

# **Exploring Test Value**

Clinical Informatics Lecture

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# Learning objectives

- Describe the overlap and distinction between test accuracy and test value
- Apply Bayesian analysis to update prior given a test result
- Appreciate that lab tests have associated risks and harms
- Apply decision analysis to model test value
- List non-analytical factors that impact the value of a lab result

Course materials at: [https://github.com/MarkZayzman/PathologyInformatics\\_2021.git](https://github.com/MarkZayzman/PathologyInformatics_2021.git)

# Why this lecture matters

- Decisions regarding test utilization should be based on the value provided by testing
- Accuracy metrics provide an incomplete description of test value
- There is a critical need to define and quantify value in order to optimize test utilization

A 50 year old man with a history of HTN, HLD, T2DM, and obesity presents to the ED with squeezing chest pain, shortness of breath, and dizziness.

**A STAT ECG reveals ST-segment elevations in consecutive leads.**

What is the most appropriate next step in management?

1. Order CK-MB
2. Order LDH
3. Order conventional cardiac troponins
4. Order high sensitivity cardiac troponins
5. Cardiac catheterization

# Key Concepts

1. The value of a test result may vary with context
2. The value of the test depends on more than just the accuracy of the test

# **Test value is multifactorial**

## **A valuable test provides**

- actionable information
- to the right person
- at the right time
- in the right format

**A test can be accurate but fail to provide value**

## **Actionable Information**

1. Changes the clinical scenario in a 'non-negligible' way
2. This change warrants some action that would not have otherwise occurred
3. Resources are available to take the indicated action
4. There is a net benefit to patient outcomes

# Key Question

*How can we quantify the impact of test result on a clinical scenario?*

(Hint: we could use Bayes Theorem)

# Bayes Theorem

$$P(D|+) = \frac{P(D)P(+/D)}{P(+)} \quad (\textit{Bayes Theorem})$$

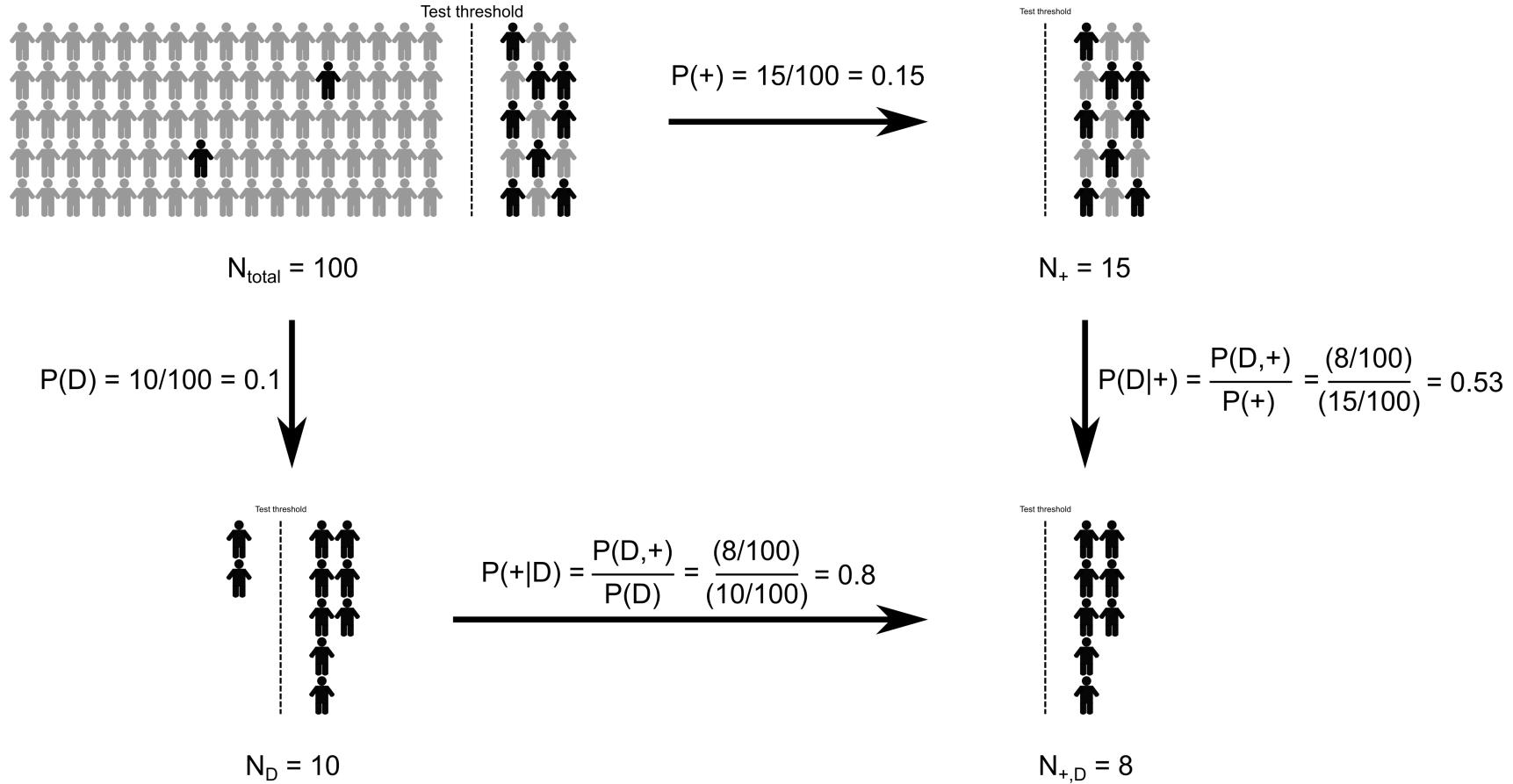
- Bayes' theorem allows us to update a prior belief in light of new evidence
- Bayes' theorem relates the probability of the hypothesis given the evidence to the probability of the evidence given the hypothesis

# Conditional probability

$$P(D|+) = \frac{P(D \cap +)}{P(+)}$$

- $P(D|+)$  : "The probability of disease given a positive test"
- $P(D \cap +)$  : "The probability of disease and a positive test"
- $P(+)$  : "The probability of a positive test"

