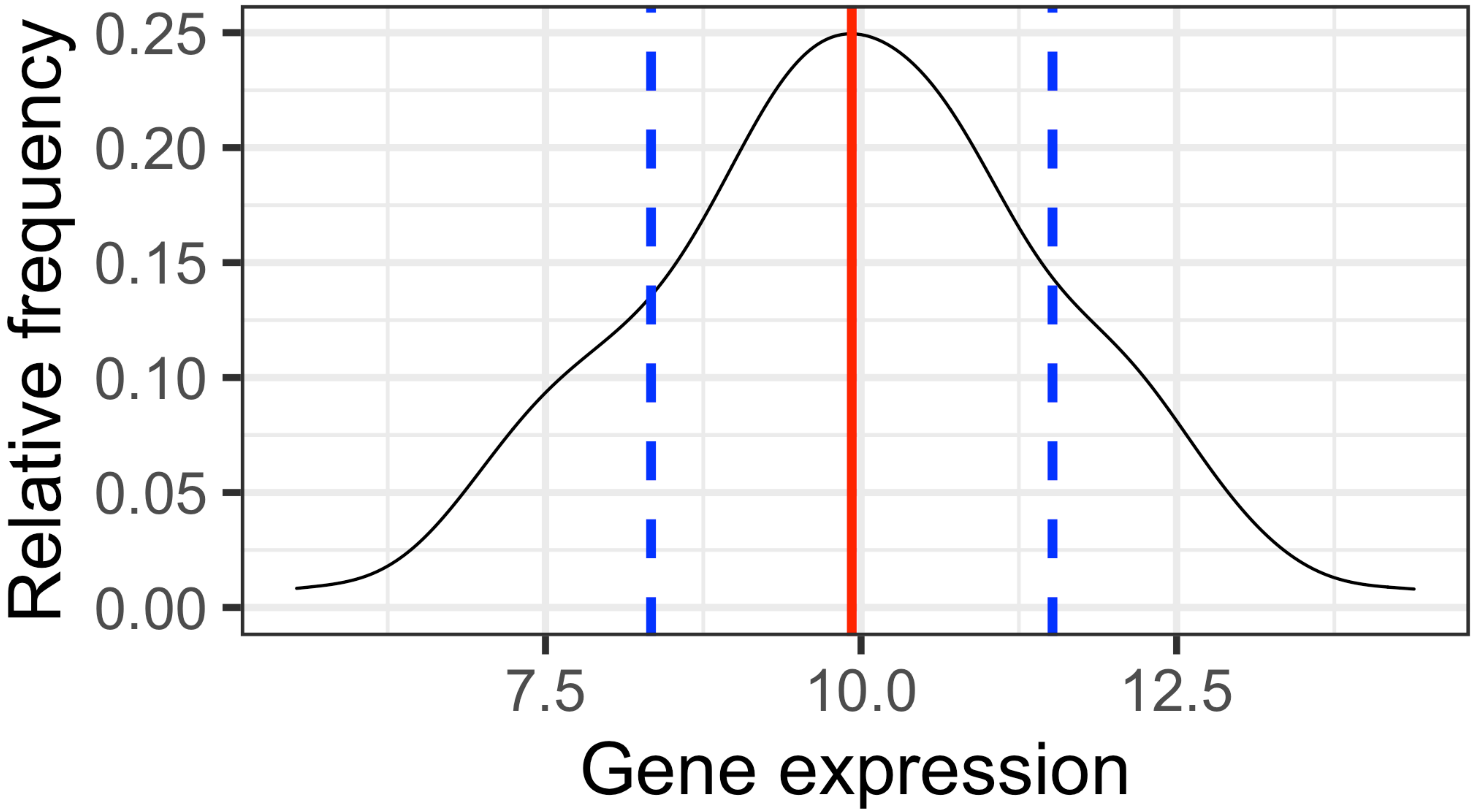
$(0-0.9)^2(0.343)$
$+ (1-0.9)^2*(0.441)$
$+ (2-0.9)^2*(0.189)$
$+ (3-0.9)^2*(0.027)$

