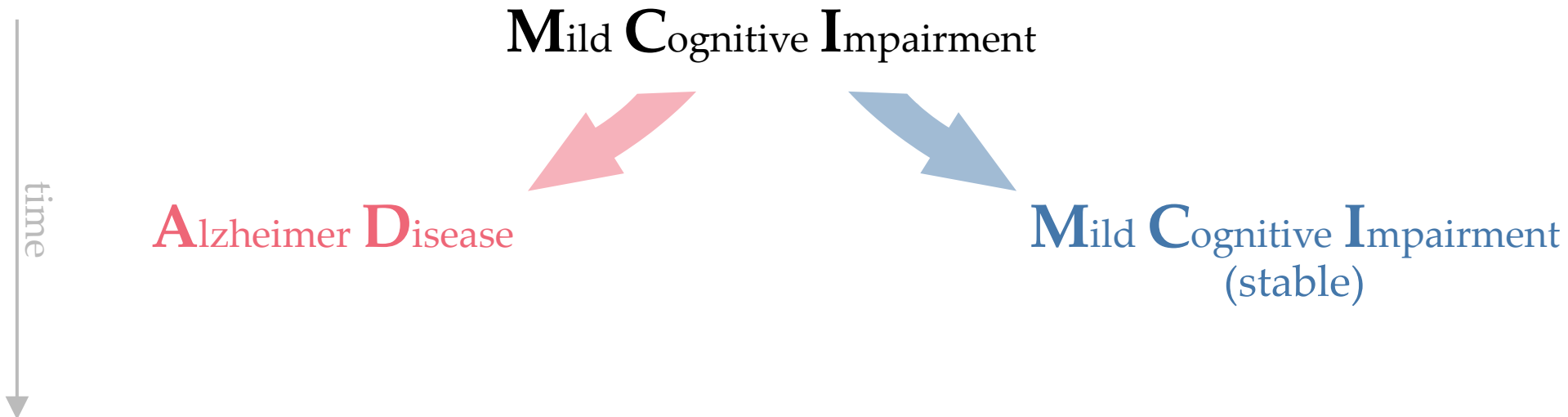
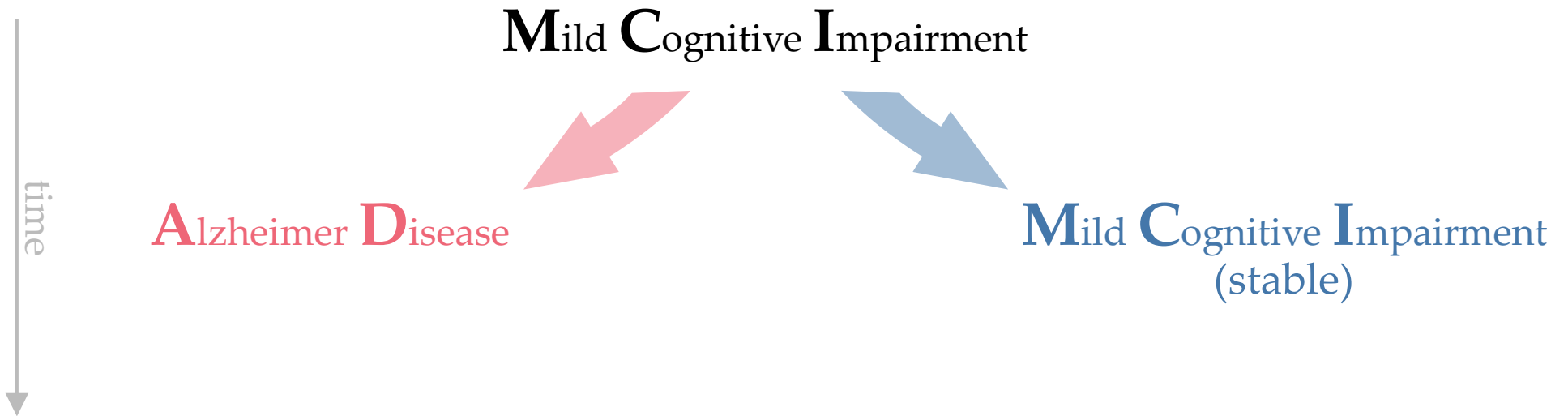


Analysis of some features  
for prognosis of Alzheimer onset:  
Probability theory & Information theory

*Luca, Alexandra, Ingrid  
MMIV-ML group meeting, 13 January 2022*

# Mild Cognitive Impairment





 Gender

 AGE

 RAVLT

 ANARTERR

 GDTOTAL

 TRABSCOR

 CATANIMSC

 TRAASCOR

 AVDELTOT

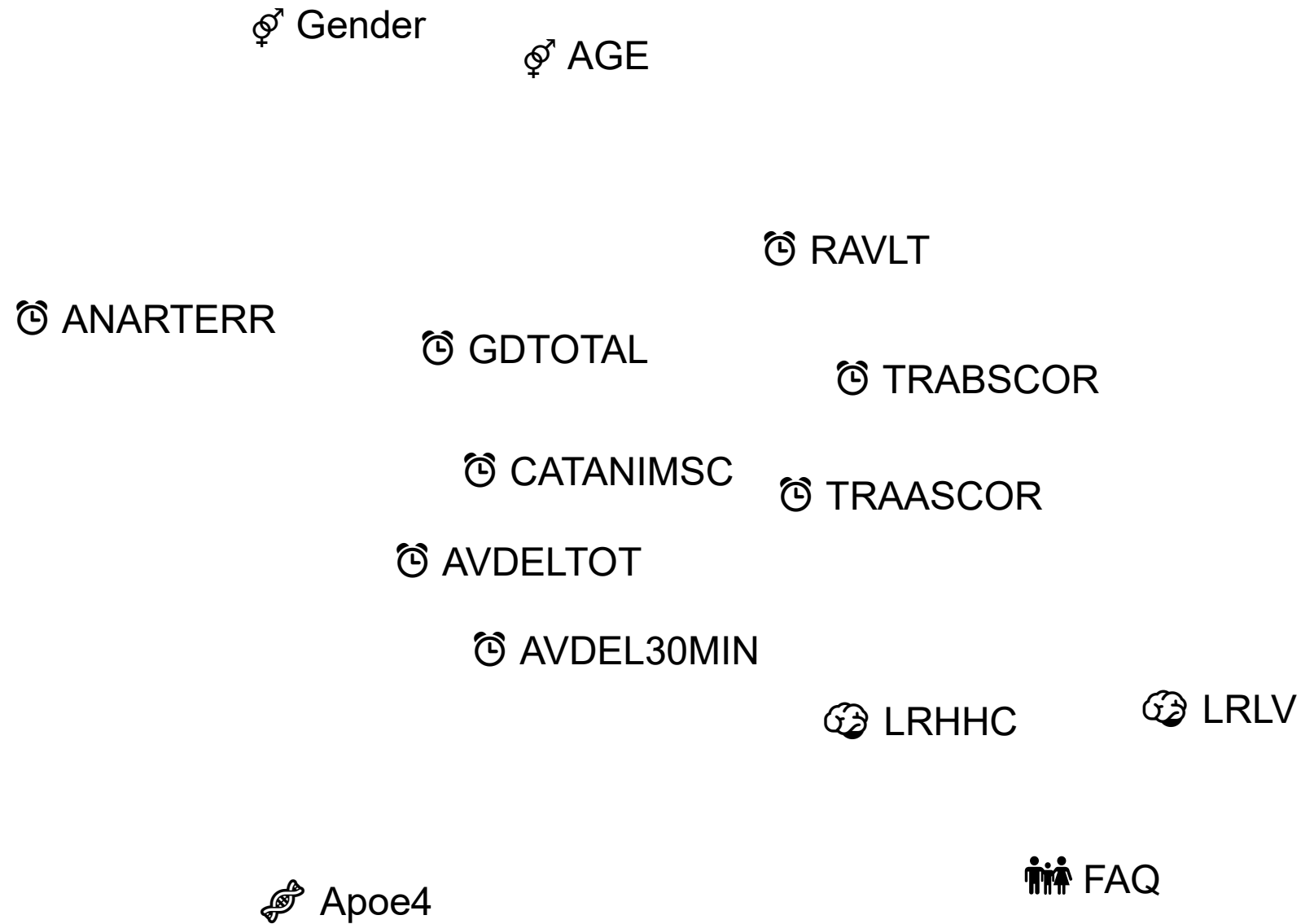
 AVDEL30MIN

 LRHHC

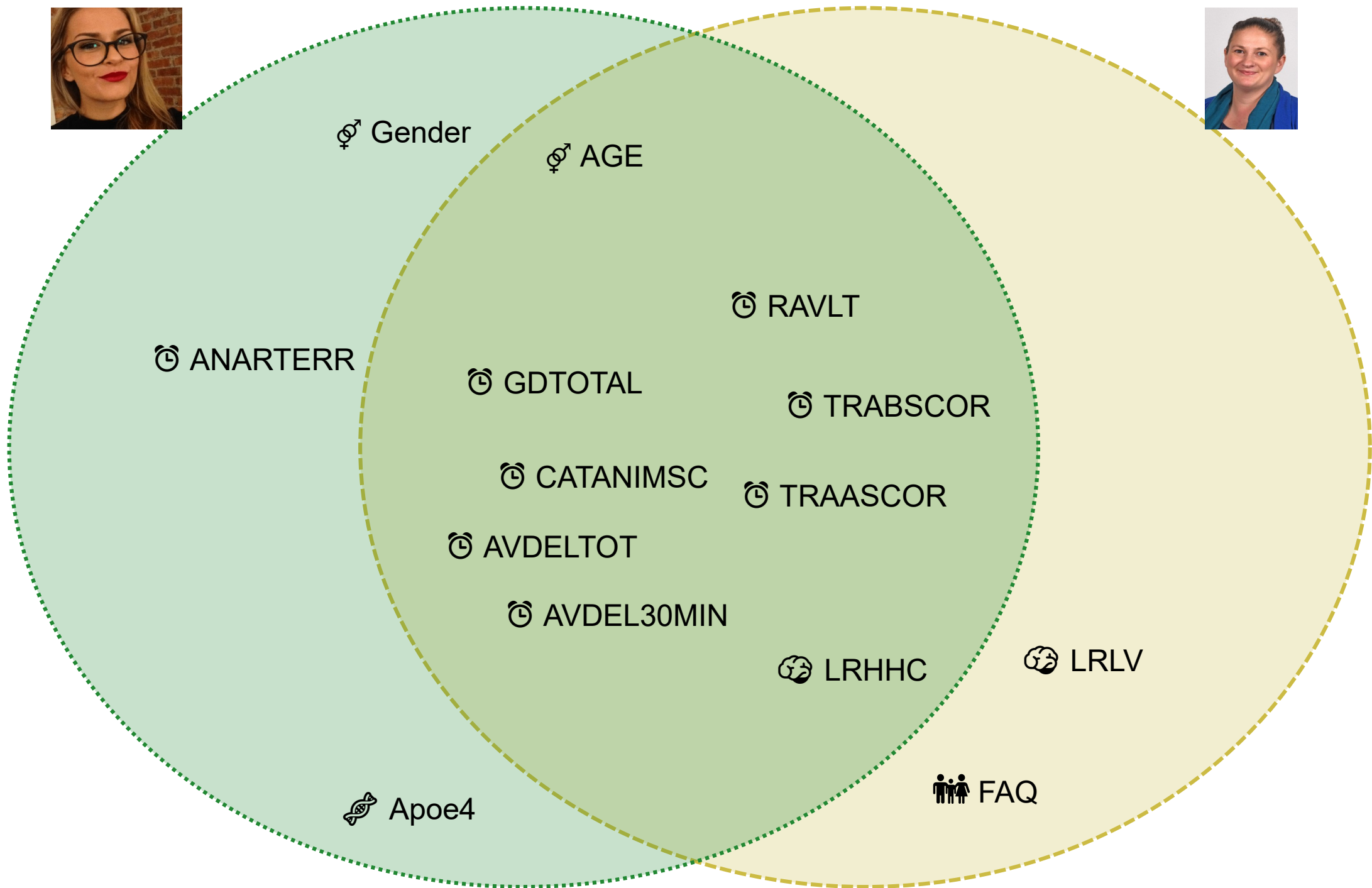
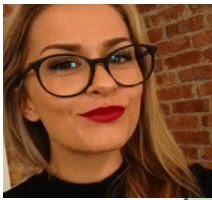
 LRLV

 Apoe4

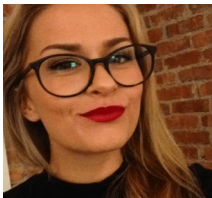
 FAQ



How 'good' are these features at prognosing the later onset of Alzheimer?



