# Hypothesis testing in public health

Seth D. Temple
Statistics Ph.D. candidate
UW Biostatistics Teaching Demo
January 18, 2024

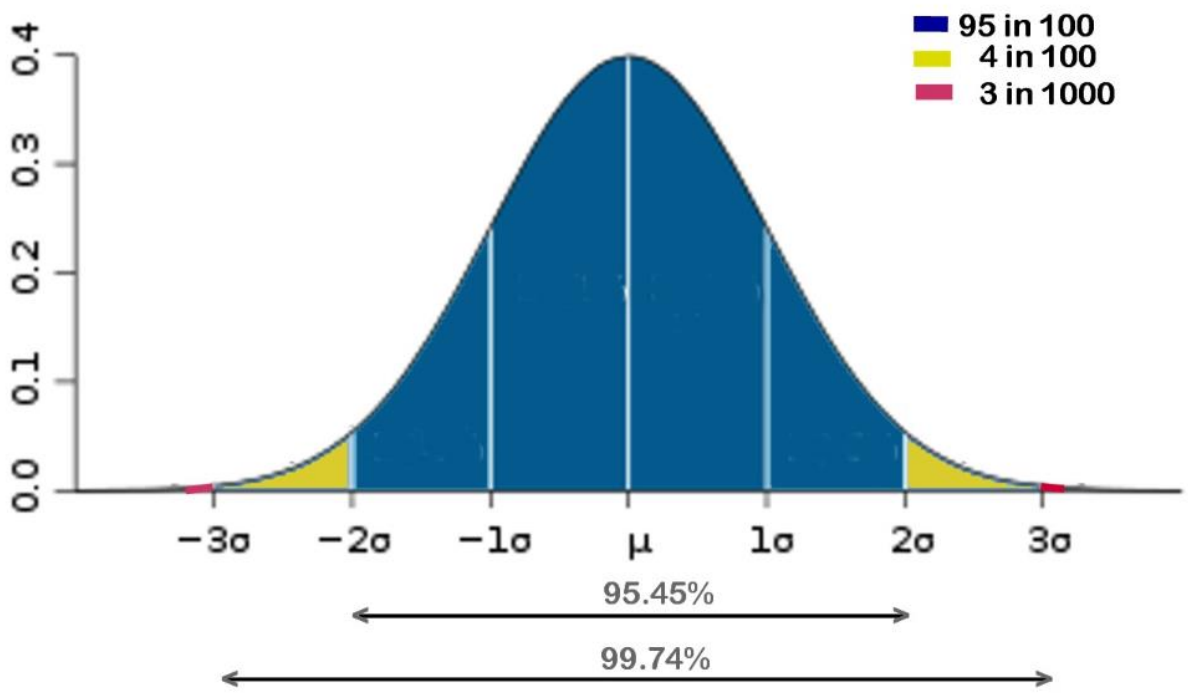
# Last class

**Parameter:**

- Feature of a population
- Model for data generation

**Statistic:**

- Feature of a sample
- Estimate parameter from data



# Learning objectives

- Frame a research question as a statistical question
- Define Type 1 and Type 2 Error
- Discuss their importance in a research study

* Not graded

# Participation* expectations

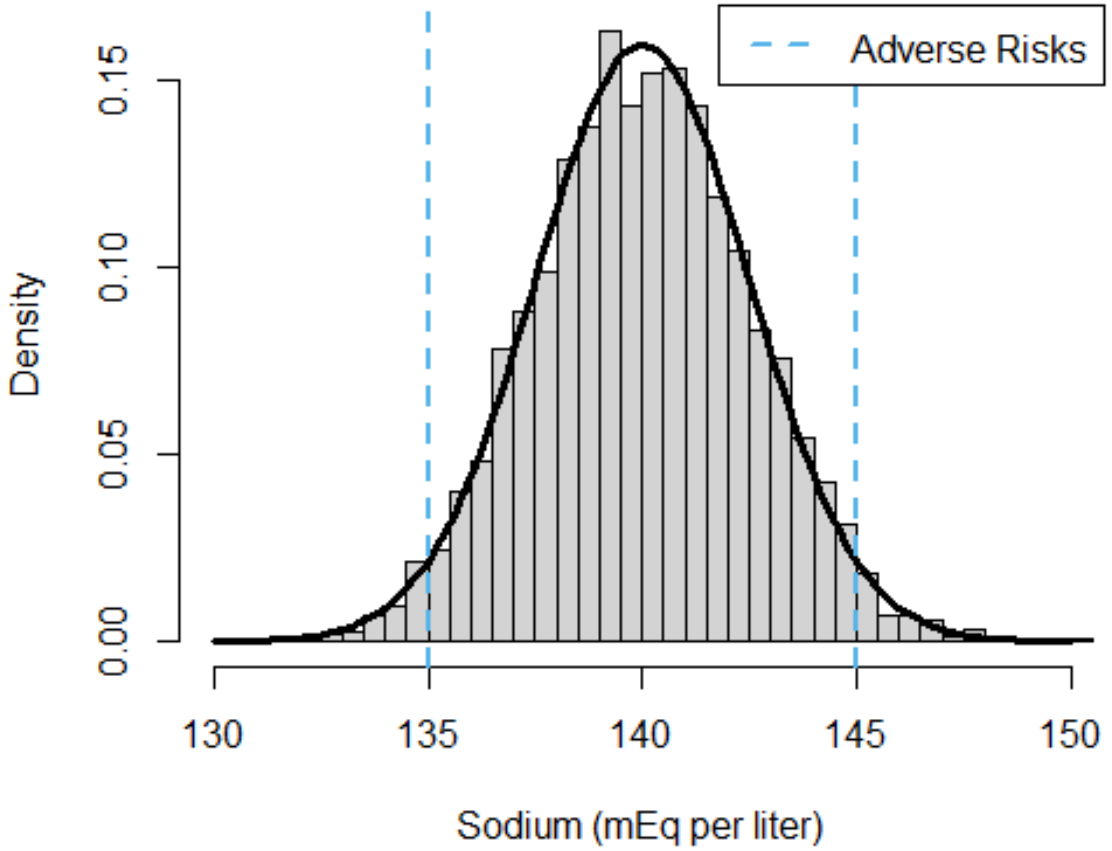
- Exercise 1
  1. Chatter in small group, or write response on notes (~60 sec.)
  2. Solicit responses for larger discussion

- Exercise 2
  - Think about your response privately (5 sec.)
  - Quick “Yes/No” poll after countdown

- Show respect; no judgment

# Example 1: Sodium homeostasis

- Sodium is important to biological processes
- Too little may lead to health consequences
- Lamotrigine helps treat bipolar disorder. It may affect sodium levels.