# Realistic test (from last class)



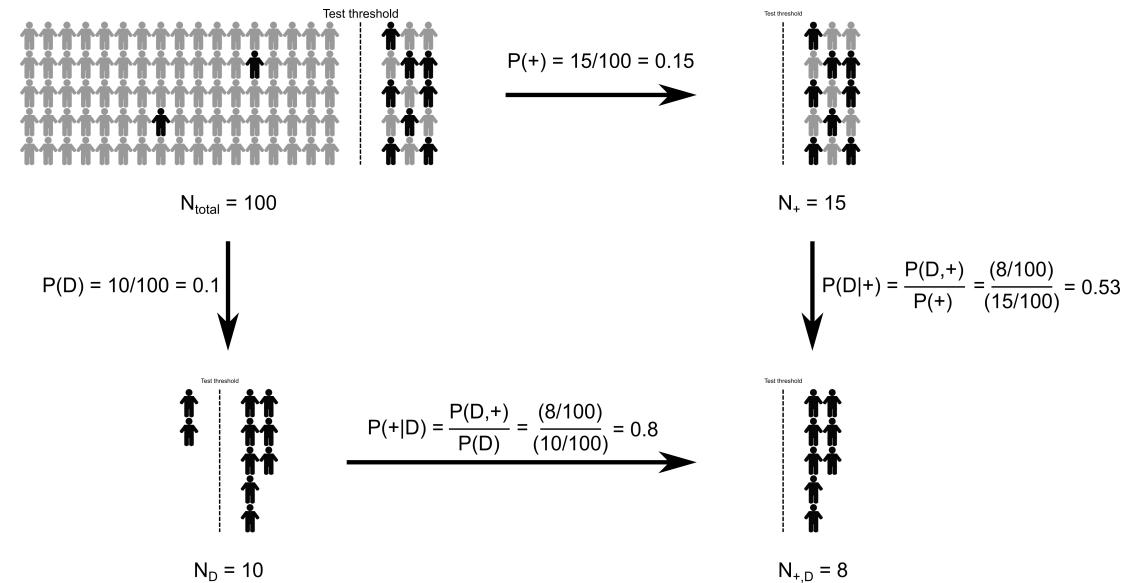
# Bayes' theorem (proof)

$$N_{TP} = N_{total} P(+) P(D|+)$$

$$= (100)(0.15)\left(\frac{8}{15}\right) = 8$$

$$N_{TP} = N_{total} P(D) P(+|D)$$

$$= (100)(0.10)\left(\frac{8}{10}\right) = 8$$



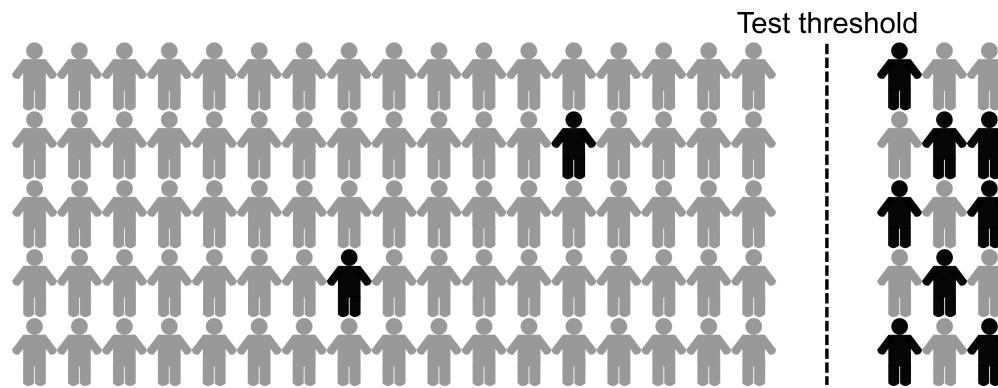
$$\cancel{N_{total}} * P(+) * P(D|+) = \cancel{N_{total}} * P(D) * P(+|D)$$

$$P(D|+) = \frac{P(D) * P(+|D)}{P(+)} \quad (\textit{Bayes Theorem})$$

# **What does Bayes theorem mean?**

The answer to this question becomes more evident if we convert from probability to odds

## Probability versus odds



Probability of disease - ratio of # diseased individuals to the total of individuals

$$P(\text{disease}) = \frac{N_{\text{diseased}}}{N_{\text{diseased}} + N_{\text{healthy}}} = \frac{10}{10 + 90} = \frac{1}{10} = 0.1$$

Odds of disease ratio of diseased to not diseased (healthy ) individuals

$$O(\text{disease}) = \frac{N_{\text{diseased}}}{N_{\text{Total}} - N_{\text{diseased}}} = \frac{N_{\text{diseased}}}{N_{\text{healthy}}} = \frac{10}{90} = \frac{1}{9} = 0.11$$

## Converting between odds and probabilities

$$O(\text{disease}) = \frac{P(\text{disease})}{1 - P(\text{disease})}$$

$$P(\text{disease}) = \frac{O(\text{disease})}{1 + O(\text{disease})}$$

# Expressing Bayes' theorem in terms of odds

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

$$P(+) = P(+|D)P(D) + P(+|H)P(H)$$

$$P(D|+) = \frac{P(D)P(+|D)}{P(+|D)P(D) + P(+|H)P(H)}$$

$$\times \frac{\frac{1}{P(D)P(+|D)}}{\frac{1}{P(D)P(+|D)}}$$

$$P(D|+) = \frac{1}{1 + \frac{P(+|H)P(H)}{P(+|D)P(D)}}$$

$$\frac{P(+|H)}{P(+|D)} = \frac{1}{LR^+}, \quad \frac{P(H)}{P(D)} = \frac{1-P(D)}{P(D)} = \frac{1}{O_{pre}(D)}$$