How 'good' are these features at prognosing the later onset of Alzheimer?



## Functional Activities Questionnaire

### Administration

Ask informant to rate patient's ability using the following scoring system:

- Dependent = 3
- Requires assistance = 2
- Has difficulty but does by self = 1
- Normal = 0
- Never did [the activity] but could do now = 0
- Never did and would have difficulty now = 1

Writing checks, paying bills, balancing checkbook	
Assembling tax records, business affairs, or papers	
Shopping alone for clothes, household necessities, or groceries	
Playing a game of skill, working on a hobby	
Heating water, making a cup of coffee, turning off stove after use	
Preparing a balanced meal	
Keeping track of current events	
Paying attention to, understanding, discussing TV, book, magazine	
Remembering appointments, family occasions, holidays, medications	
Traveling out of neighborhood, driving, arranging to take buses	
<b>TOTAL SCORE:</b>	

### Evaluation

Sum scores (range 0-30). Cutpoint of 9 (dependent in 3 or more activities) is recommended to indicate impaired function and possible cognitive impairment.

Pfeffer RI et al. Measurement of functional activities in older adults in the community. J Gerontol 1982; 37(3):323-329. Reprinted with permission of The Gerontological Society of America, 1030 15<sup>th</sup> Street NW, Suite 250, Washington, DC 20005 via Copyright Clearance Center, Inc.

These guidelines/tools are informational only. They are not intended or designed as a substitute for the reasonable exercise of independent clinical judgment by practitioners considering each patient's needs on an individual basis. Guideline recommendations apply to populations of patients. Clinical judgment is necessary to design treatment plans for individual patients. For more information, visit our Web site at [www.aviviahealth.com](http://www.aviviahealth.com). To contact our Chief Medical Officer, please call 1-888-4AVIVIA (1-888-428-4842).

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ANART

ABSCOR

SCOR

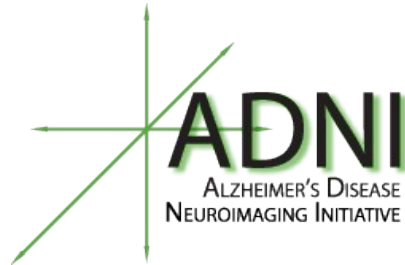
HHC

LRLV

FAQ



Data source:



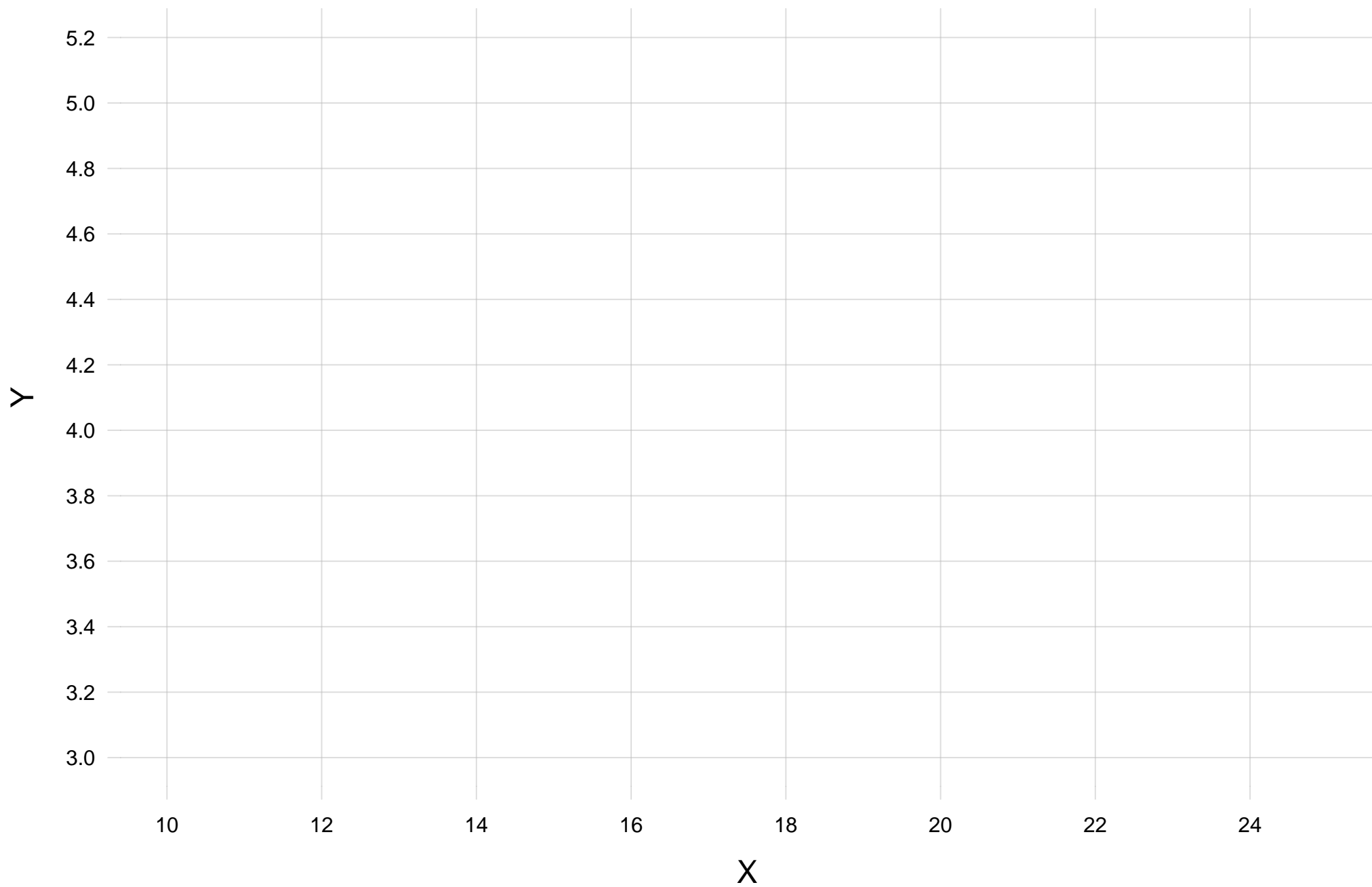
**Ingrid's study:** 12 + 1 variates, 678 datapoints

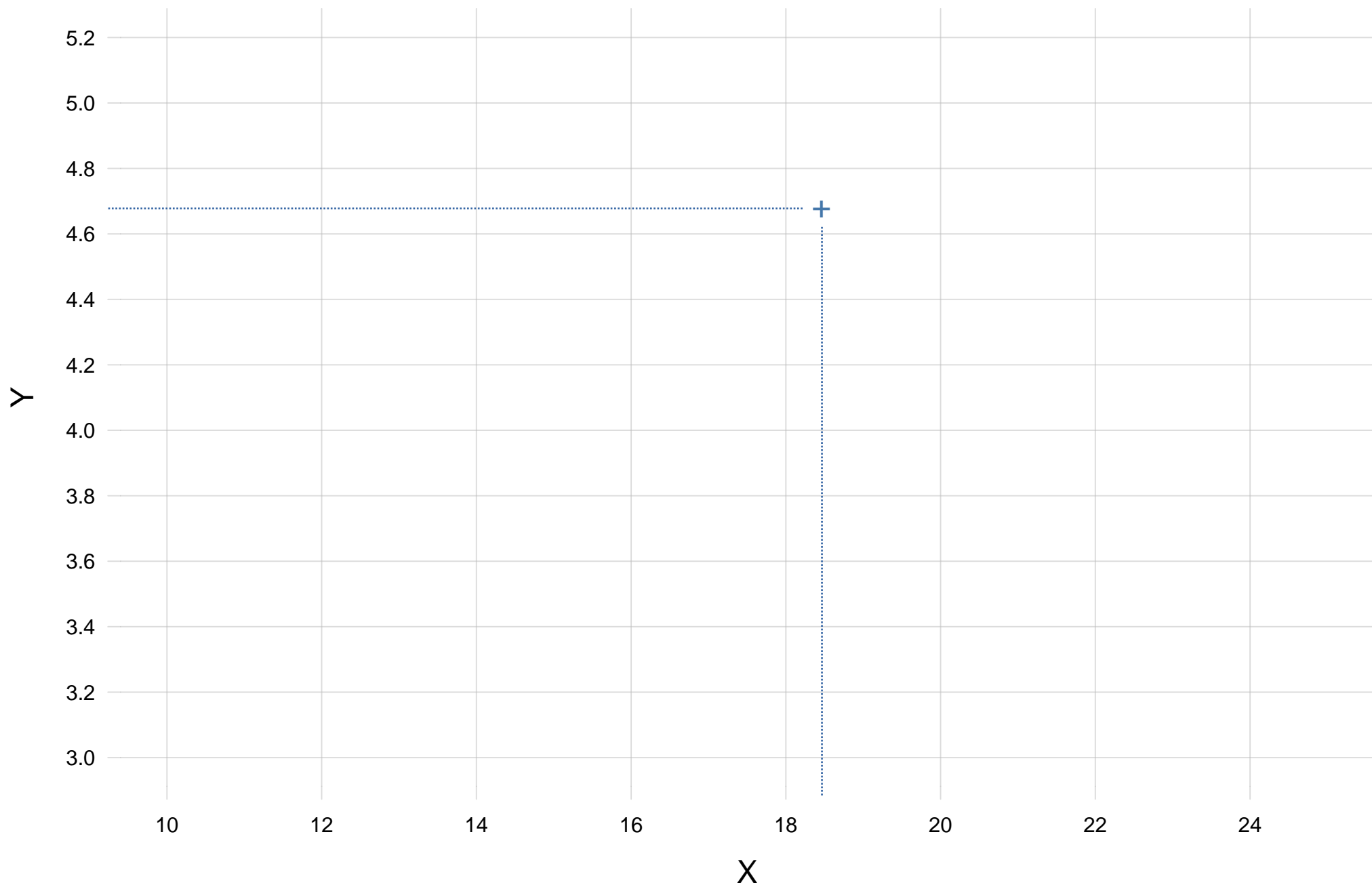
**Alexandra's study:** 11 + 1 variates, 708 datapoints (43 missing values)