## Research Question

- Does **lamotrigine** affect levels of **sodium**?

## Statistical Question

- $\mu_0$ is “average” parameter based on prior study
- $\mu_D$ is parameter for population taking lamotrigine
- Does the **sample mean $\bar{X}_D$** sodium give enough evidence to reject that $\boldsymbol{\mu_D = \mu_0}$?

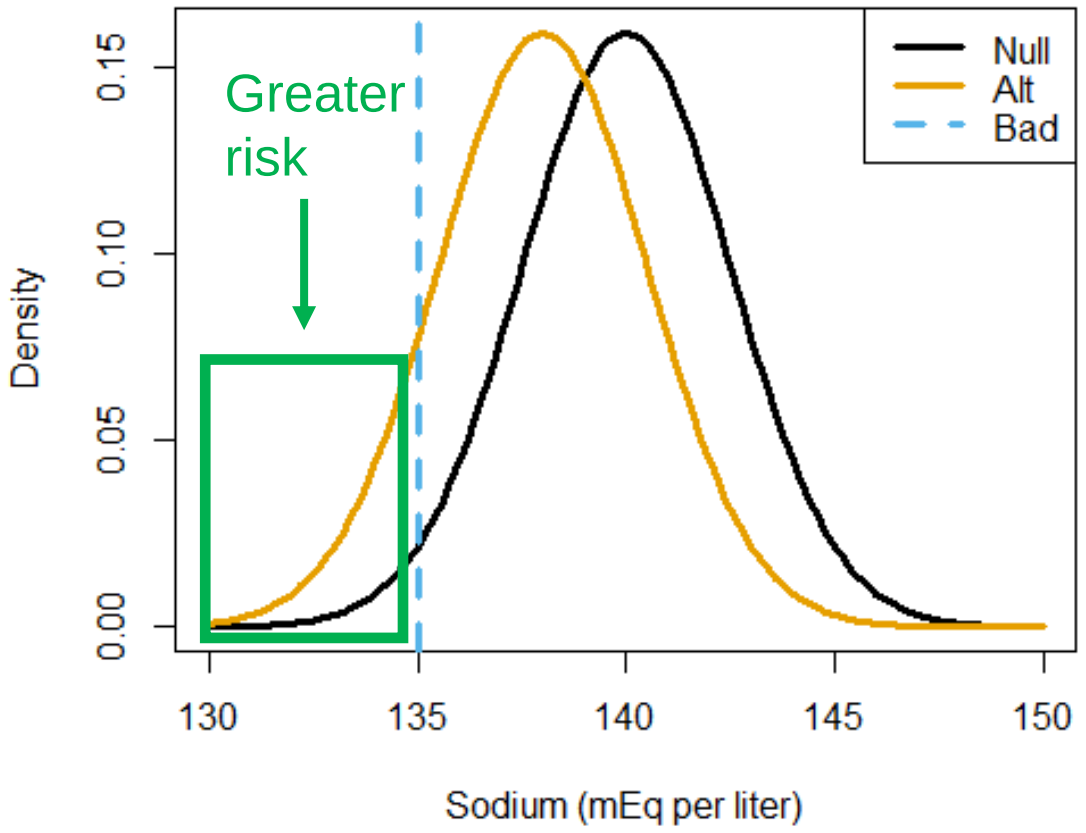
# Why do we care about hypothesis tests?

**Reward**

- Prescribe patients an effective treatment

**Risk**

- Do harm to patients



# Type 1 Error. We reject that $\mu_D = 140$ even though it is.

* This definition generalizes to other hypothesis tests.

# Type 2 Error. We fail to reject $\mu_D = 140$ given that $\mu_D = 138$.

* This definition generalizes to other hypothesis tests, say $\mu_D \neq 140$.

(Have you taken a COVID test before?)