$$P(D|+) = \frac{1}{1 + \frac{1}{LR^+ O_{pre}(D)}}$$

*rearrange*

$$\frac{1-P(D|+)}{P(D|+)} = \frac{1}{LR^+ O_{pre}(D)}$$

$$\frac{1-P(D|+)}{P(D|+)} = \frac{1}{O_{post}(D)}$$

$$O_{post}(D) = LR^+ O_{pre}(D)$$

## Bayes allows us to refine a prior belief in light of new evidence

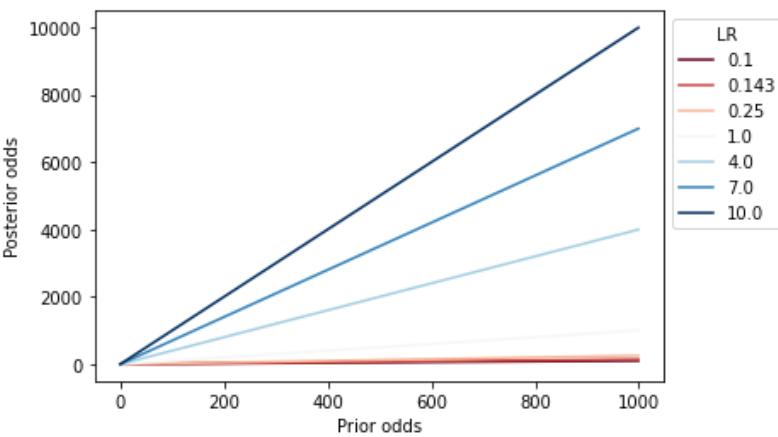
$$O_{post}(D) = LR * O_{pre}(D)$$

*posterior belief* = *evidence* \* *prior belief*

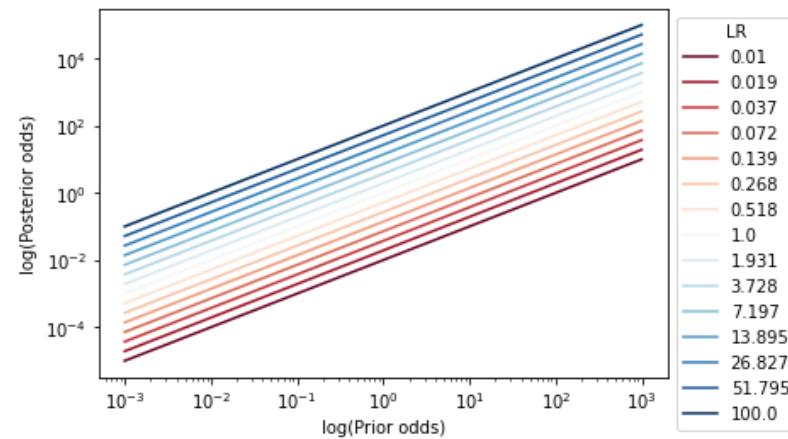
Note that our new (posterior) belief depends on:

- the strength of the prior belief
- the strength of the evidence

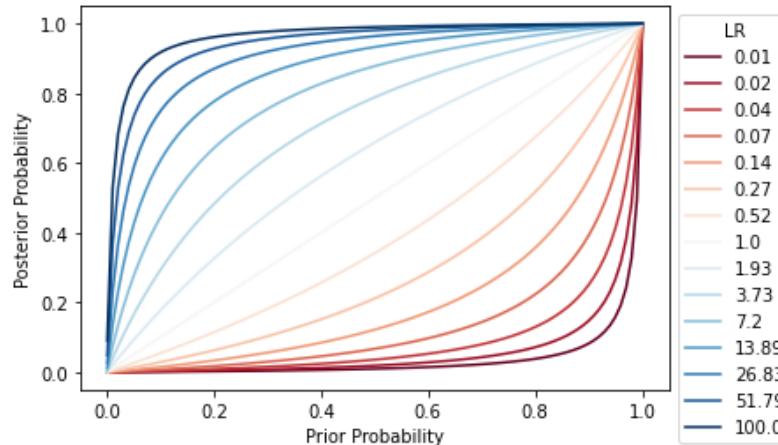
$$Post_{odds} = LR * Pre_{odds}$$

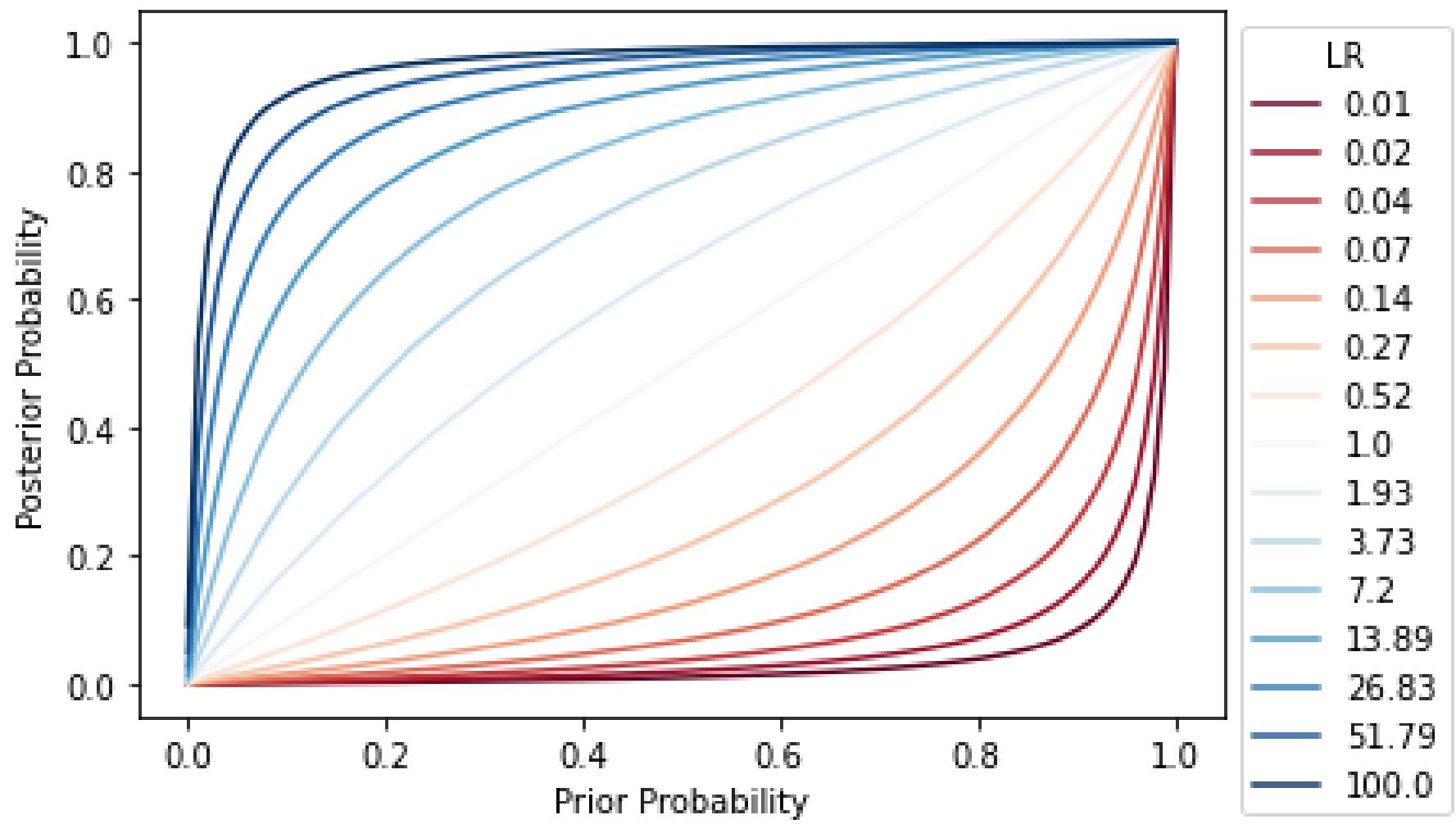


$$\log Post_{odds} = \log LR + \log Pre_{odds}$$



$$Post_{prob} = \frac{1}{1 + \frac{1 - Pre_{prob}}{LR * Pre_{prob}}}$$





A patient has a positive mammogram ( $Se = 97\%$ ,  $Sp = 64.5\%$ ). The background prevalence of breast cancer among similar patients is 0.2%. She has no significant additional risk factors.