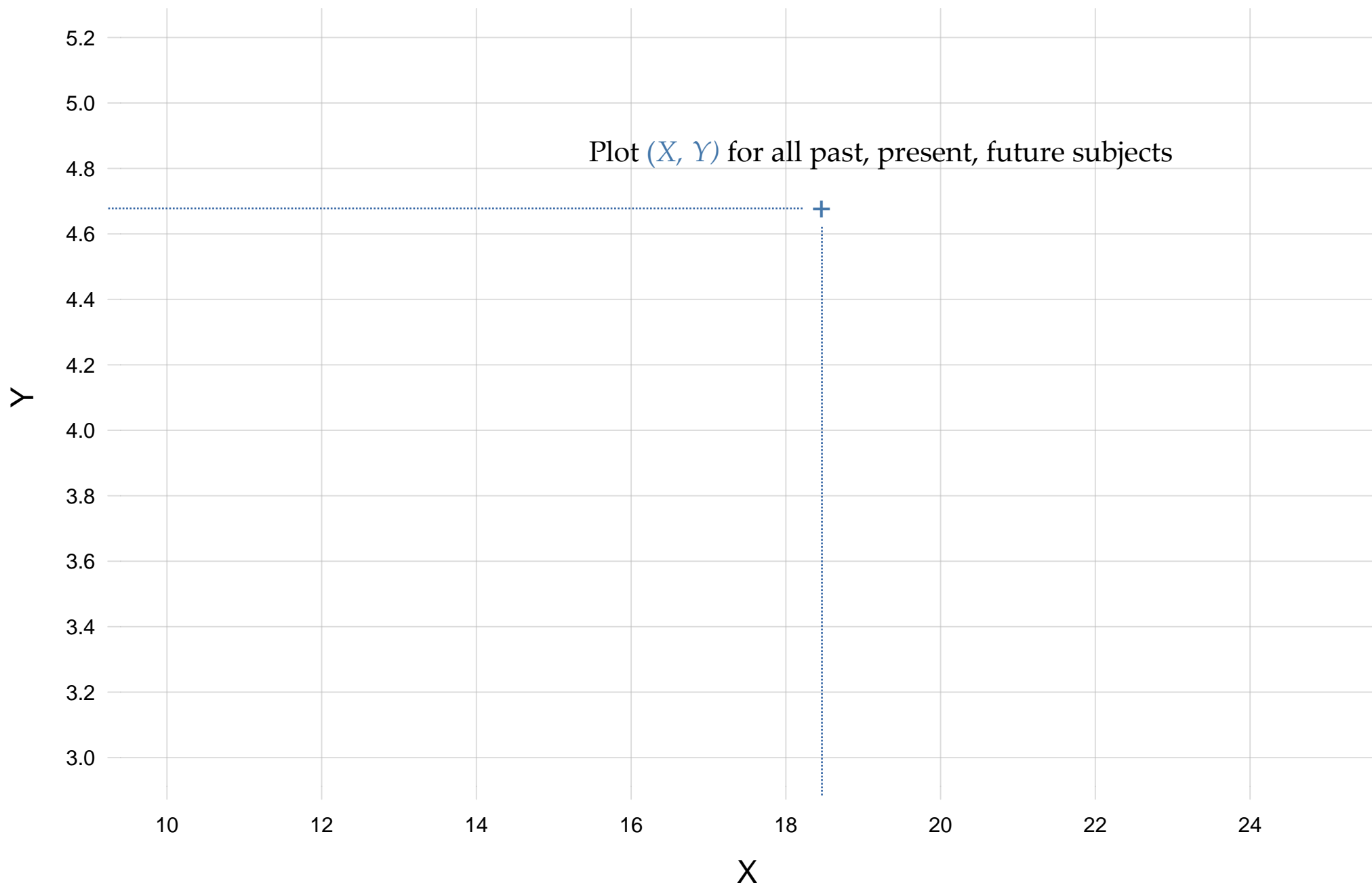
Computation time: ~65 h/study (3 parallel sessions to assess numeric convergence)