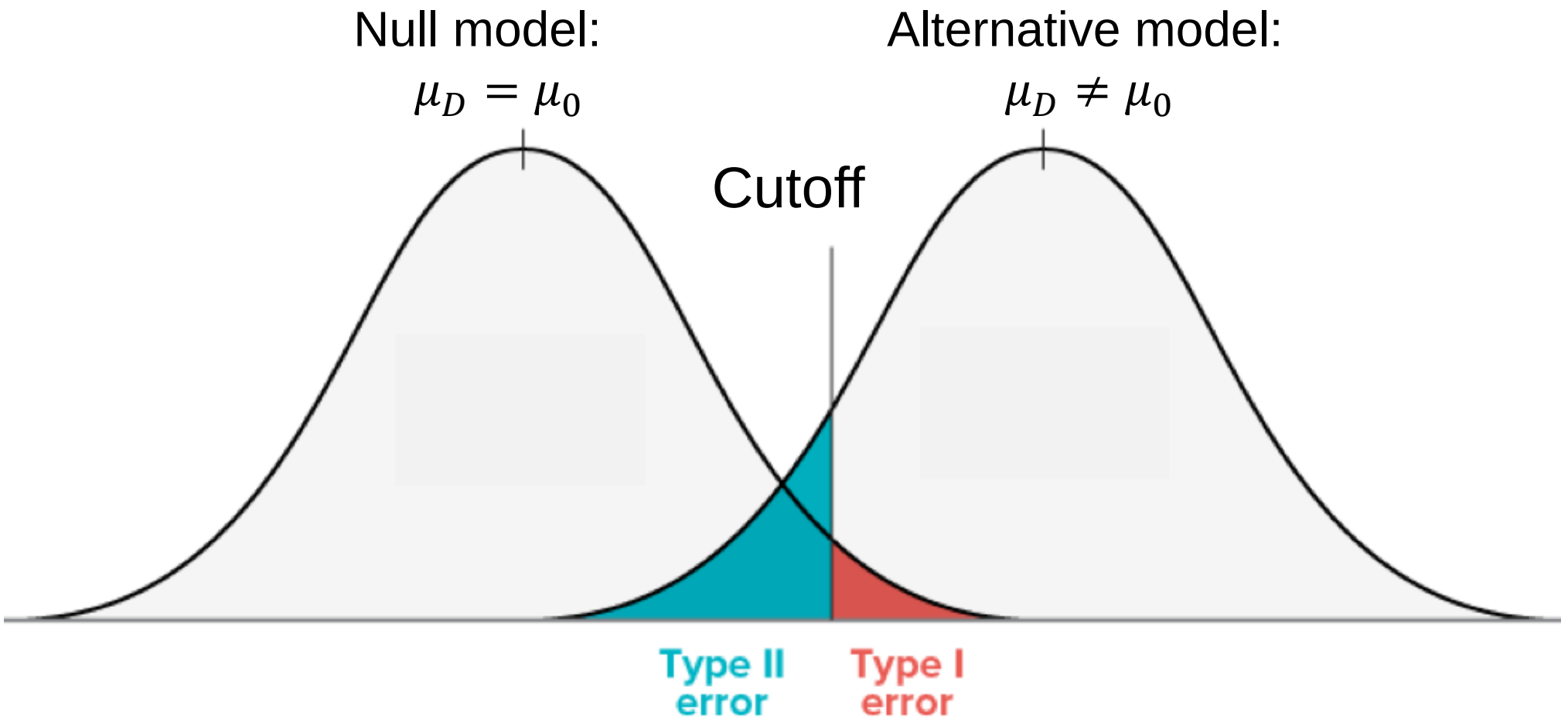
# Warm-up viral tests


| Predicted / Concluded \ Actual | + | - |
|---|---|---|
| + | True positive | False positive |
| - | False negative | True negative |

Type 1 error

Type 2 error

# Visualizing Type I,II errors

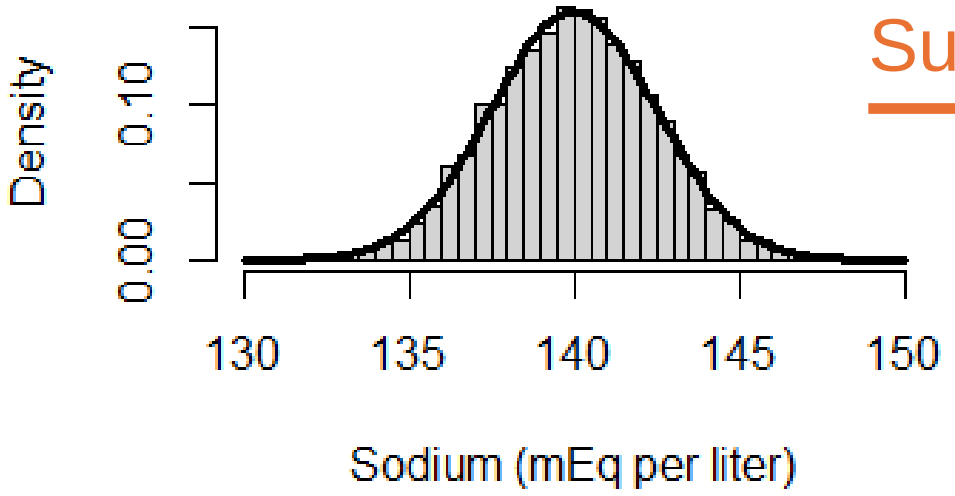


# Hypothesis test calculation

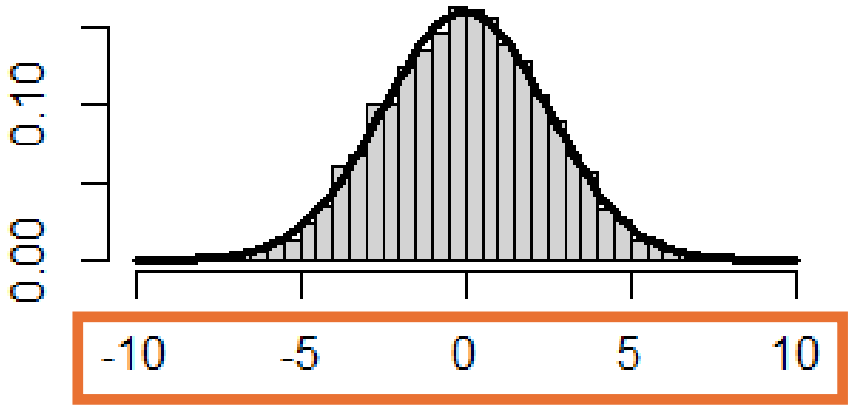
- Collect blood work from 30 individuals
- $X_1, \ldots, X_{30}$ are their sodium levels
- Compute the mean

$$\bar{X}_D = \frac{X_1 + \cdots + X_{30}}{30}$$

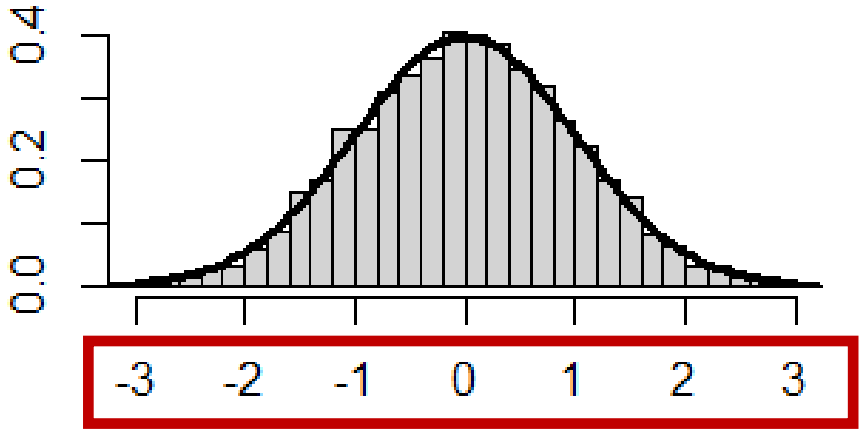
$***$ $X_D$ is statistic estimating $\mu_D$ $***$