VAR(Y) = 0.63

SD(Y) = 0.79

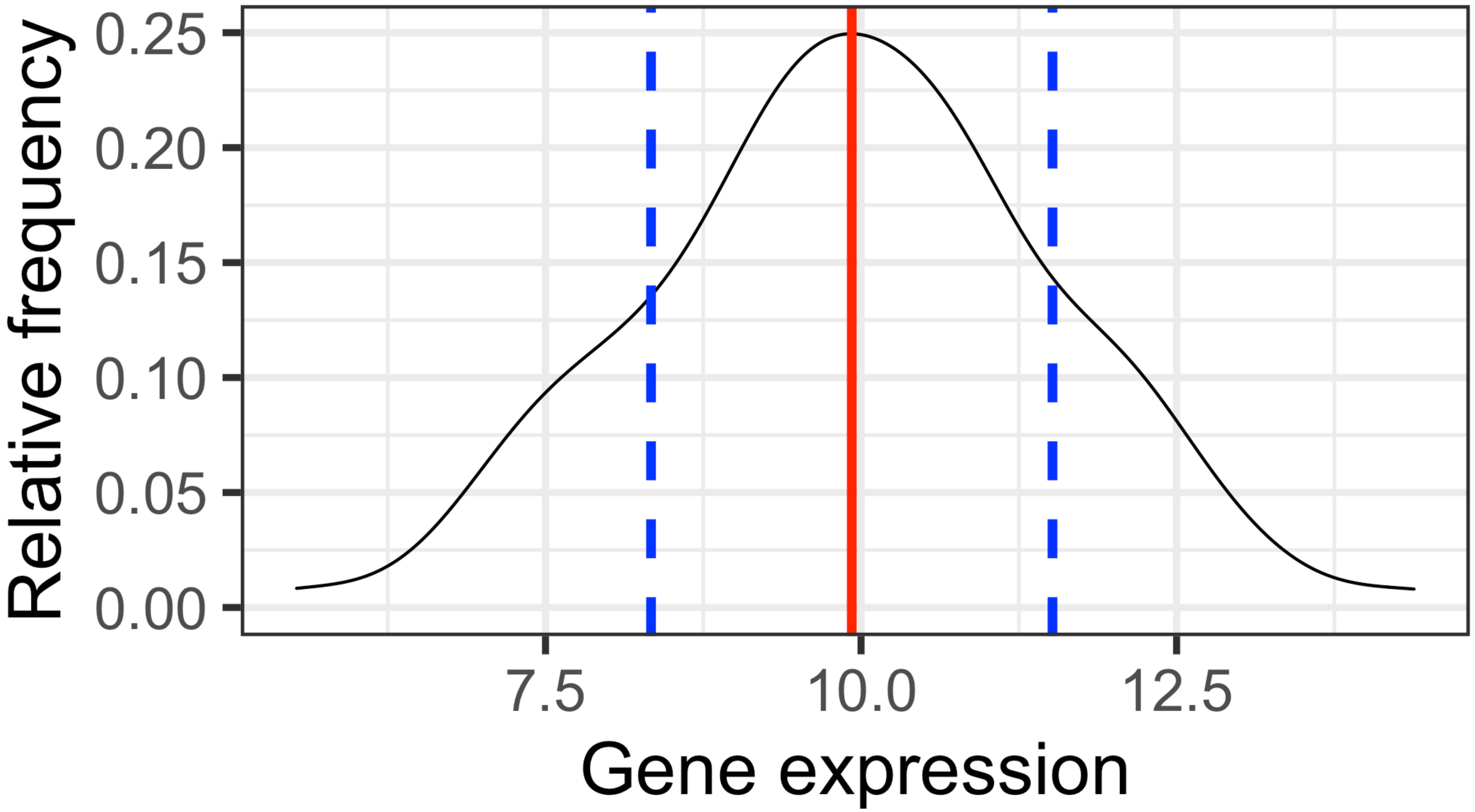
Adding and subtracting random variables

Let's say you performed single-cell RNA-seq within a specific population and found the distribution of your gene of interest to have a mean of 10 units with a standard deviation of 1.5 units:



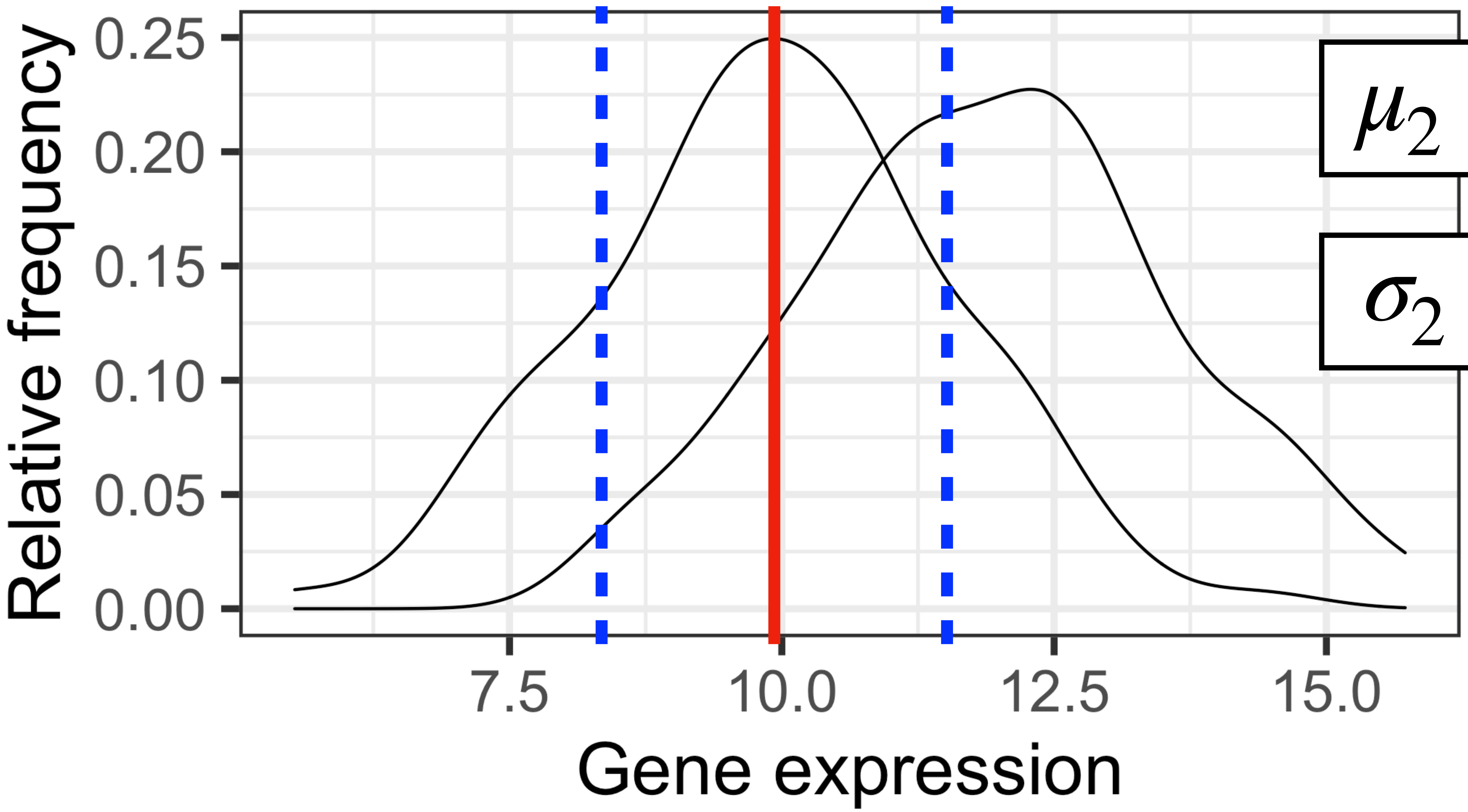
Adding and subtracting random variables

Let's say you performed single-cell RNA-seq within a specific population and found the distribution of your gene of interest to have a mean of 10 units with a standard deviation of 1.5 units. <u>If you know your second gene of interest is expressed, on average, two units more than the first, what should its distribution look like?</u>



Adding and subtracting random variables

Let's say you performed single-cell RNA-seq within a specific population and found the distribution of your gene of interest to have a mean of 10 units with a standard deviation of 1.5 units. If you know your second gene of interest is expressed, on average, two units more than the first, what should its distribution look like?



$$\boxed{\mu_2 = \mu_1 + 2}$$

$$\boxed{\sigma_2 = \sigma_1}$$

Adding and subtracting random variables

- (1) If we **add** two random variables that are *independent* of one another, then we **add their variances**
- (2) If we **subtract** two random variables that are *independent* of one another, then we **add their variances**
- (3) **standard deviation** = square root of **variance**