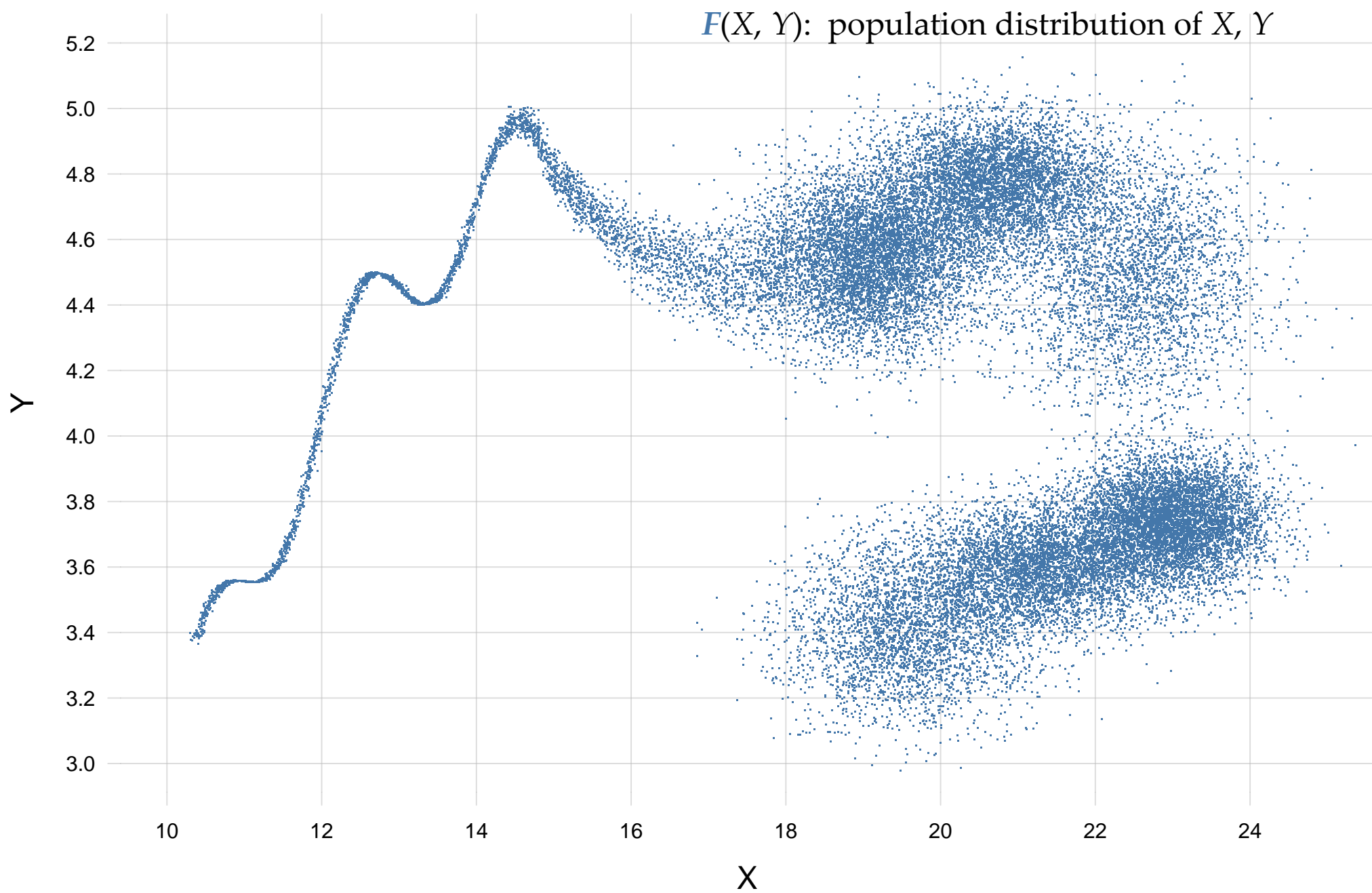
HPC **UNINETT** jigma2



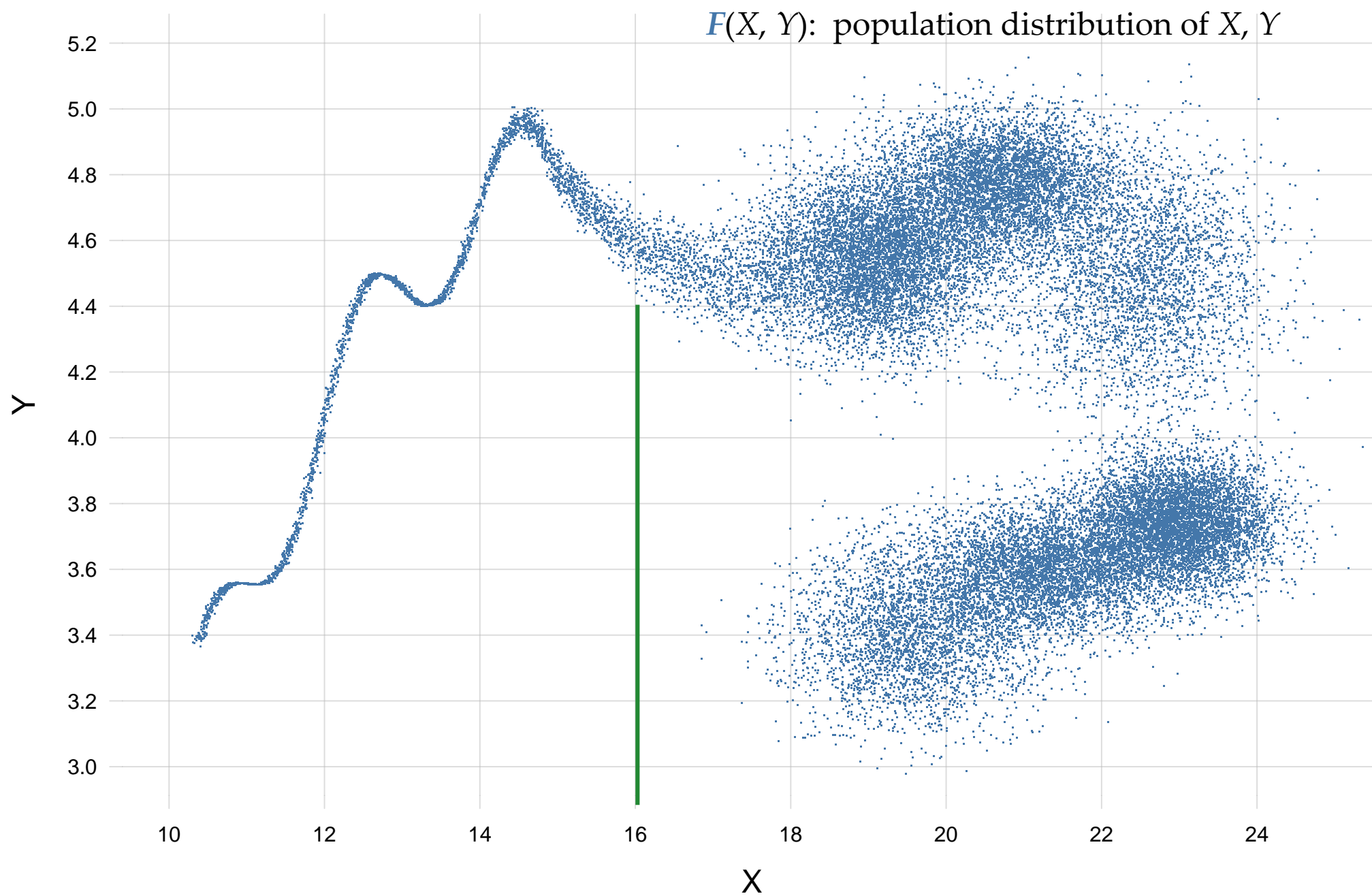






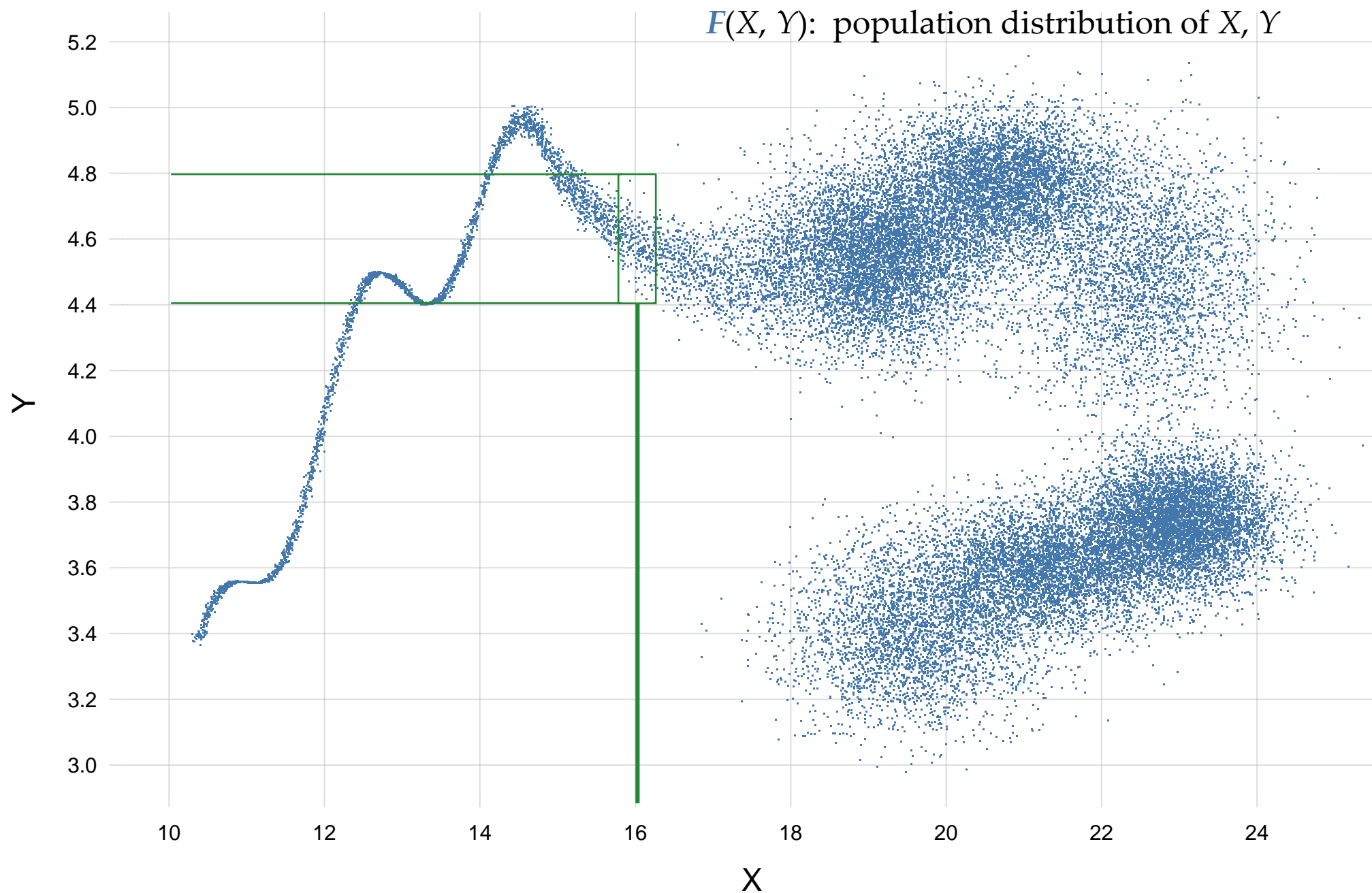


New patient:  $X = 16$



New patient:  $X = 16$

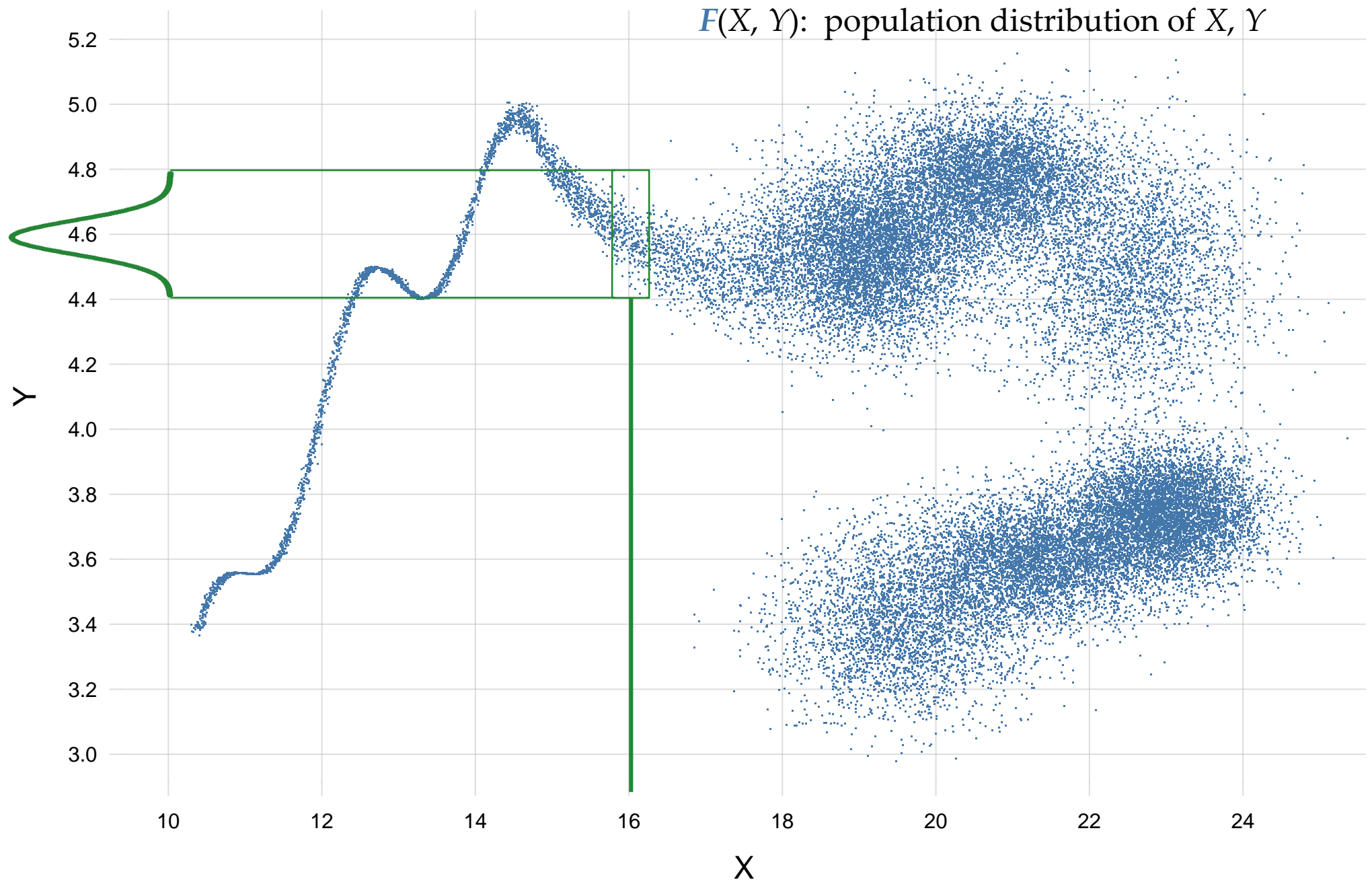
$\Rightarrow Y \approx 4.5-4.7$



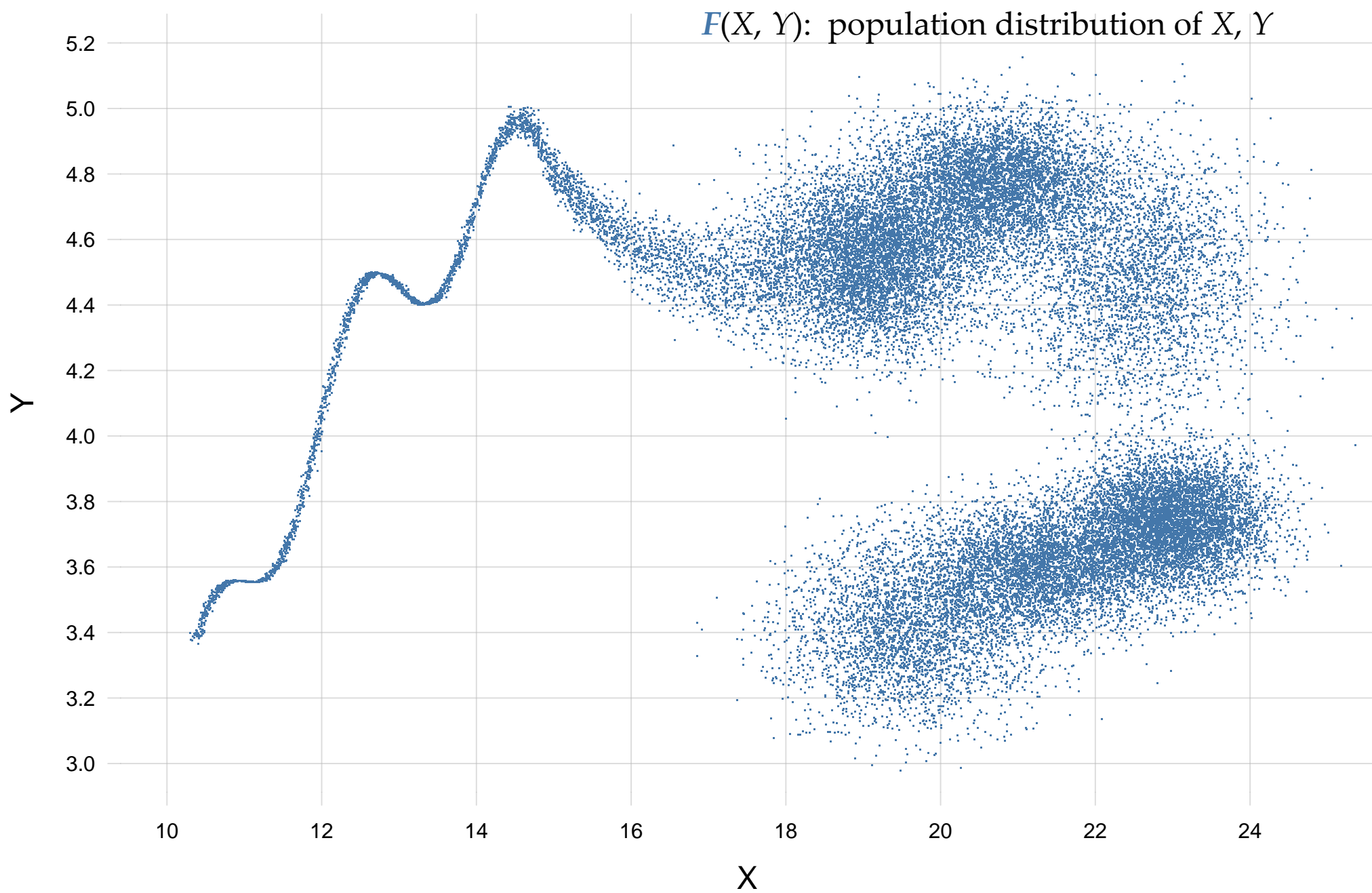


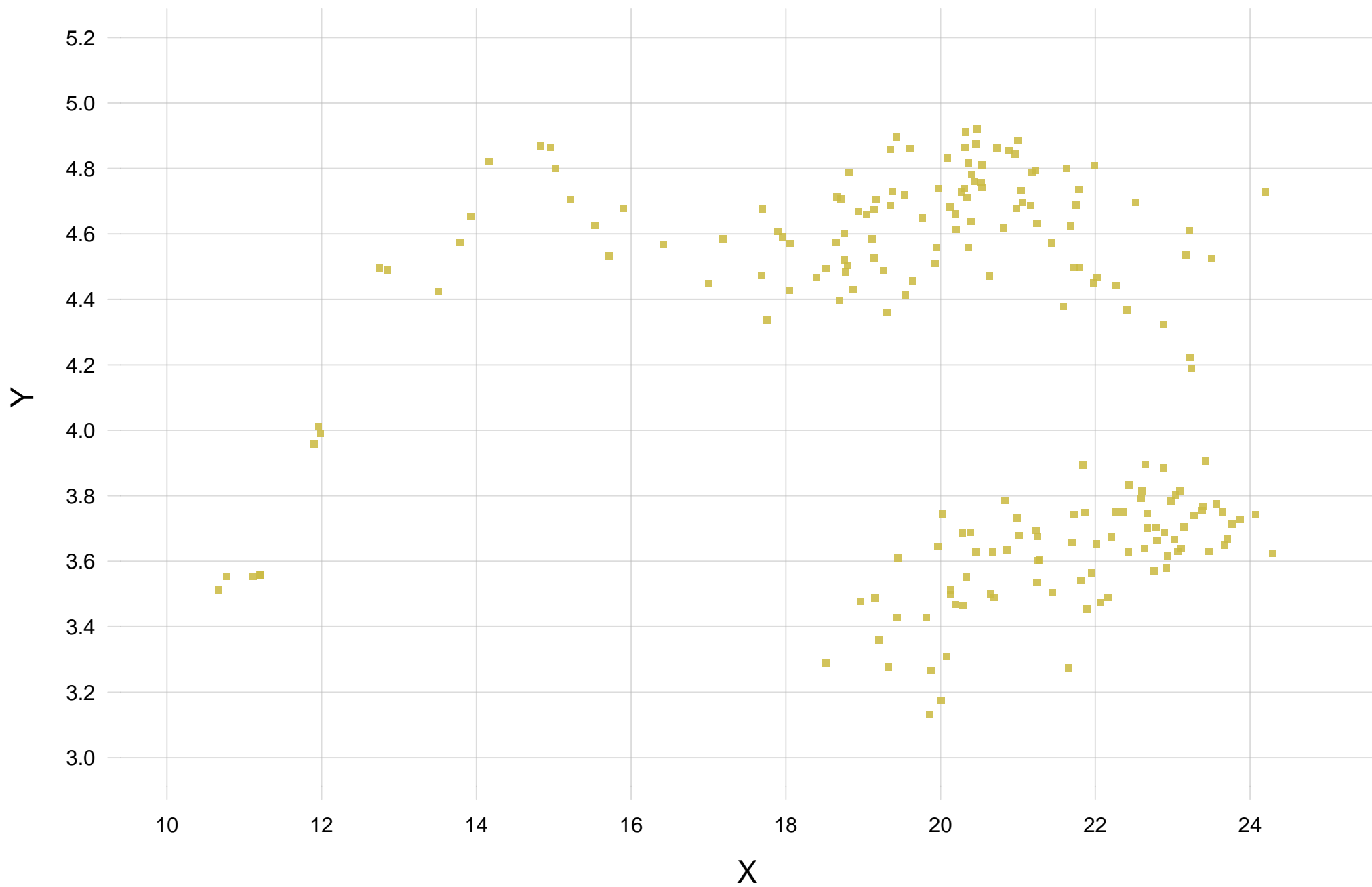
New patient:  $X = 16$

$\Rightarrow Y \approx 4.5-4.7$



$$P(y \mid x) = \textcolor{blue}{F}(y \mid x)$$





$$P(y \mid x) = F(y \mid x)$$

$$P(y \mid x) = \int F(y \mid x) \, p(F \mid \text{data}) \, dF$$

probability = average over all possible population distributions

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probability = average over all possible population distributions