Subtract




Divide




# Put the statistic on a common scale

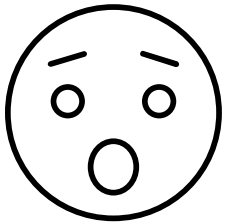
# Hypothesis test calculation

Sodium levels $X_1, \ldots, X_{30}$ from patients taking lamotrigine

$$\boldsymbol{\bar{X}_D = 138.42}$$

$$\boldsymbol{Z_D = \sqrt{30} \times \frac{(\bar{X}_D - 140)}{2.5} = -3.46}$$

$p$-value: probability mean as extreme is 0.0005 !!!



# $p$-value: the probability of observing a statistic as extreme as in our sample

Here our statistic is the mean

Under the null model

# Type 1 error simulations

- Assume model $N(\mu_0 = 140, \sigma = 2.5)$
- Run 1000 experiments
  1. Simulate 30 samples from model
  2. Compute $Z_D$ statistic
  3. If $|Z_D| > 1.96$, add 1 to running count

I found $|Z_D| > 1.96$ to occur $\frac{53}{1000} \approx 0.05$.

# Discussion activity (60 sec.)

Study effect of lamotrigine on # **of mood swings**

- 50 participants in Drug D group
- 50 participants in Placebo P group

1. How would you phrase the statistical question in this study?
2. How would you phrase the Type 1 error?

# My answer key

1. Does the difference of sample means $\boldsymbol{\bar{X}_D - \bar{X}_P}$ give enough evidence to reject that $\boldsymbol{\mu_D - \mu_P = 0}$?

2. We reject initial assumption $\mu_D = \mu_P$ despite $\mu_D = \mu_P$.

# Back to sodium homeostasis example

# Alternative Hypothesis Experiment

- Run an experiment 1000 times
  1. Simulate 30 samples from model $N(\boldsymbol{\mu_D}, \sigma = 2.5)$
  2. Compute $Z_D = \sqrt{30} \times (\bar{X}_D - 140)/2.5$
  3. If $|Z_D| > 1.96$, add 1 to a running count

| True Parameter $\mu_D$ | Type 2 Error | Power = 1 - Type 2 |
|---|---|---|
| 139.75 | 0.91 | 0.09 |
| 139.50 | 0.81 | 0.19 |
| 139.00 | 0.42 | 0.58 |
| 138.00 | 0.01 | 0.99 |

# Sample Size Experiment

Same as before, except # of people varies

The true drug effect $\mu_D$ is 139

| Sample Size | Type 2 Error |
|---|---|
| 10 | 0.77 |
| 20 | 0.57 |
| 30 | 0.42 |
| 50 | 0.28 |

# Confidence level experiment

Same as before, except controlling Type 1 error varies

The true drug effect $\mu_D$ is 139

| Confidence | Type 2 Error |
|---|---|
| 0.10 | 0.29 |
| 0.05 | 0.41 |
| 0.01 | 0.65 |
| 0.001 | 0.86 |

# My answer key

Type II error probability depends on specifying tolerance for Type I error.

We may want to make few Type 1 errors.