1. ***Compute the pre test and post test odds of breast cancer for this patient***
2. ***Compute post test probability***

A patient has a positive mammogram ( $Se = 97\%$ ,  $Sp = 64.5\%$ ). The background prevalence of breast cancer among similar patients is 0.2%. She has no significant additional risk factors.

$$LR^+ = \frac{P(+|D)}{P(+|H)} = \frac{Se}{1-Sp} = \frac{0.97}{1-0.645} = \frac{0.97}{0.355} = 2.7 \approx 3$$

**1. Compute the pre test and post test odds of breast cancer for this patient**

$$Pre_{odds} = \frac{0.002}{1-0.002} \approx 0.002$$

$$Post_{odds} = LR * Pre_{odds} = 3 * 0.002 = 0.006$$

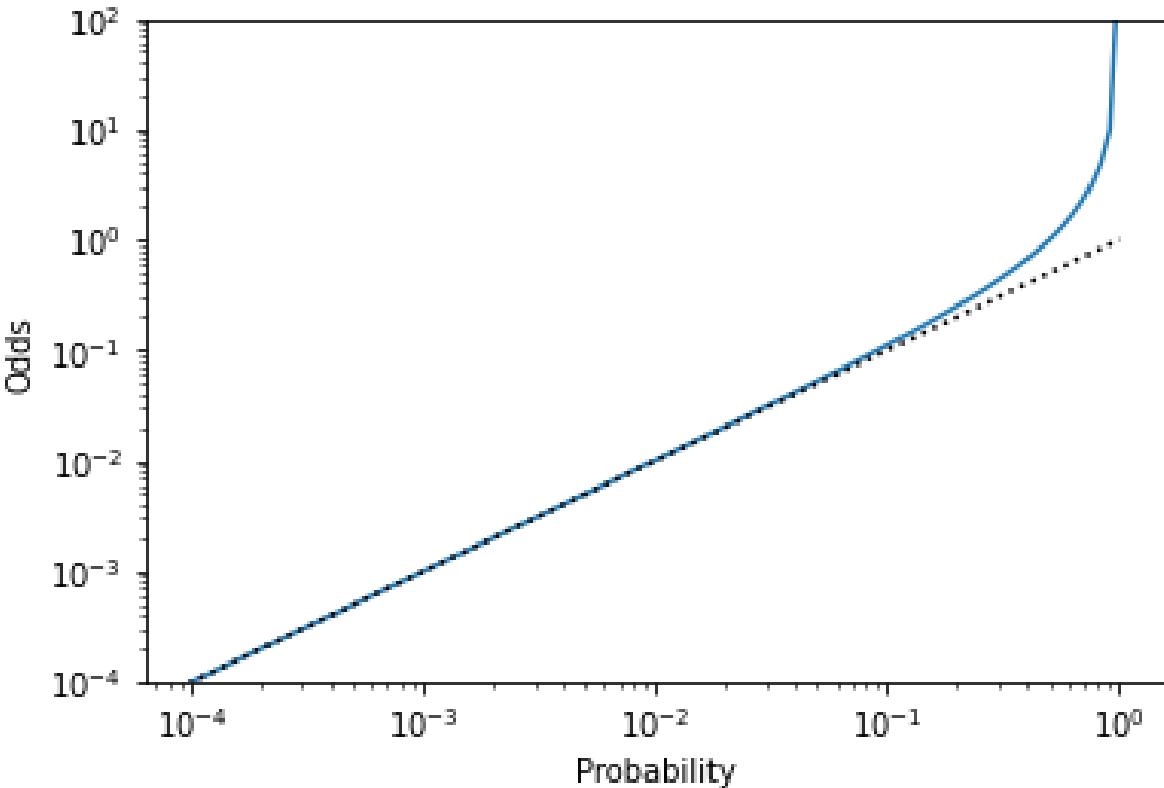
**2. Compute post test probability**

$$Post_{prob} = \frac{0.006}{1-0.006} = 0.00603 \approx 0.006$$

Note how similar the odds and probabilities were in this case

# Odds and probability are similar when low

$$O(disease) = \frac{P(disease)}{1-P(disease)}$$



$$\lim_{P(disease) \rightarrow 0} (1 - P(disease)) \approx 1$$

$$\therefore \lim_{P(disease) \rightarrow 0} O(disease) \approx P(Disease)$$

# This can come in handy on an exam or in practice

## Question 999

*Blah blah blah prevalence is 1% blah blah blah blah Sensitivity is 0.8, specificity is 0.9 blah blah*

What is the probability that the patient has the disease?

- A. 1%
- B. 4%
- C. 10%
- D. 20%
- E. 50%

## Question 999

**Blah blah blah prevalence is 1% blah blah blah Sensitivity is 0.8, specificity is 0.9 blah blah**

What is the probability that the patient has the disease?

$$LR^+ = \frac{Se}{1-Sp} = \frac{0.8}{1-0.9} = \frac{0.8}{0.1} = 8$$

$$Odds_{post} = LR^+ Odds_{pre} = 8 * \frac{0.01}{1-0.01} \approx 8 * 0.01 = 0.08$$

- A. 1%
- B. 7%
- C. 10%
- D. 20%
- E. 50%

## Caution: this doesn't work if the prevalence is not low

*Blah blah blah prevalence is 25% blah blah blah blah Sensitivity is 0.8, specificity is 0.9 blah blah*

What is the probability that the patient has the disease?