$$p(F \mid \text{data}) \propto \underbrace{F(y_1, x_1) \times F(y_2, x_2) \times F(y_3, x_3) \times \dots}_{\text{how well the 'candidate' distribution fits the data}}$$



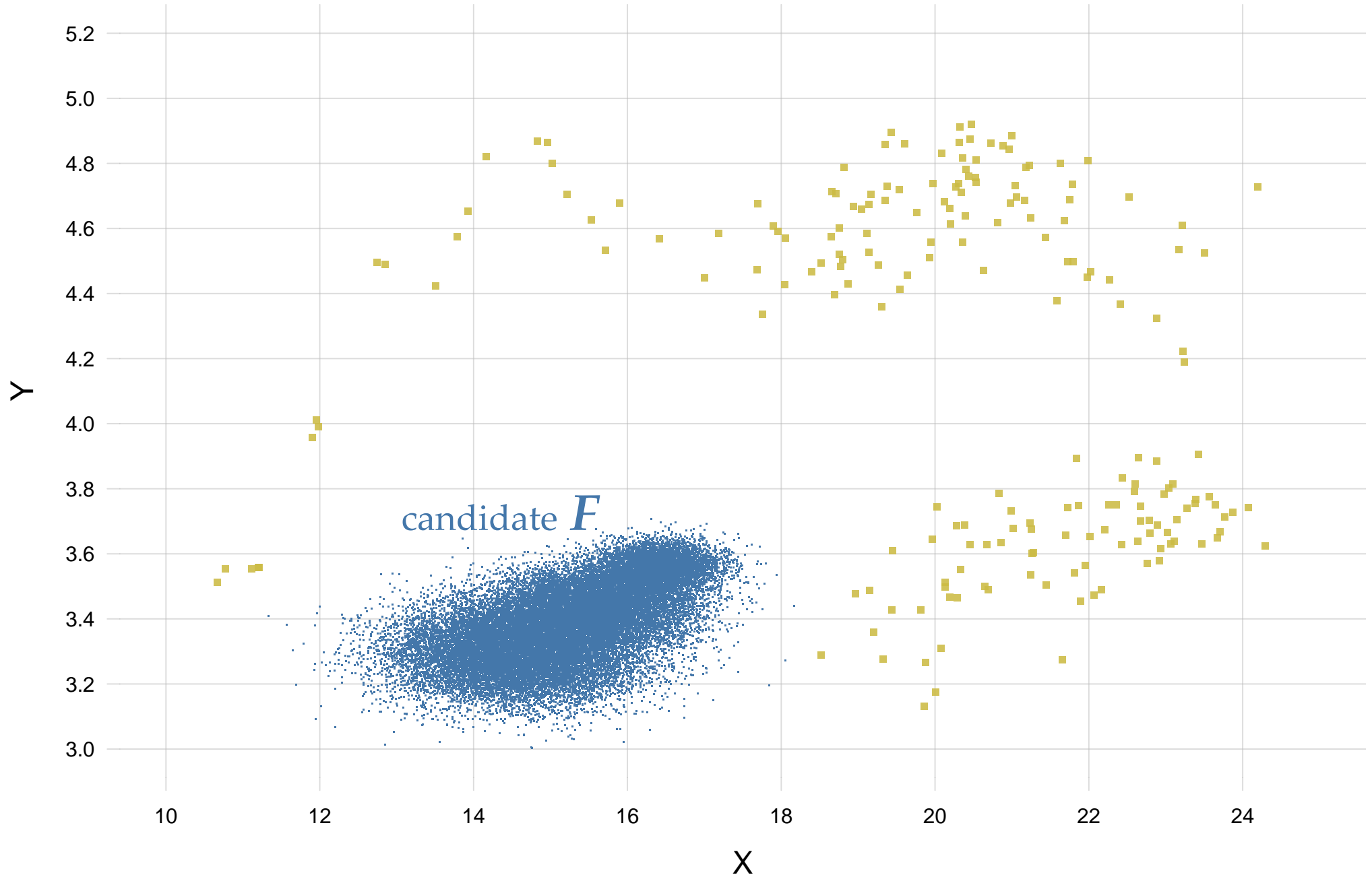
$$P(y \mid x) = \int F(y \mid x) \, p(F \mid \text{data}) \, dF$$

probability = average over all possible population distributions

$$p(F \mid \text{data}) \propto \underbrace{F(y_1, x_1) \times F(y_2, x_2) \times F(y_3, x_3) \times \dots}_{\text{how well the 'candidate' distribution fits the data}} \times \underbrace{p(F \mid \text{prior info})}_{\text{extra-data knowledge}}$$

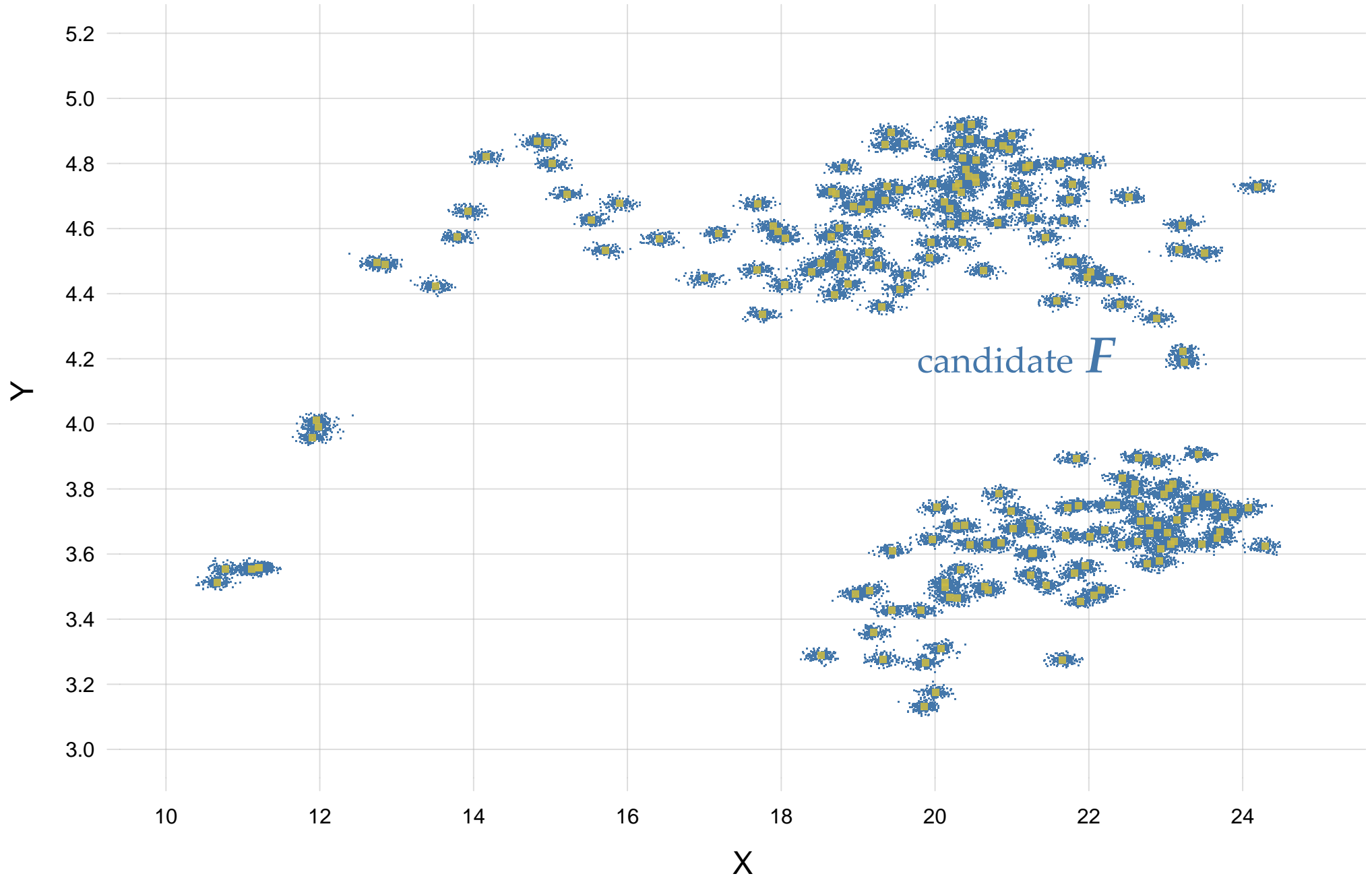
poor candidate: doesn't fit the data

$$\underbrace{F(y_1, x_1) \times F(y_2, x_2) \times F(y_3, x_3) \times \dots}_{\text{low}} \times \underbrace{p(F \mid \text{prior info})}_{\text{high}}$$