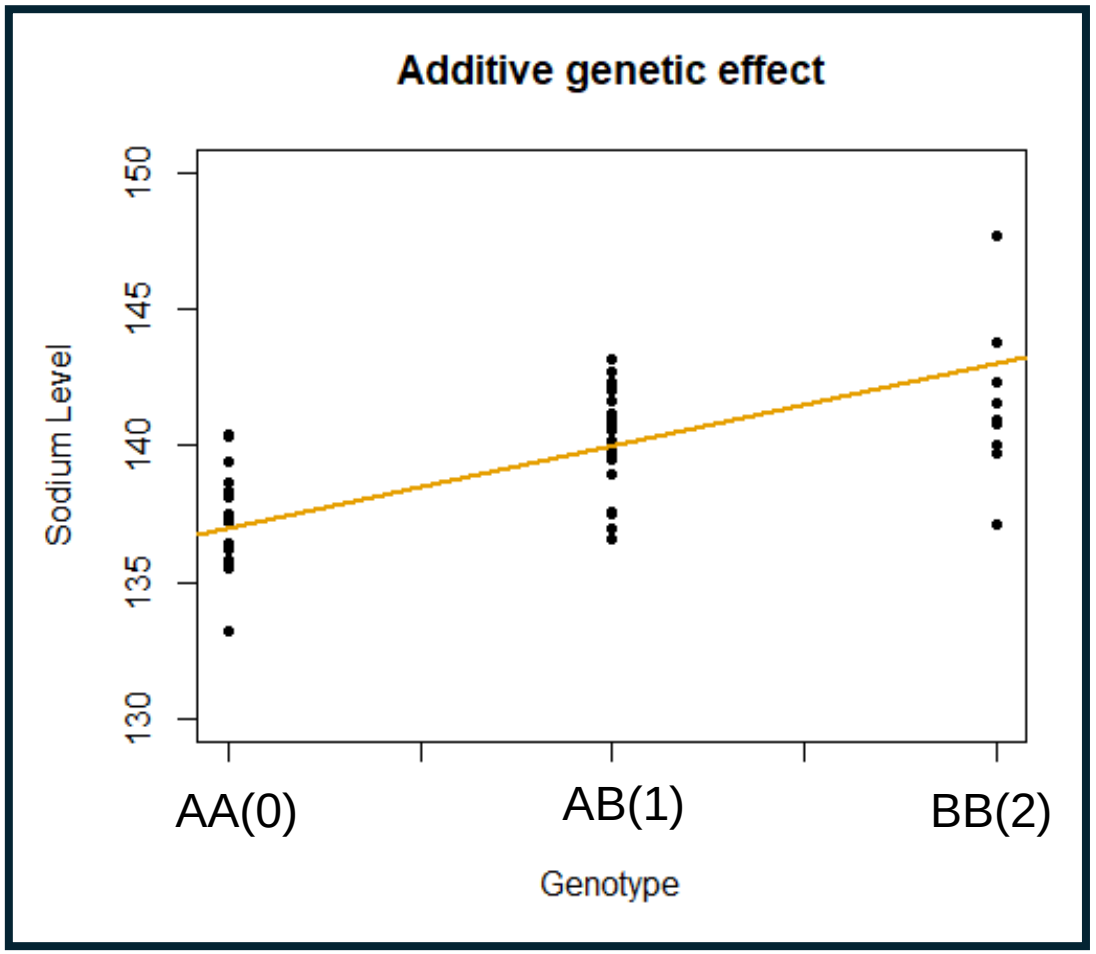
# Beyond $p$-values

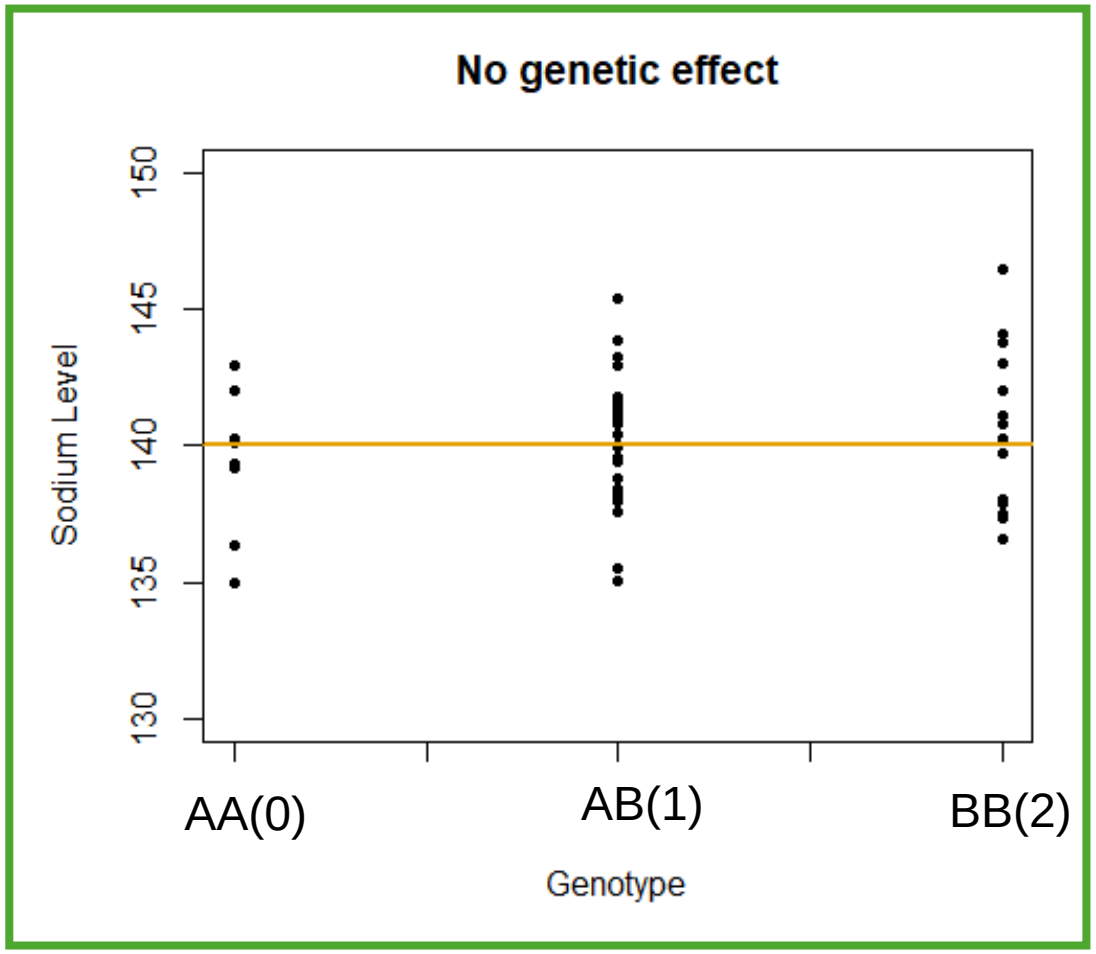
- Lamotrigine shows “significant” effect on mood! Why worry about sodium levels?
  - How effective is significant? 😕
  - $\mu_0$ is based on non-representative study. 😕
  - Prescription costs 😕
  - Studies had few participants ☹
  - Electrolytes are effective supplement ☺

# Example 2: Genetic associations

- Genotypes AA (0), AB (1), BB (2)
- $(Y_1, \ldots, Y_n)$ sodium levels
- $(X_1, \ldots, X_n)$ genotypes
- $\epsilon_i$ random noise

$$Y_i = \underbrace{\beta_0}_{\text{Intercept}} + \underbrace{\beta_1}_{\text{Slope}} \times X_i + \epsilon_i$$


Additive genetic effect
Sodium Level
150
145
140
135
130
AA(0)
AB(1)
BB(2)
Genotype


No genetic effect
Sodium Level
150
145
140
135
130
AA(0)
AB(1)
BB(2)
Genotype

# Simulate additive genetic effect

1. Draw roughly $\frac{1}{3}, \frac{1}{3}, \frac{1}{3}$ genotypes AA, AB, BB
2. Draw 50 errors $\epsilon \sim N(\mu = 0, \sigma = 2.5)$
3. Compute $Y$
   - Intercept $\beta_0 = 137$
   - Slope $\beta_1 = 3$
4. Compute $p$-value from average $\bar{Y}$

Would you reject that slope is zero?