$$LR^+ = \frac{Se}{1-Sp} = \frac{0.8}{1-0.9} = \frac{0.8}{0.1} = 8$$

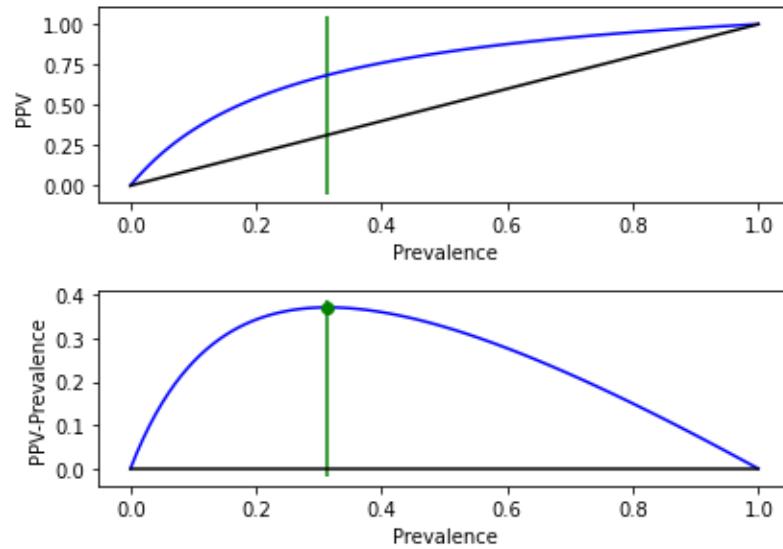
$$Odds_{post} = LR^+ Odds_{pre} = 8 * \frac{0.25}{1-0.25} = 8 * 0.33 = 2.64$$

$$Prob_{post} = \frac{Odds_{post}}{1+Odds_{post}} = \frac{2.64}{1+2.64} = \frac{2.64}{3.64} = 0.73$$

**Let's take a break to discuss the activity**

[https://hughesdrew.shinyapps.io/hit\\_survey/](https://hughesdrew.shinyapps.io/hit_survey/)

Applying Bayes theorem we can quantify the difference between the posterior and prior disease probability, **but how do we know when this difference is clinically meaningful?**



### *Prevalence Threshold*

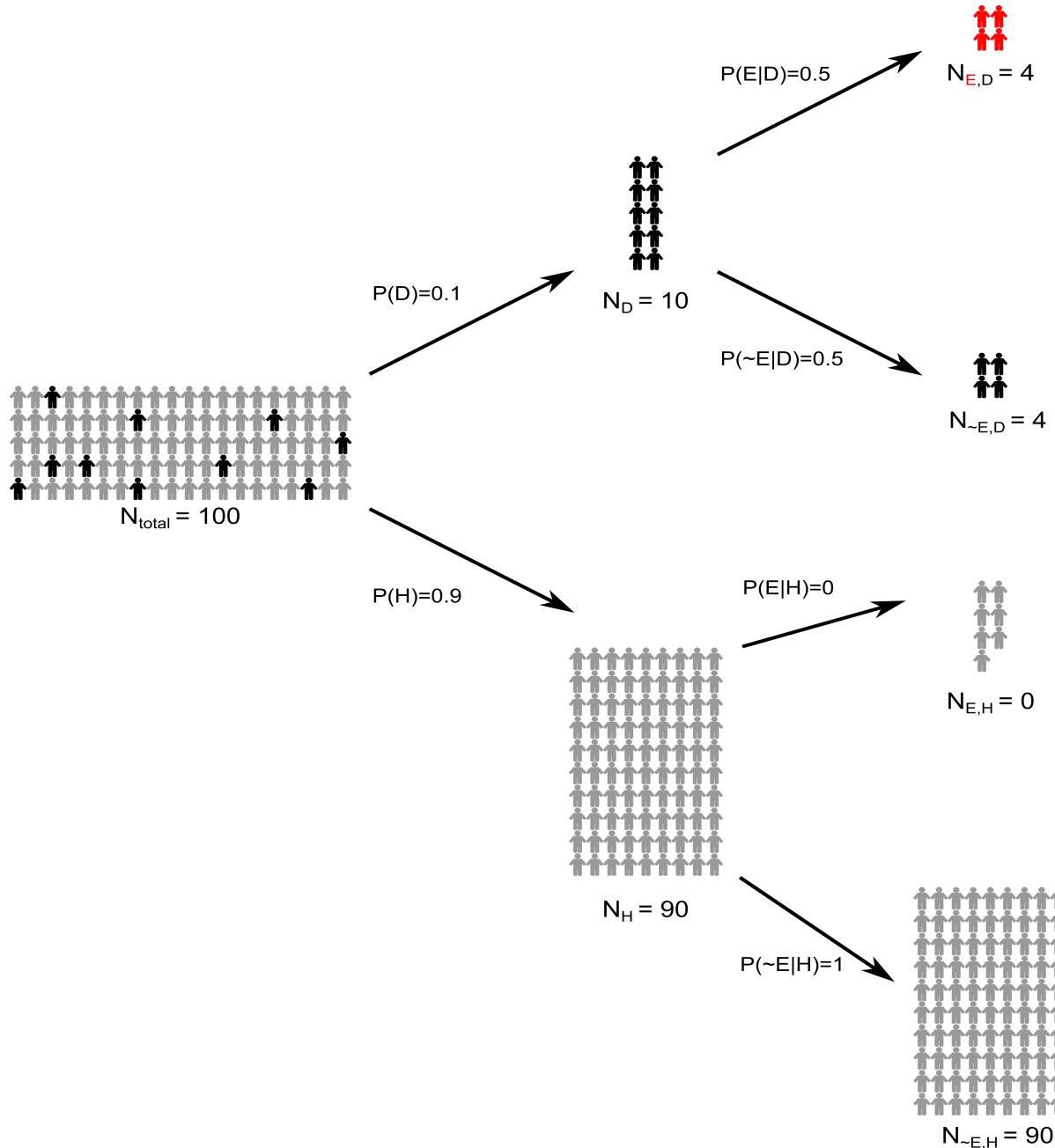
We have to define decision thresholds - at what probability do we treat?

(For more on prevalence threshold see J. Balayla 2020 PLoS One)