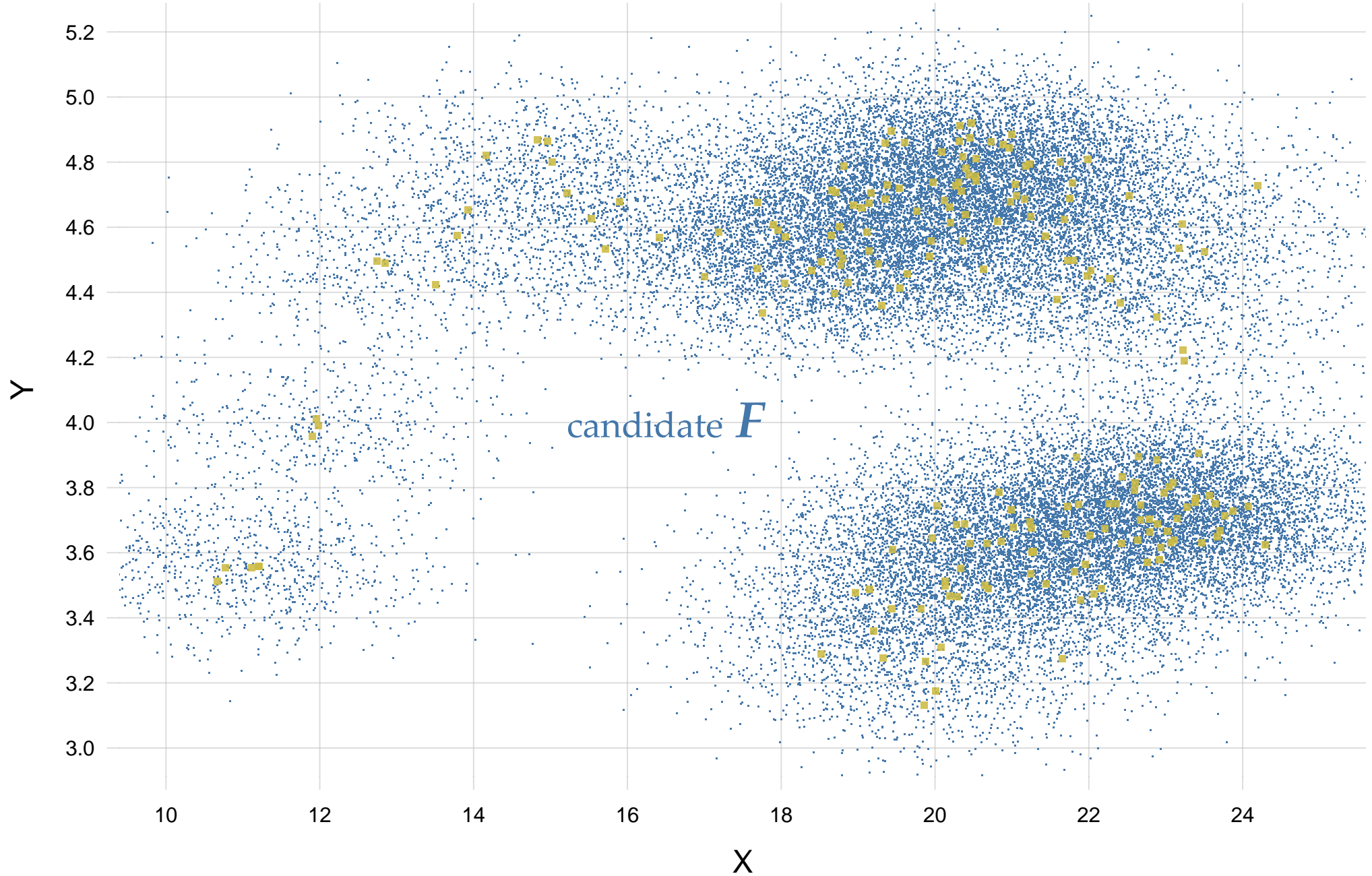
poor candidate: biologically implausible

$$\underbrace{F(y_1, x_1) \times F(y_2, x_2) \times F(y_3, x_3) \times \dots}_{\text{high}} \times \underbrace{p(F \mid \text{prior info})}_{\text{low}}$$



reasonable candidate

$$\underbrace{F(y_1, x_1) \times F(y_2, x_2) \times F(y_3, x_3) \times \dots}_{\text{high}} \times \underbrace{p(F \mid \text{prior info})}_{\text{high}}$$