# Studying one variant

Simulated additive effect model:

$$Y = 137 + \mathbf{3} \times X + \epsilon$$

| Parameter | Estimate | p-value |
|---|---|---|
| Slope | 2.91 | 2e-16 |

# Simulate no genetic effect

1. Draw roughly $\frac{1}{3}, \frac{1}{3}, \frac{1}{3}$ genotypes AA, AB, BB
2. Draw 50 errors $\epsilon \sim N(\mu = 0, \sigma = 2.5)$
3. Compute $Y$
   - Intercept $\beta_0 = 140$
   - Slope $\beta_1 = 0$
4. Compute $p$-value from average $\bar{Y}$

Would you reject that slope is zero?

# Studying one variant

Simulated no effect model:

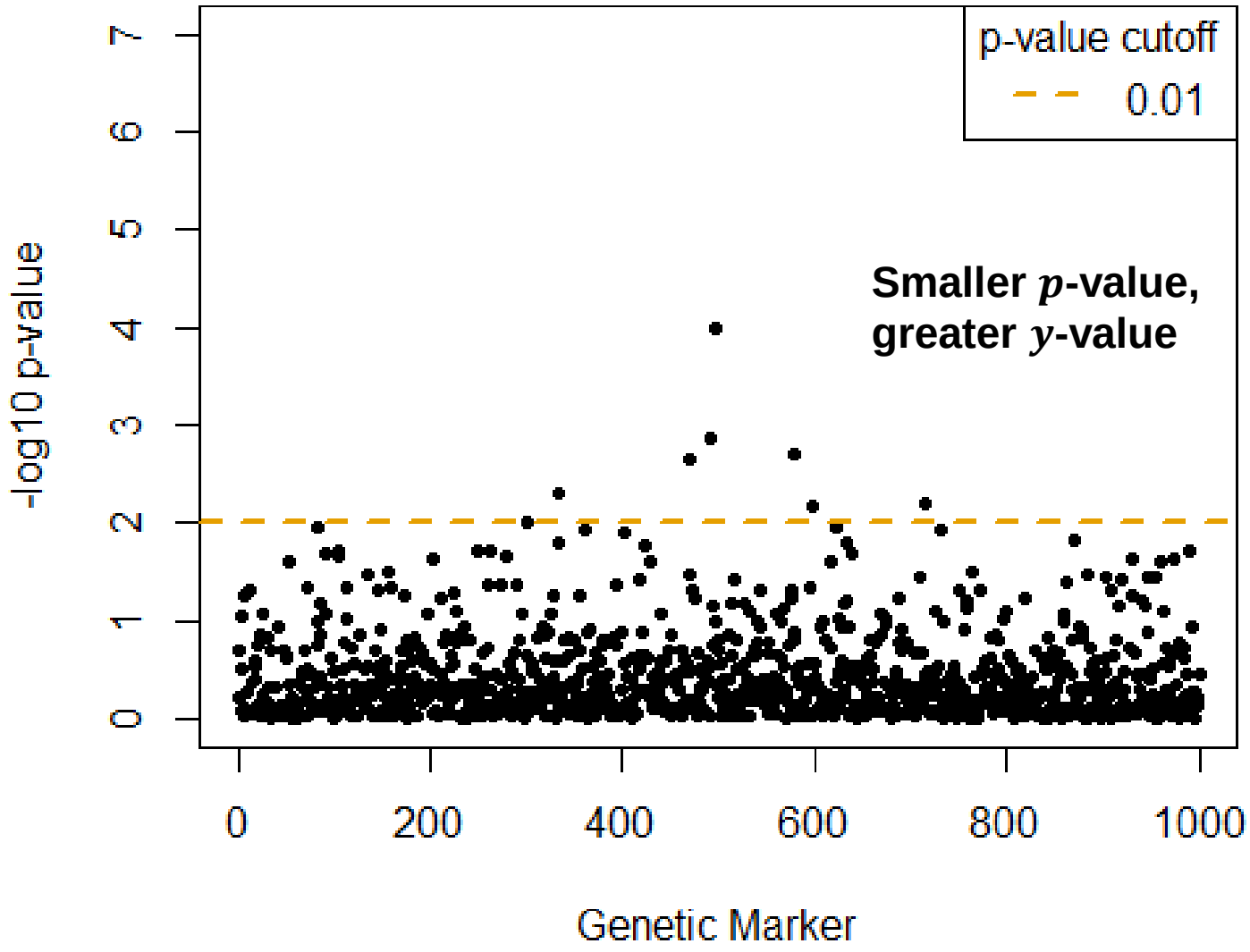
$$Y = 140 + \mathbf{0} \times X + \epsilon$$