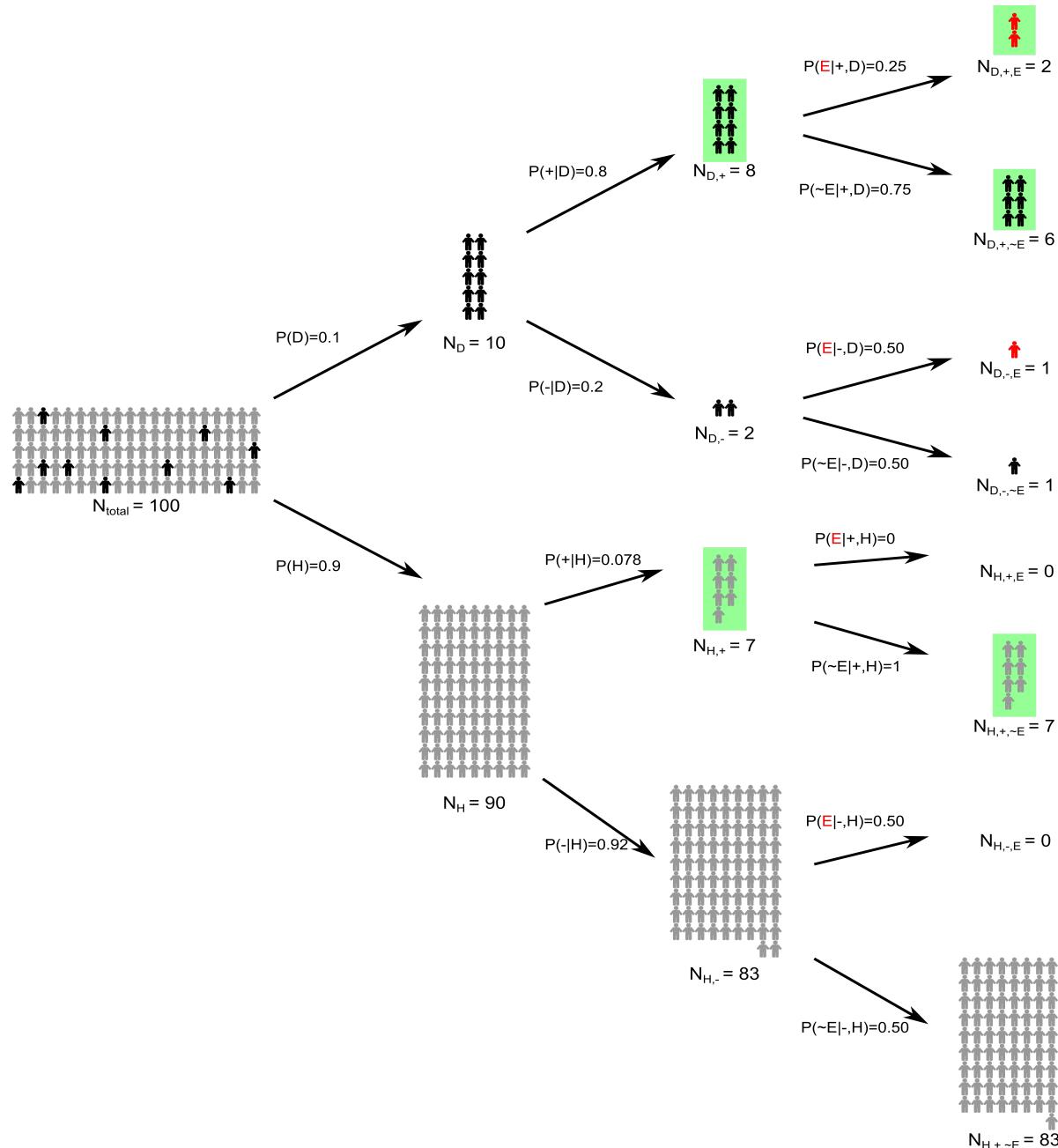
# Decision analysis

- A formal process to decision making
- Involves estimating the expected rates of desirable and undesirable outcomes
- Estimates are compared for the actions being considered
- Can incorporate objective and subjective criteria

# Expected rate of thrombosis without testing/treatment



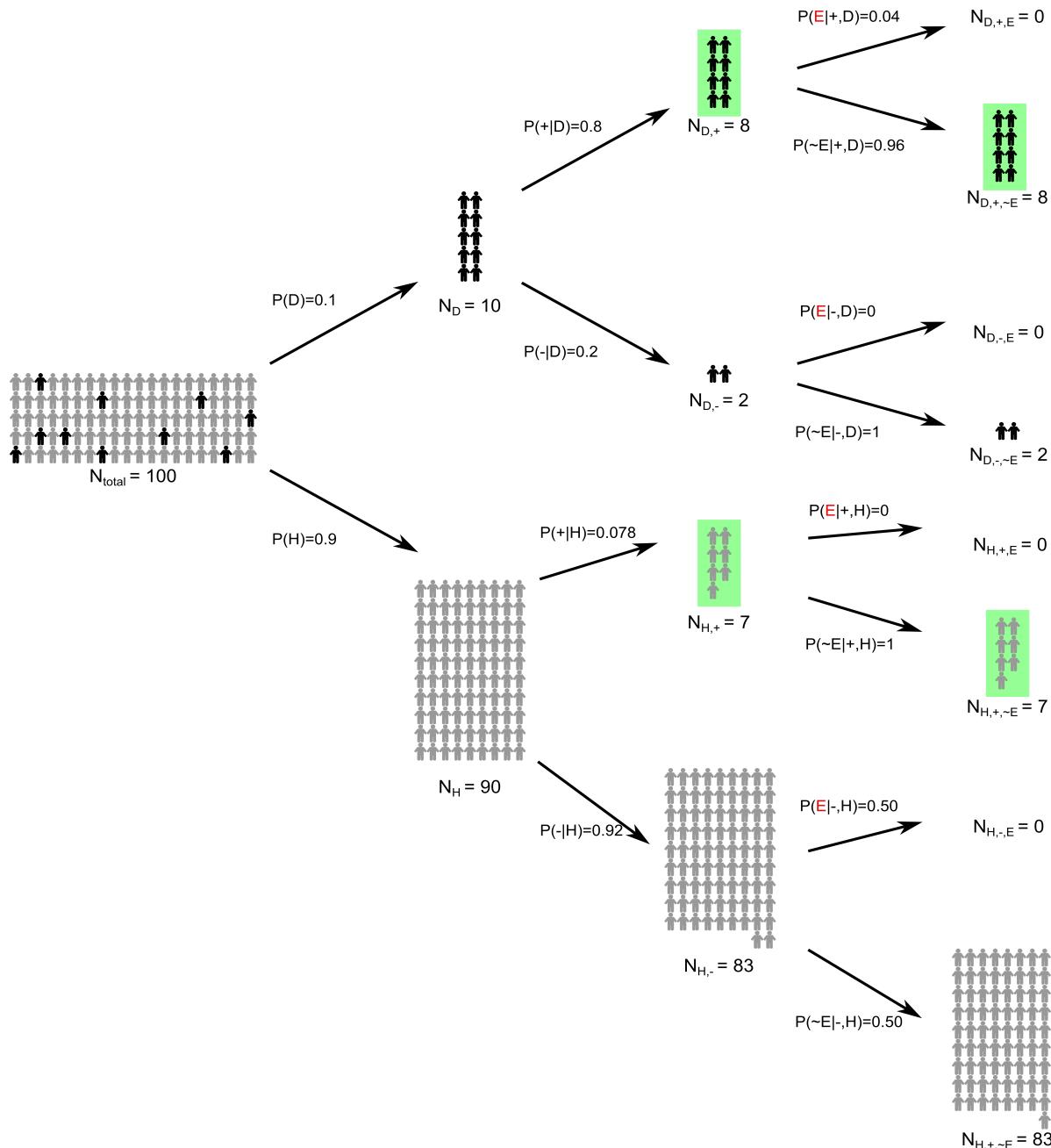
# Expected rate of thrombosis with testing based treatment