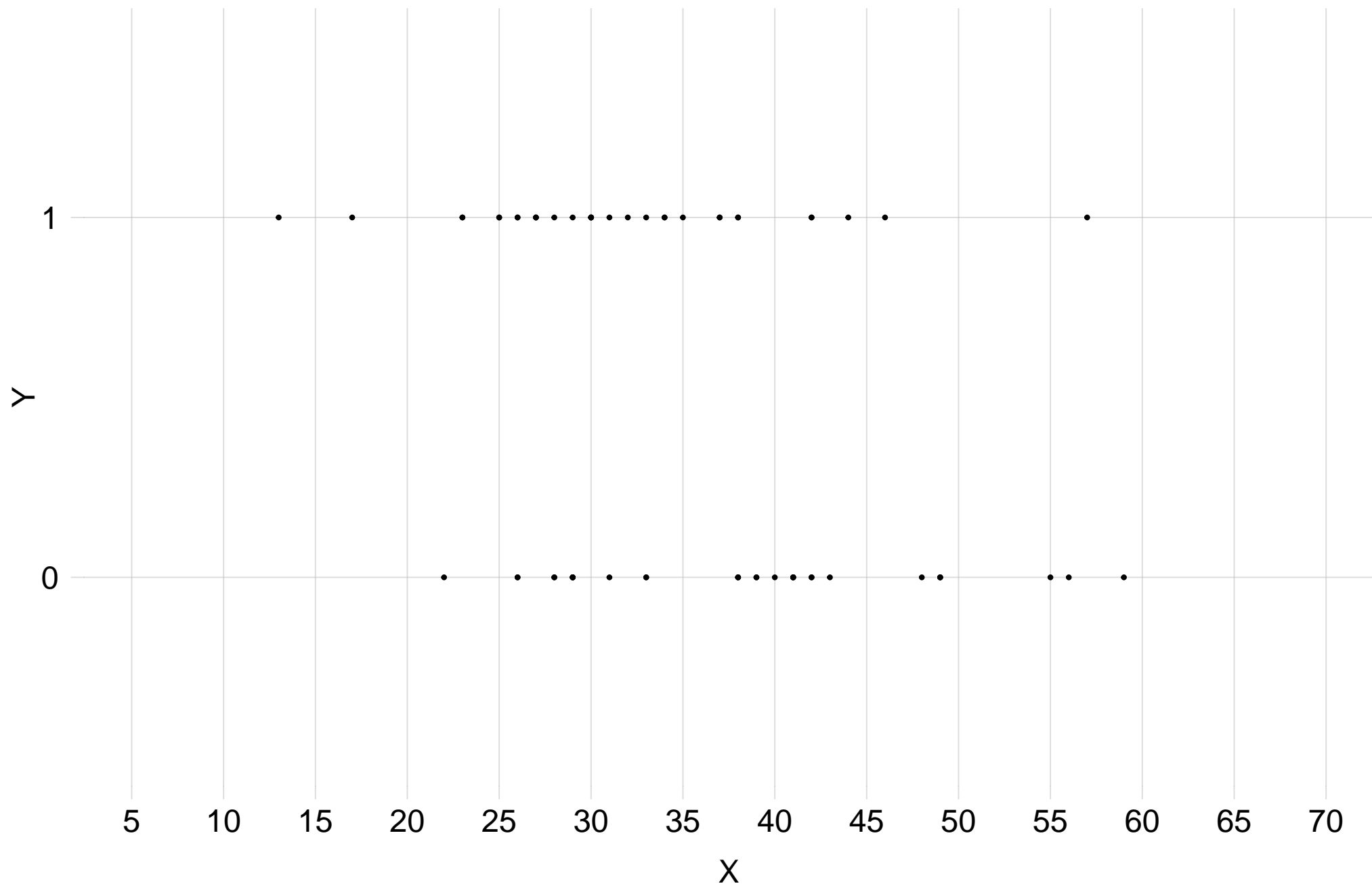


*intuition*  $\rightarrow$  *mathematics*

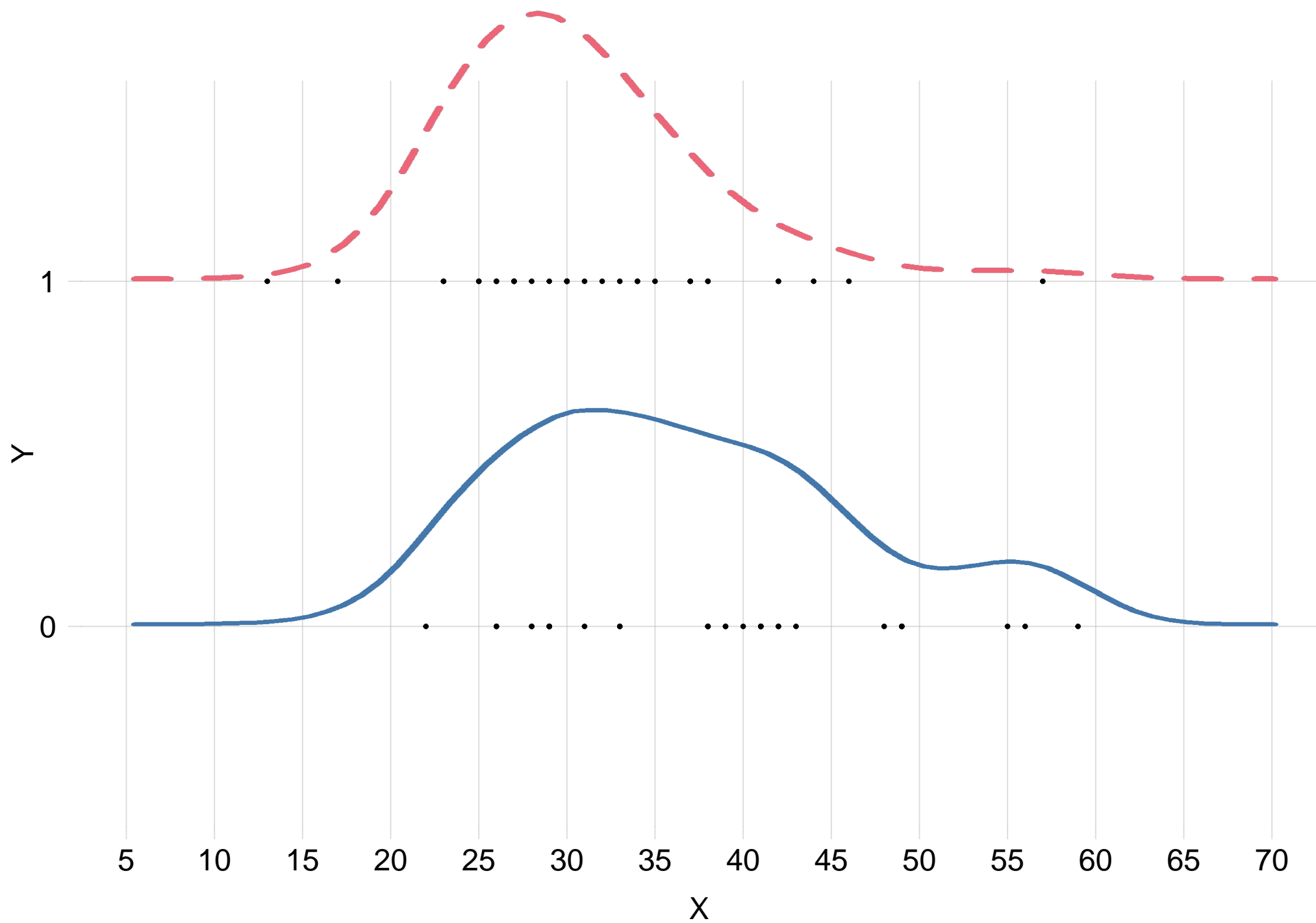
*intuition* → *mathematics*

*first principles*  $\rightarrow$  *mathematics*  $\rightarrow$  *intuition*

*(‘Bayesian’)*

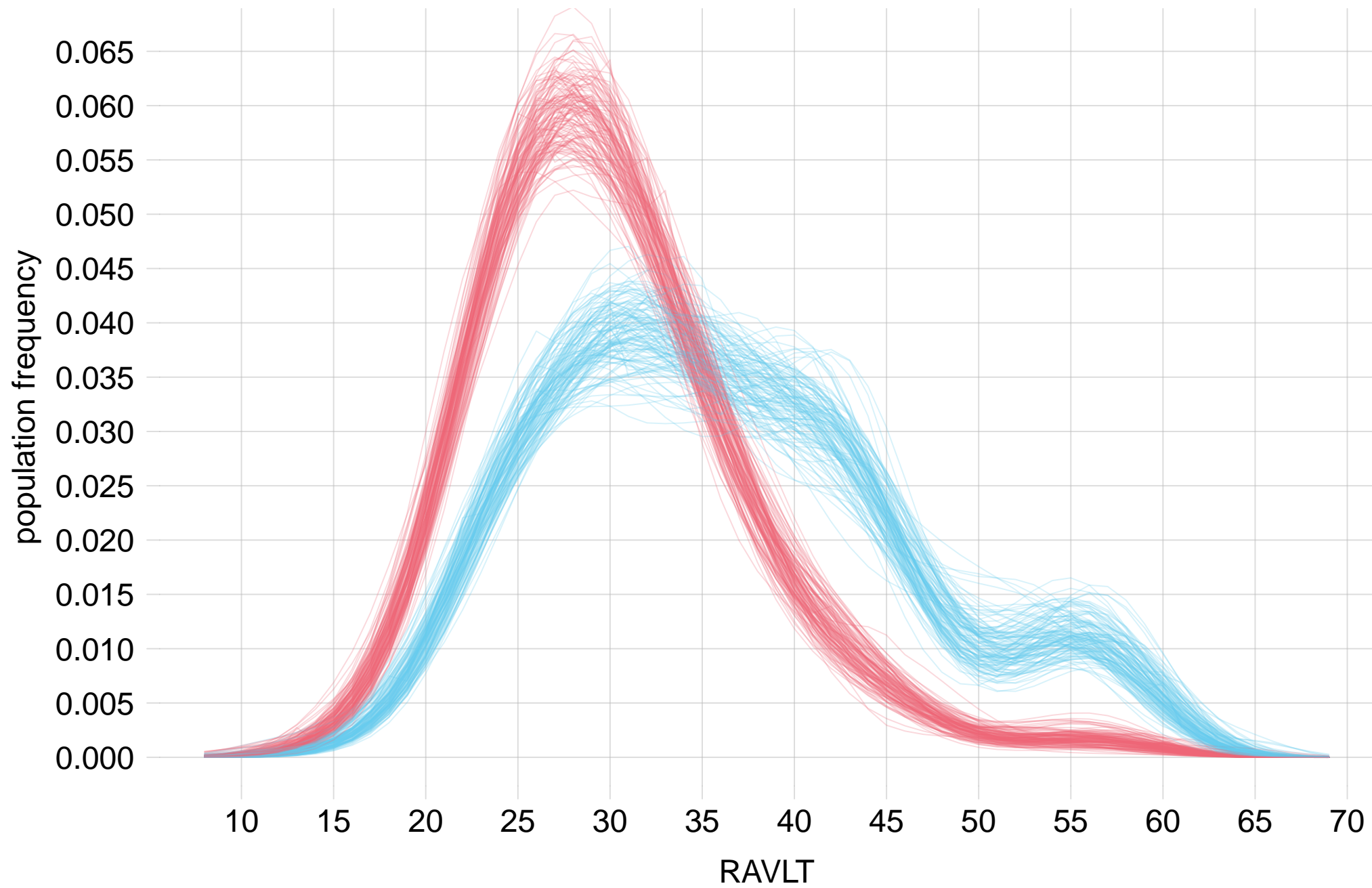




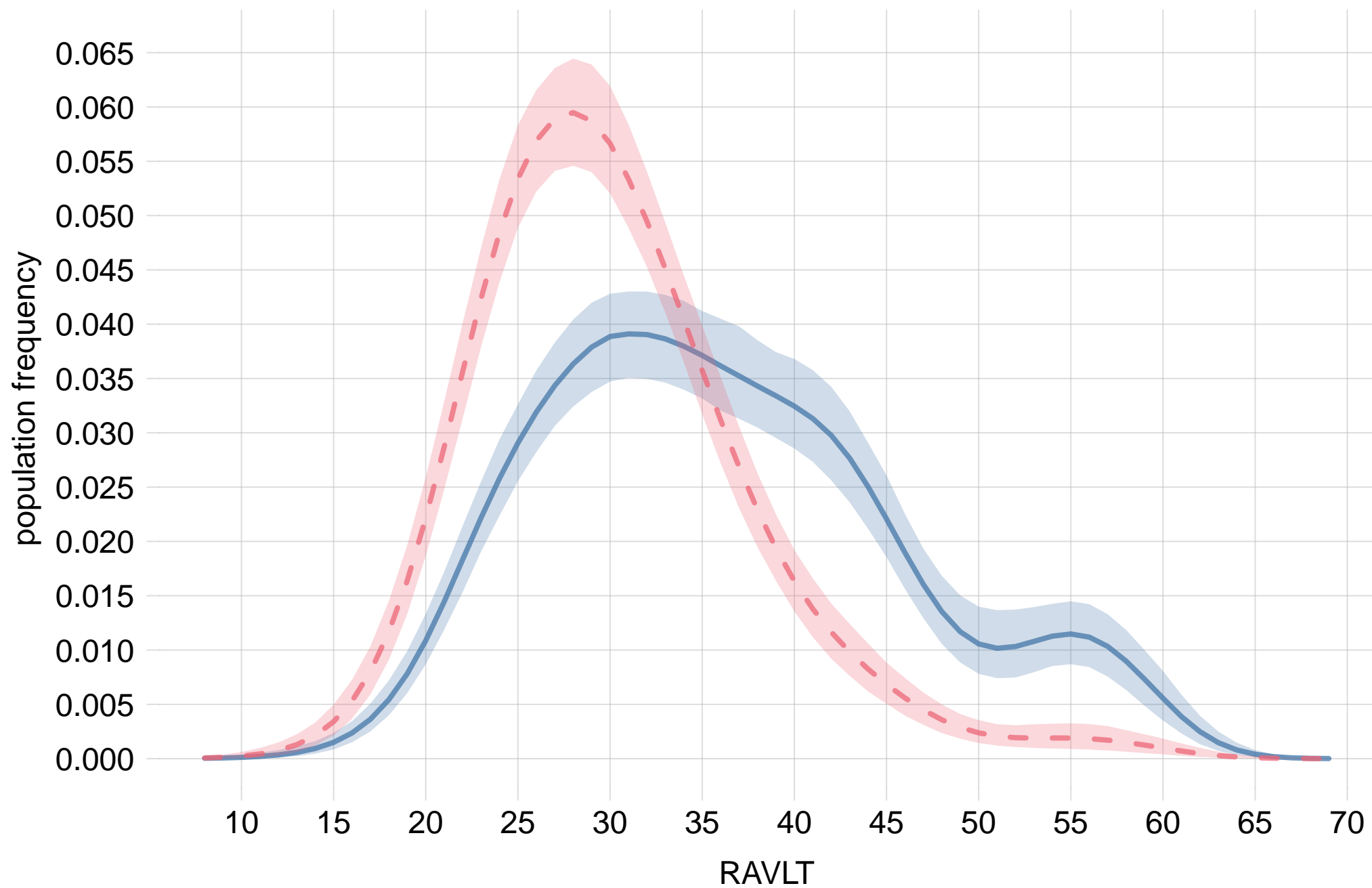




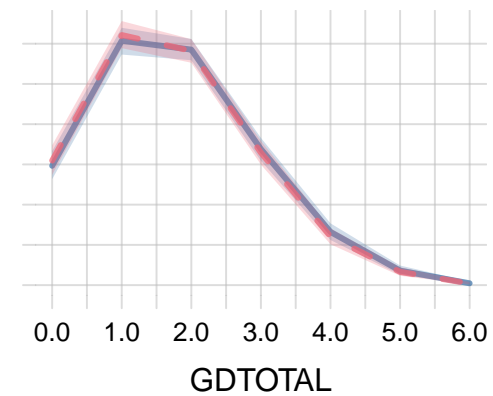
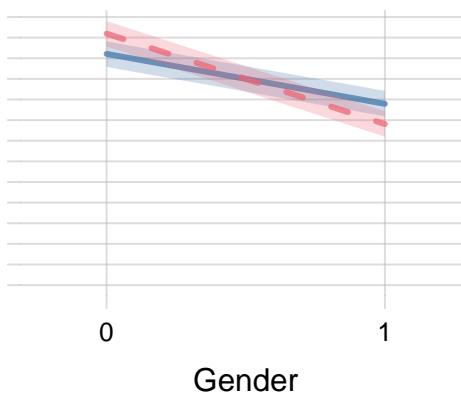
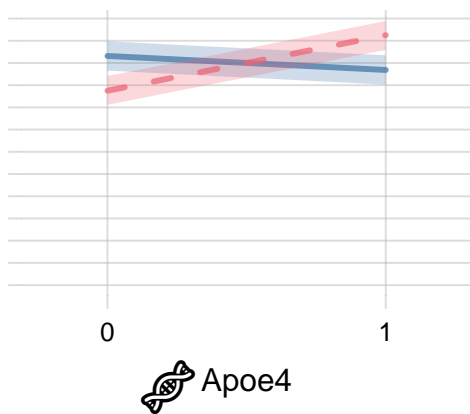
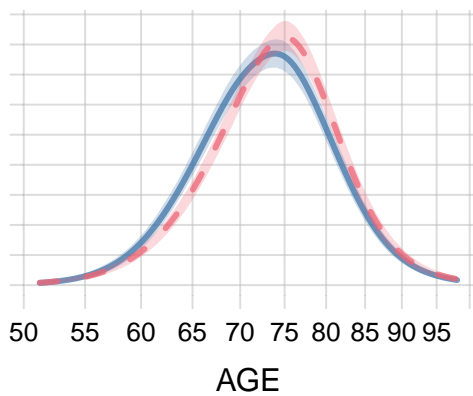
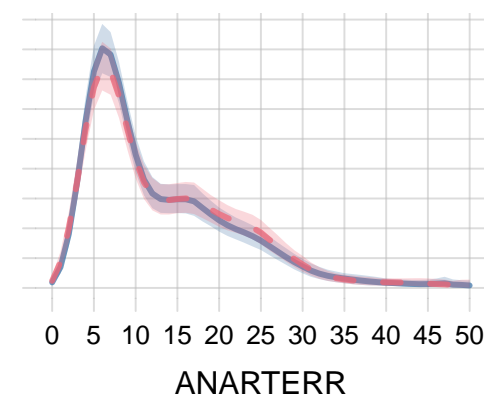
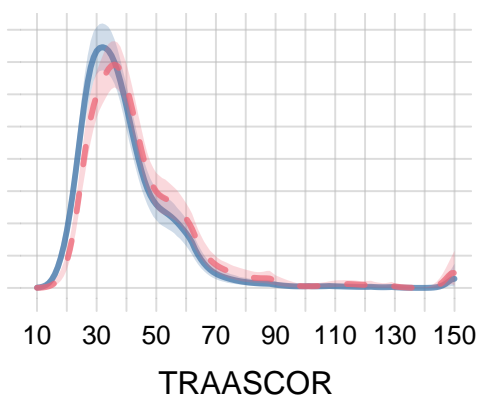
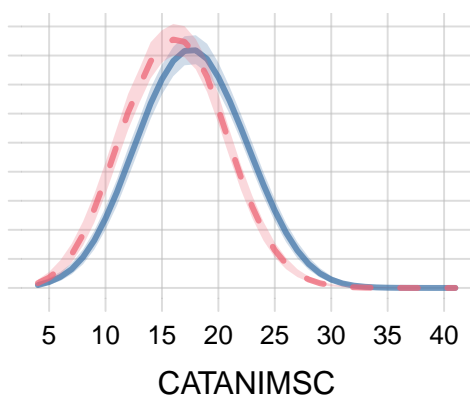
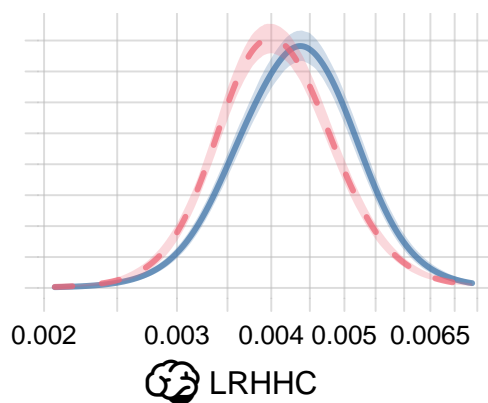
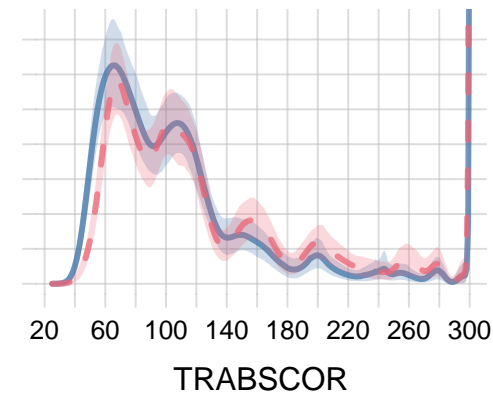
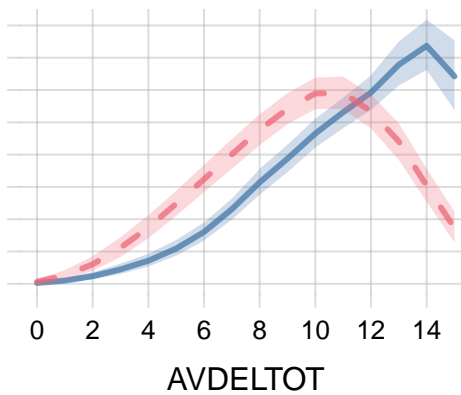
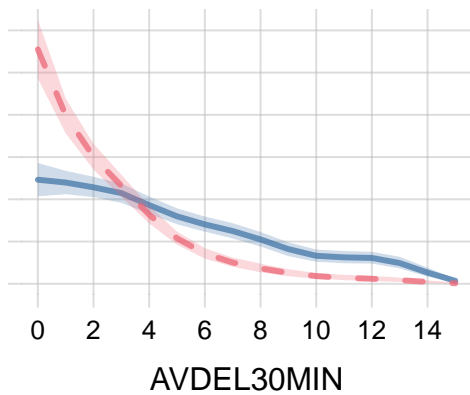
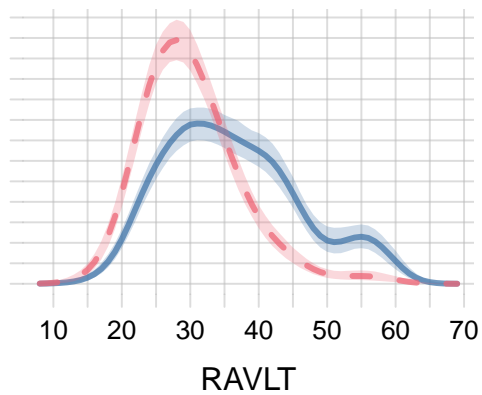
— MCI    - - - AD