Adding and subtracting random variables

$\mu_1 = 300; \sigma_1 = 22$

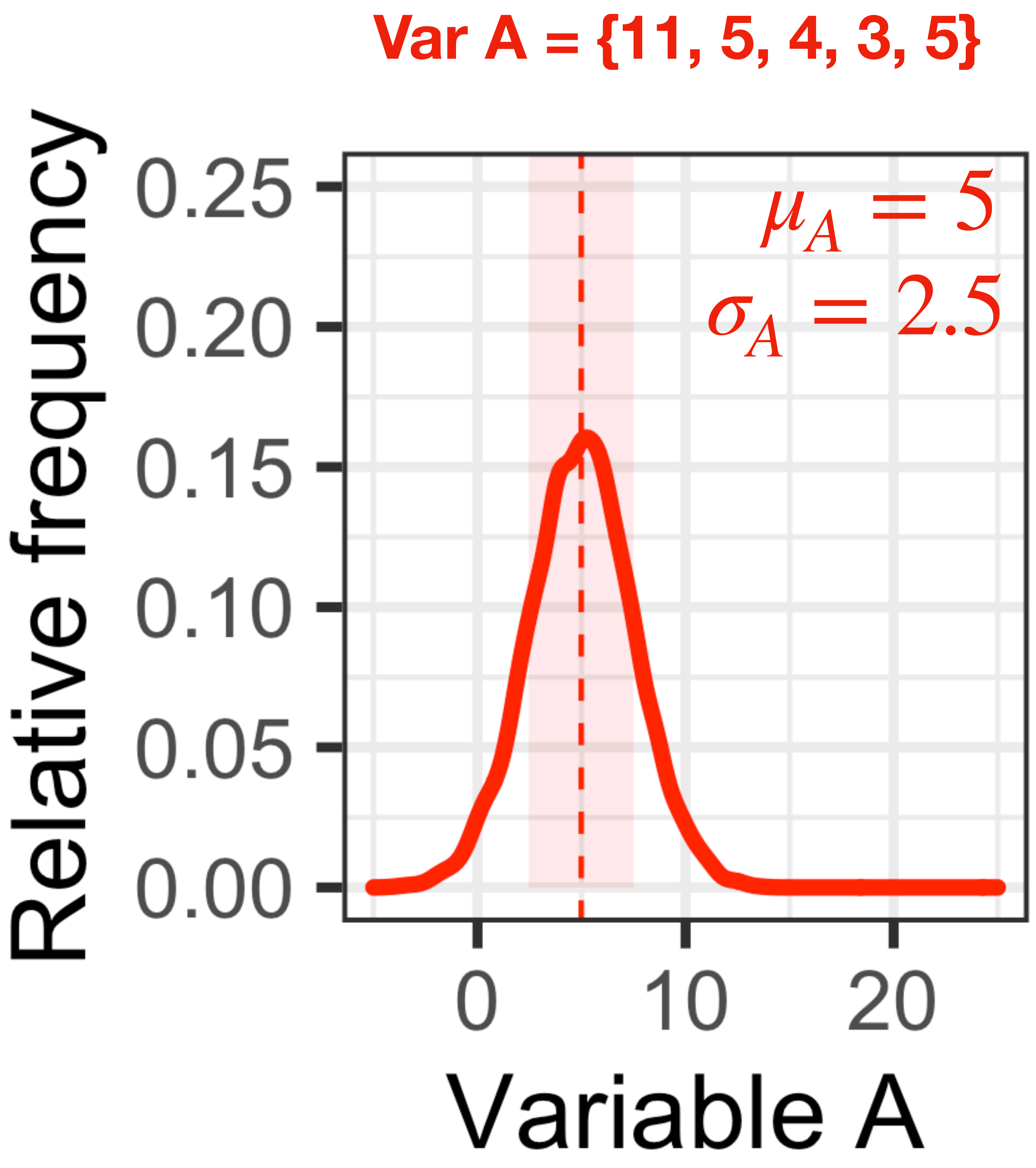
$\mu_2 = 368; \sigma_2 = 26$

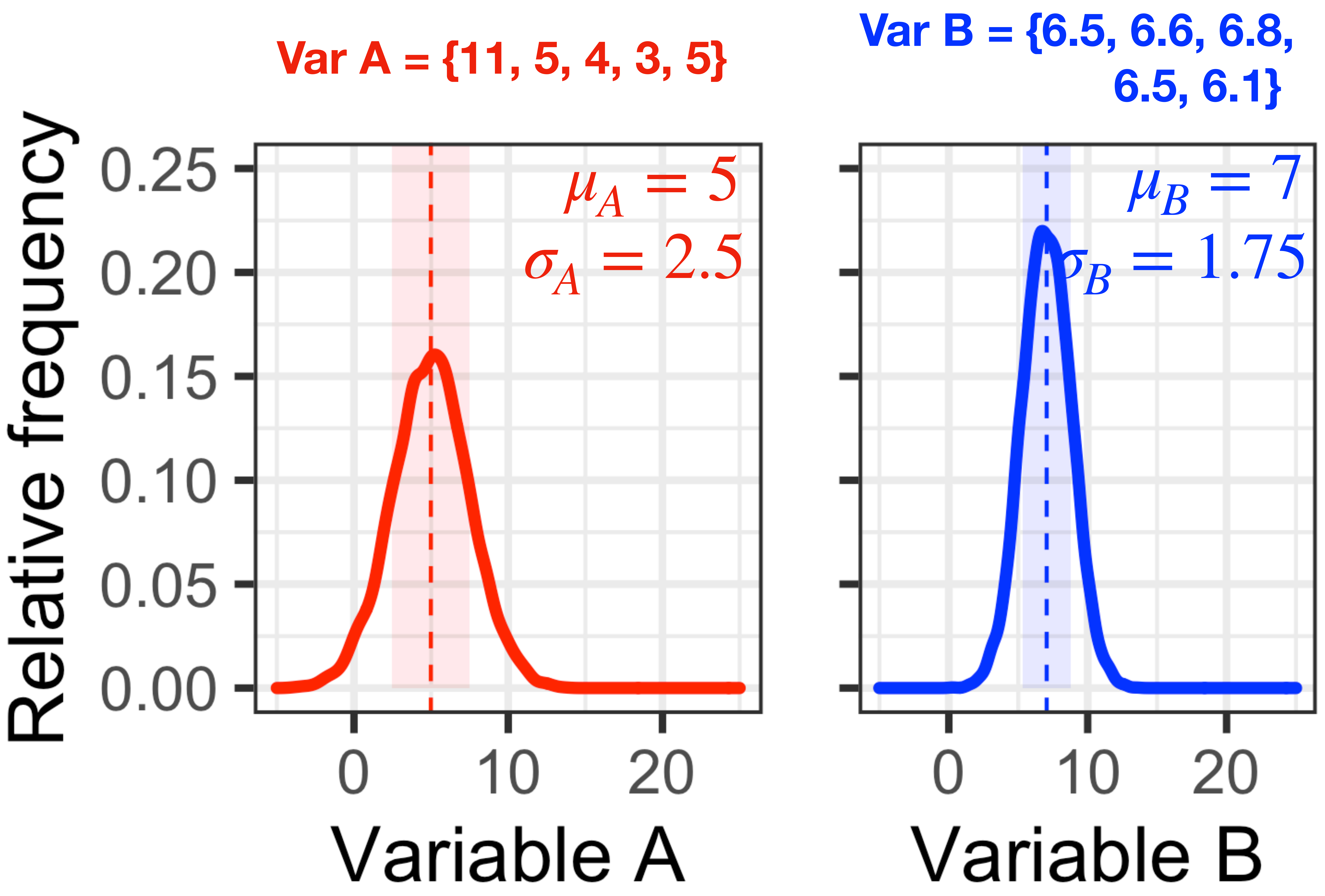
$$\mu_{1-2} = \mu_1 - \mu_2$$
$$= -68$$

What is the overall difference in means between the populations (black and white)?

$$\sigma^2_{1-2} = \sigma^2_1 + \sigma^2_2$$
$$\sigma^2_{1-2} = 22^2 + 26^2$$
$$= 1160$$
$$\sigma = 34.06$$

What is the variance in difference between these two populations?


Var A = {11, 5, 4, 3, 5}
$\mu_A = 5$
$\sigma_A = 2.5$
Relative frequency
0.25
0.20
0.15
0.10
0.05
0.00
0
10
20
Variable A


Var A = {11, 5, 4, 3, 5}
Var B = {6.5, 6.6, 6.8, 6.5, 6.1}
$\mu_A = 5$
$\sigma_A = 2.5$
$\mu_B = 7$
$\sigma_B = 1.75$
Relative frequency
0.25
0.20
0.15
0.10
0.05
0.00
0
10
20
Variable A
Variable B

Var A = {11, 5, 4, 3, 5}
Var B = {6.5, 6.6, 6.8, 6.5, 6.1}
Var (A+B) = {6.5+11, 6.6+5, 6.8+4, 6.5+3, 6.1+5}
Relative frequency
0.25
0.20
0.15
0.10
0.05
0.00
$\mu_A = 5$
$\sigma_A = 2.5$
$\mu_B = 7$
$\sigma_B = 1.75$
$\mu_{A+B} = 12$
$\sigma_{A+B} = 3.05$
0
10
20
Variable A
Variable B
Variable A + B

If you want to see the math: link here

Announcements

- Homework #1 due **at 6pm**
- TA office hours **Tuesday 4:30-5:30** and **Friday 1:30-2:30** on **zoom**
- Homework #2 is up now, due next Tuesday (Oct. 5) @ 6pm