# **Laboratory testing and resultant treatments have associated costs and harms**

- If we only consider the information we gain we risk ignoring a net loss
- Our goal is to provide a net benefit and avoid a net harm
- Not all events carry equal value, so weighting of outcomes may be necessary

# Expected number of bleeding events with testing/treatment



# Computing metrics of utility

$$ER = \frac{\#Events}{\#Patients} \quad (EventRate)$$

$$RR = \frac{Event\ Rate_{testing}}{Event\ Rate_{control}} = \frac{\frac{3+0}{100}}{\frac{4+0}{100}} = \frac{3}{4} = 0.75 \quad (Relative\ Risk)$$

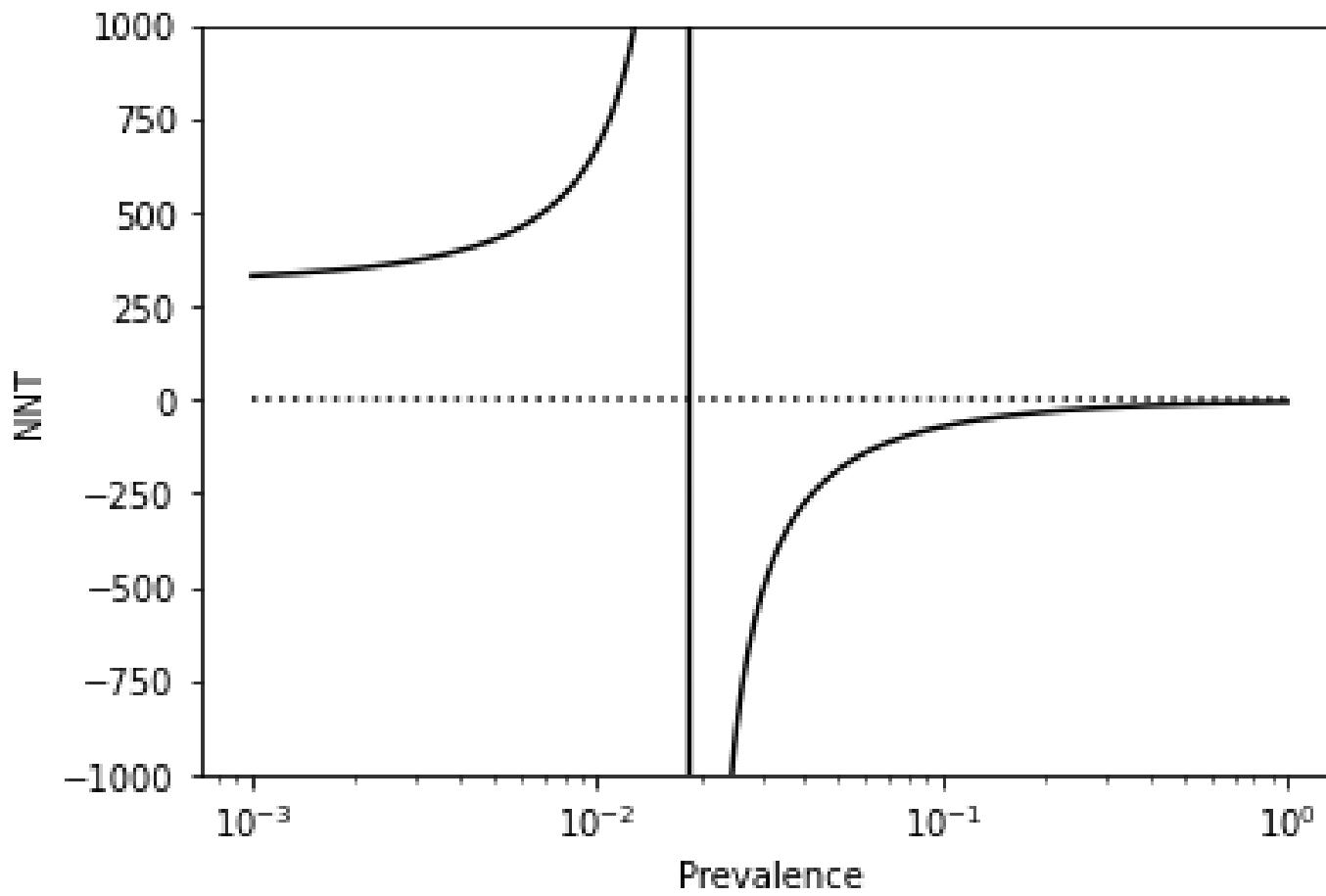
$$RRR = 1 - RR = 1 - 0.75 = 0.25 \quad (Relative\ Risk\ Reduction)$$

$$ARR = ER_{testing} - ER_{control} = \frac{3}{100} - \frac{4}{100} = -0.01 \quad (Abs\ Risk\ Reduction)$$