| Parameter | Estimate | p-value |
|---|---|---|
| Slope | -0.09 | 0.67 |

# Simulate no genetic effect for 1000 genetic markers

Markers are independent

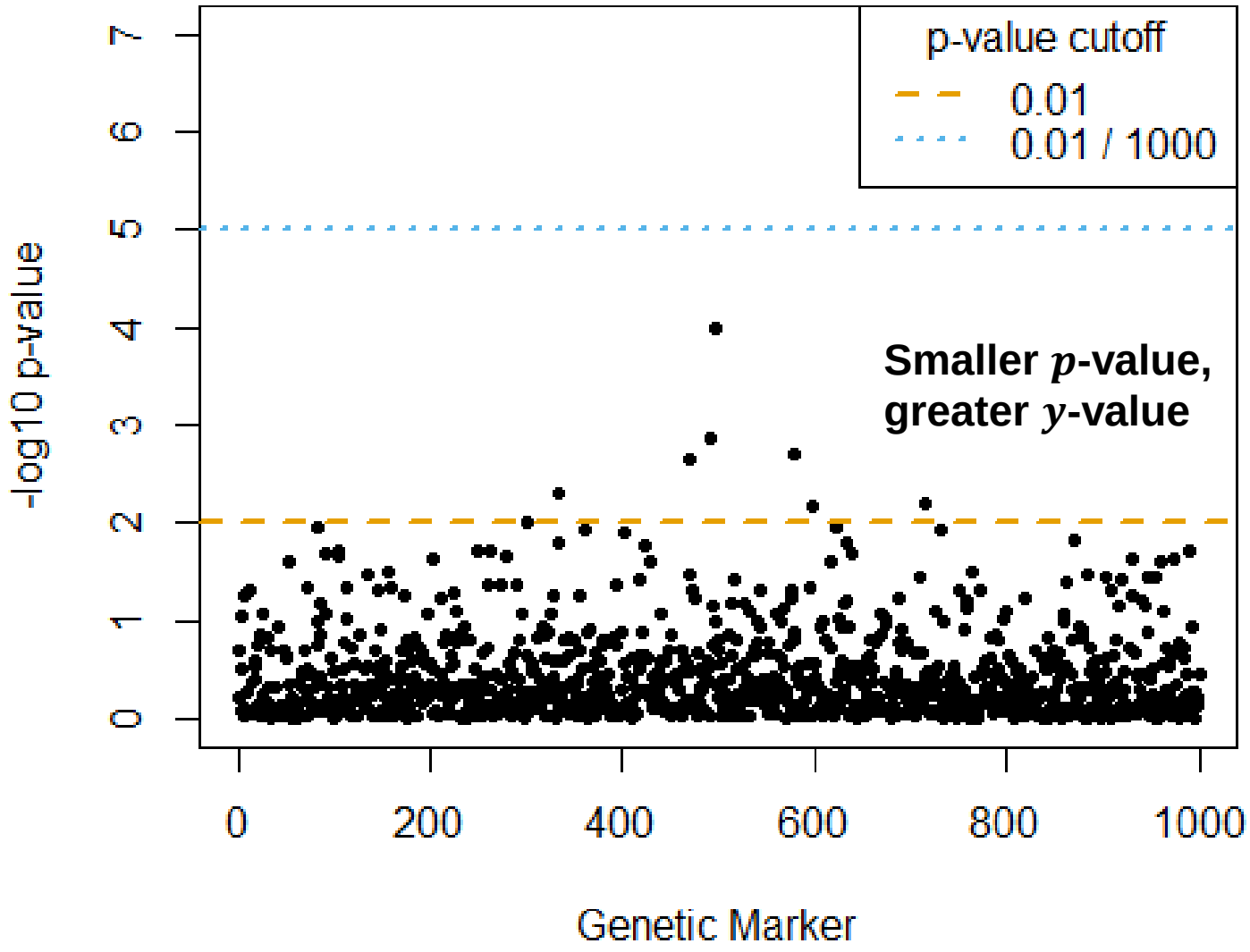
## Is sodium metabolite associated w/ genotypes?



# Why do we observe **~ 10 / 1000** "significant" associations?

- $p$-value threshold should be smaller
- Divide by # tests

# Is sodium metabolite associated w/ genotypes?



# Today's review

- Two examples of statistical analysis
  - Average sodium level (continuous)
  - Genetic association (linear relationship)

- **Type 1 error** is about controlling for false positives
  - Testing too many things
- **Power** is about identifying true positives