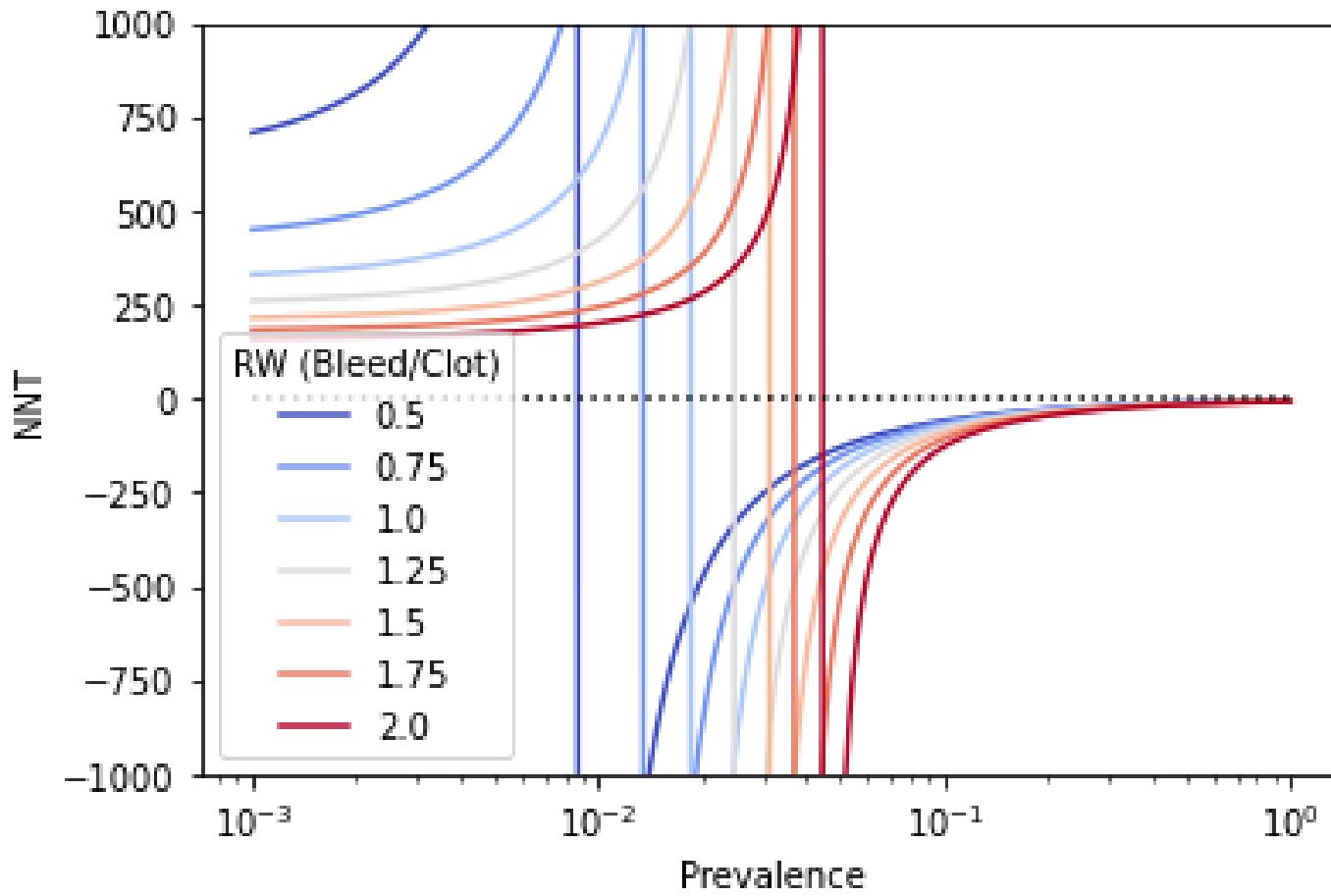
$$NNT = \frac{1}{ARR} = \frac{1}{-0.01} = -100 \quad (Number\ Needed\ to\ Test)$$

(Event = thrombosis or bleed)

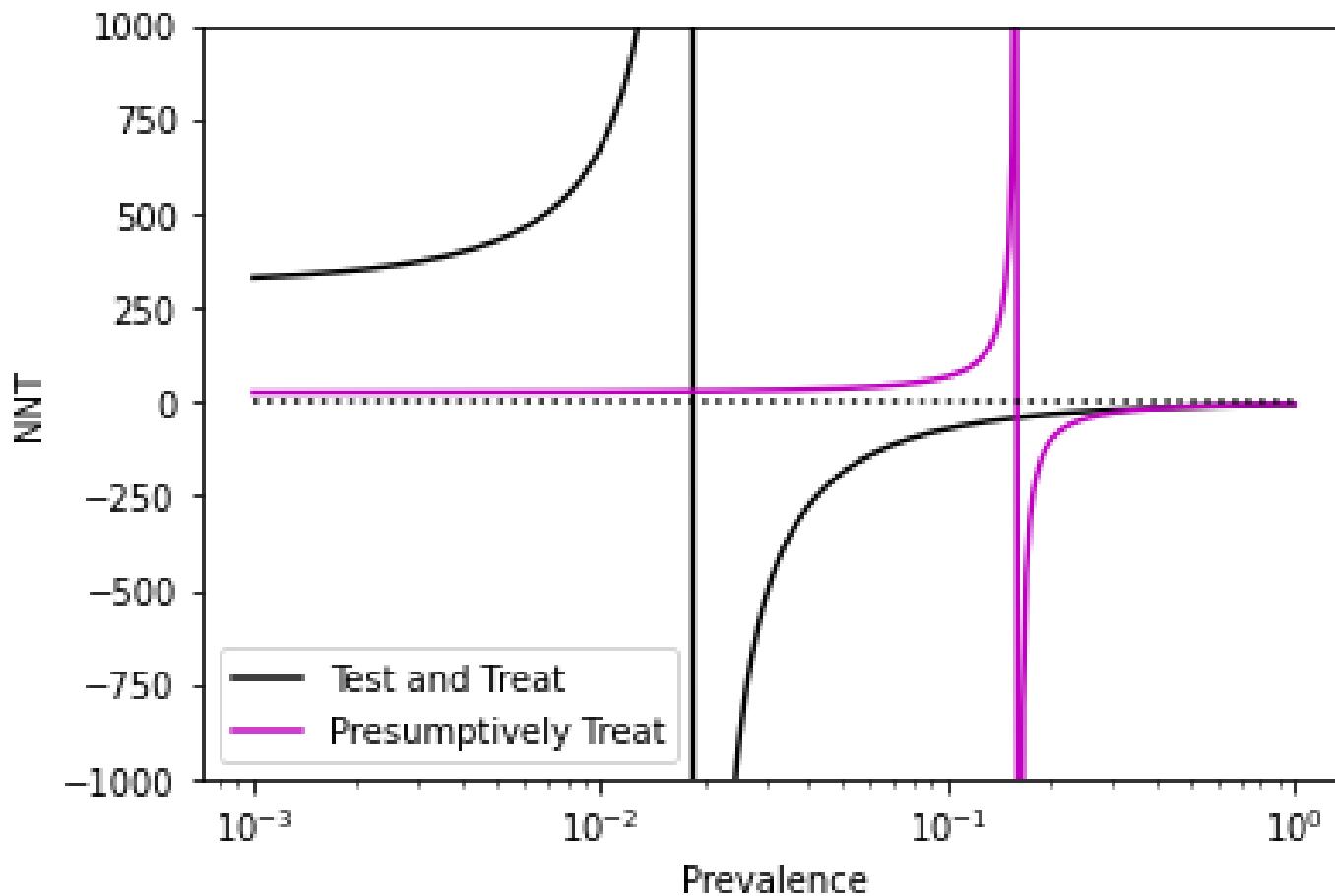
# Number needed to treat depends on prevalence



# Accounting for clinician/patient values



# What if we had just treated presumptively



## **Alternatively test value can be determined empirically**

- Results of decision analysis depends on model assumptions
- If a principled approach is not accessible an RCT paradigm can be used
  - Randomize to test vs no test, compare outcomes

# Unexpected Value (a note on secondary data uses)

- Development of EMR has provided new opportunities for secondary (i.e. not the primary intended use) uses for laboratory data
- The value engendered by secondary data uses **should not be considered** in the management of test utilization for clinical purposes
  - Ordering of clinical testing billed to patient/patient insurance for secondary use purposes constitutes fraud

# Learning objectives

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