Next class: more types of hypothesis tests

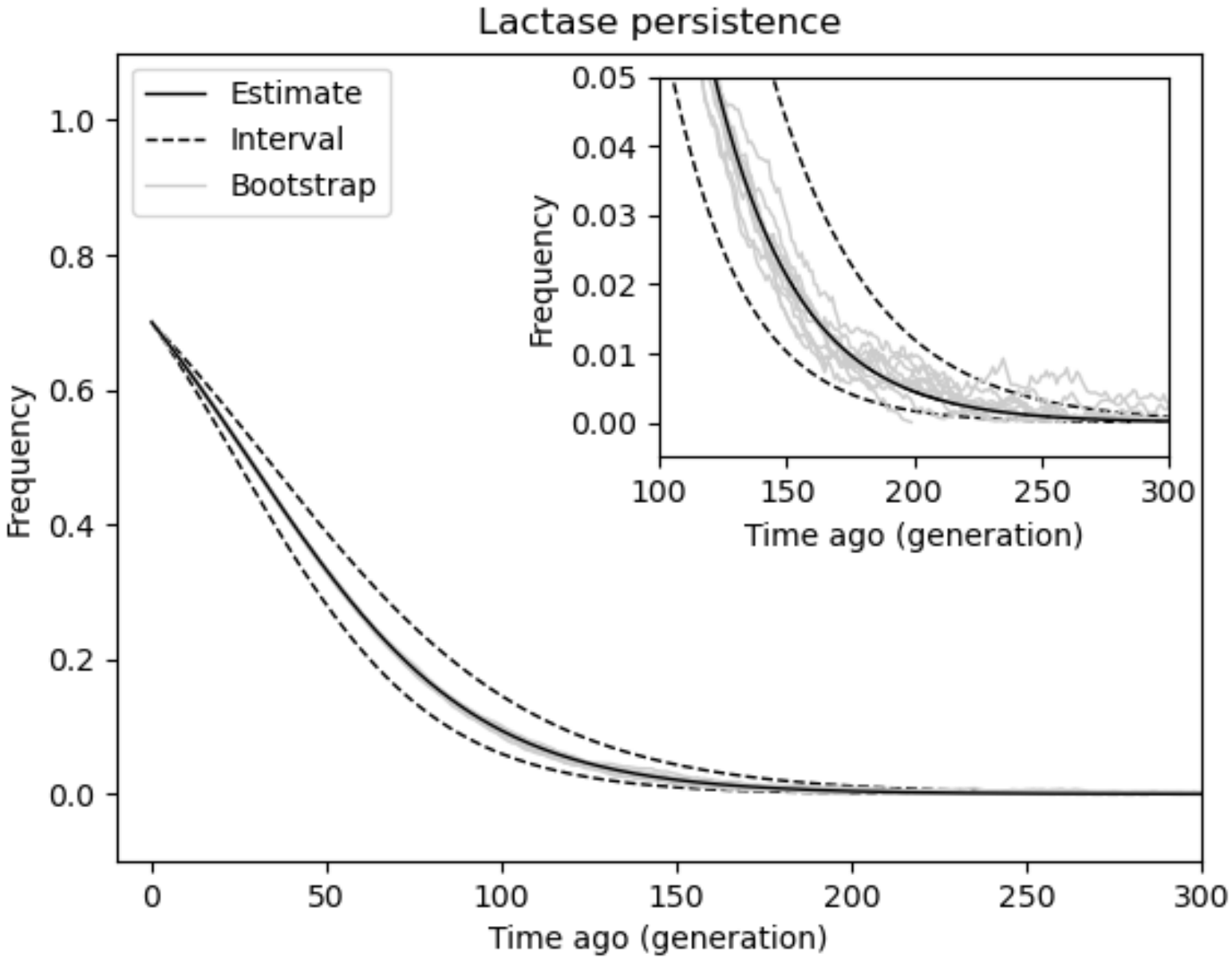
# My vision in this role

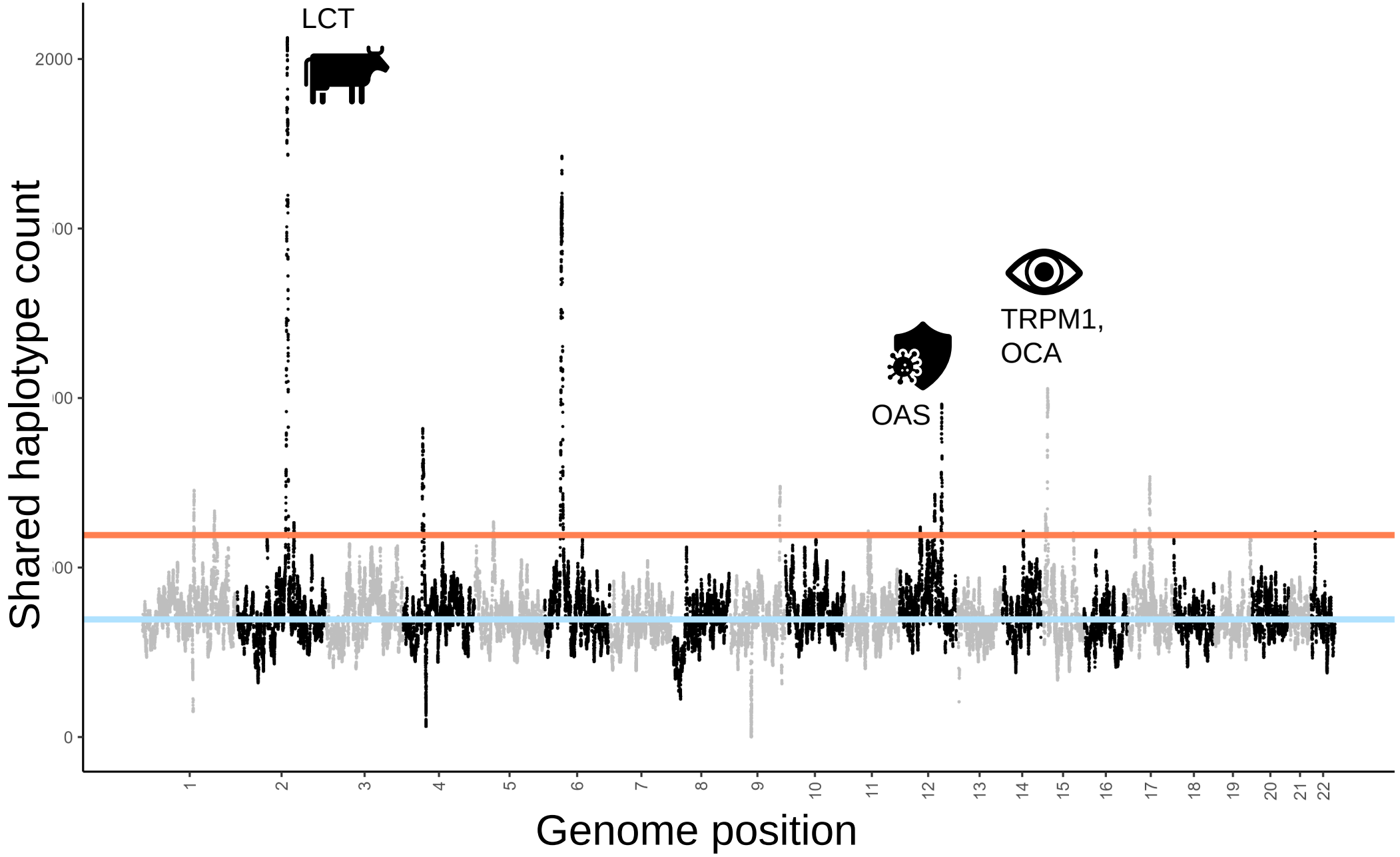
- Today: teaching undergrads in public health
- Able to teach grad courses (512, 513, 533, 570-1, …)
- Passionate about statistical genetics
  - Broadening curriculum beyond human genomics
  - Outreach (workshops, online courses)
  - An undergraduate course
  - Mentoring student research
  - Promoting DEI

sdtemple.github.io/files/teaching-demo-sdtemple.pdf
sdtemple.github.io/files/teaching-demo-sdtemple.R

# Thank you for the invite

Appendix: my research


Lactase persistence
Estimate
Interval
Bootstrap
Frequency
Time ago (generation)
0.0
0.2
0.4
0.6
0.8
1.0
0
50
100
150
200
250
300
0.00
0.01
0.02
0.03
0.04
0.05


LCT
TRPM1,
OCA
OAS
Shared haplotype count
2000
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
Genome position

# Current & future research

- Correlated binary random vector in light of unobserved process
- Recent selection in non-European or non-human studies
- Deep learning in population genetics