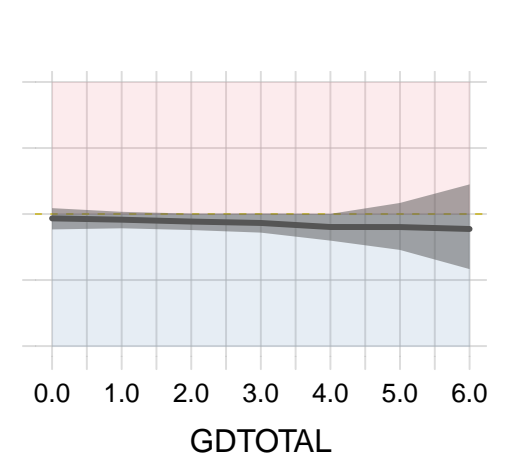
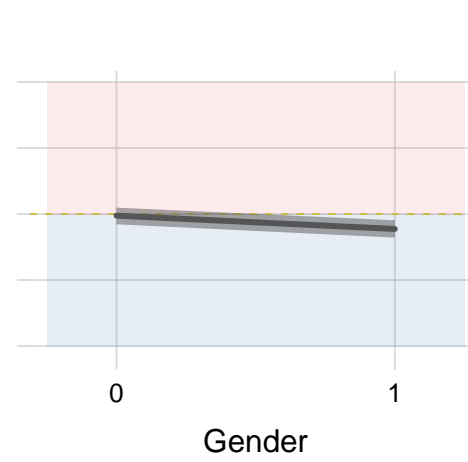
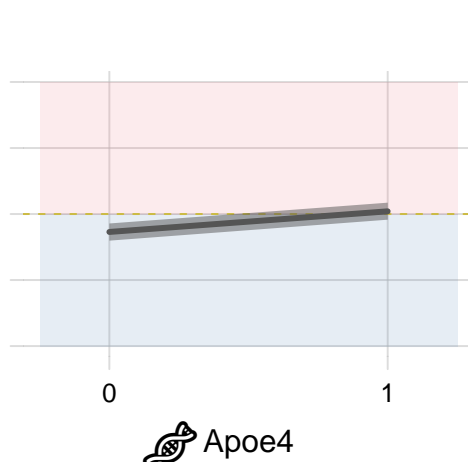
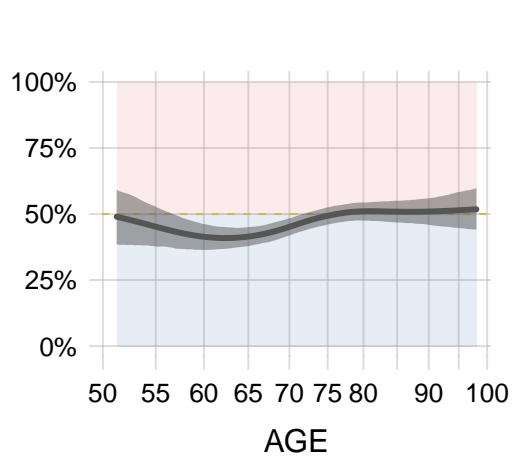
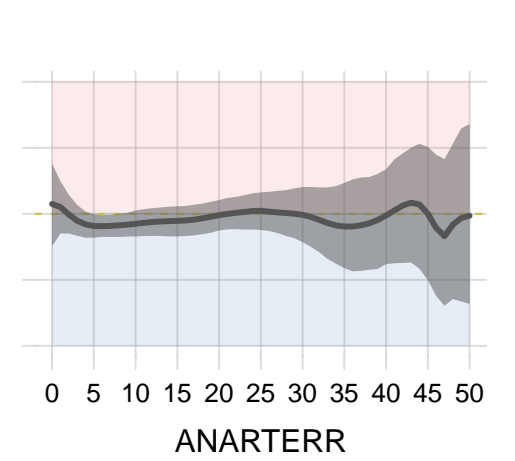
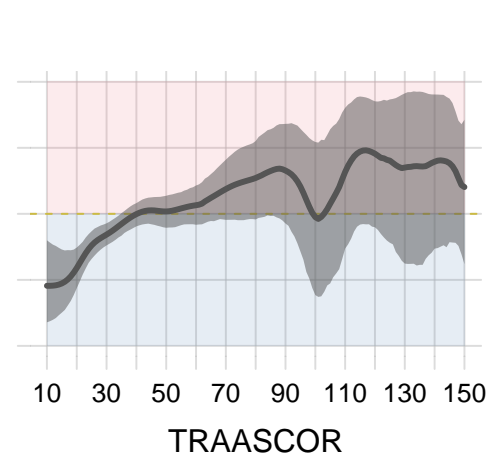
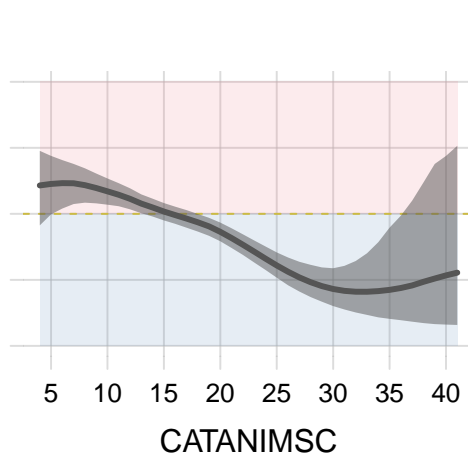
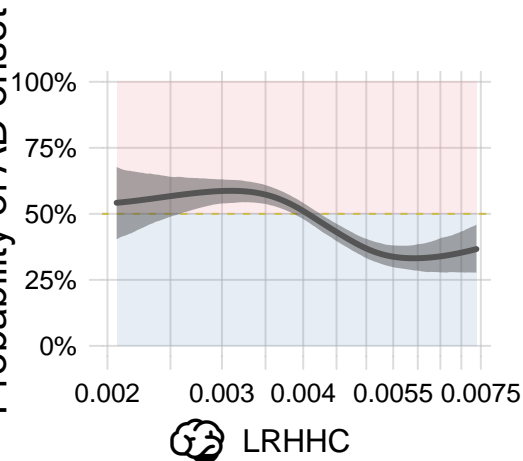
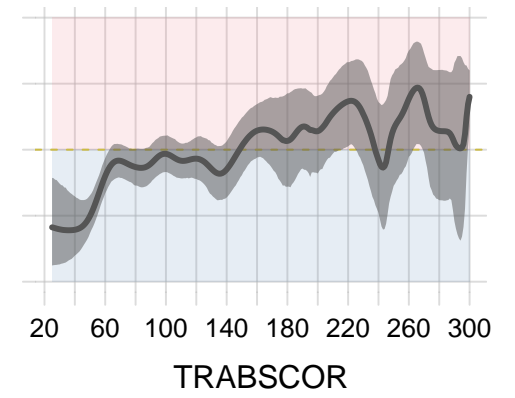
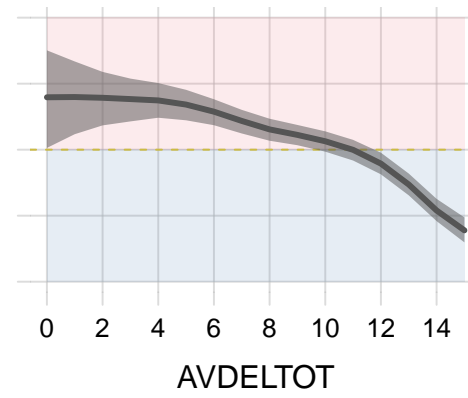
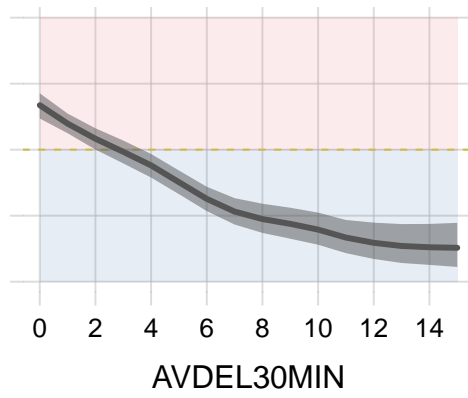
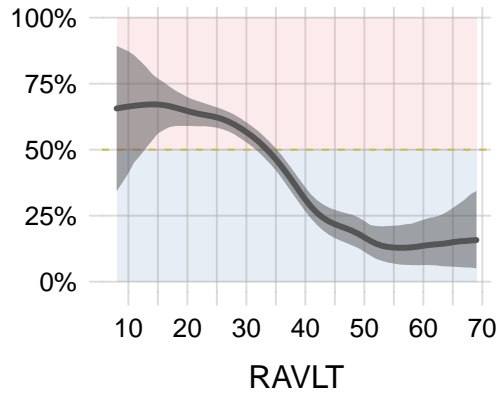
— MCI    - - - AD    87.5% credible interval

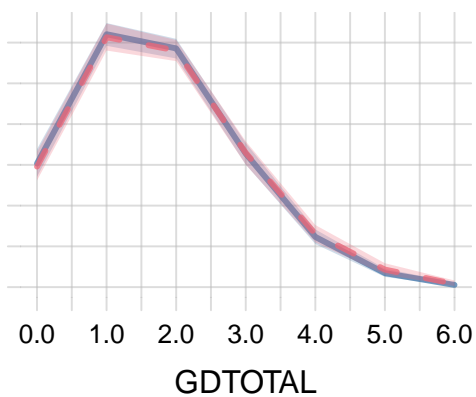
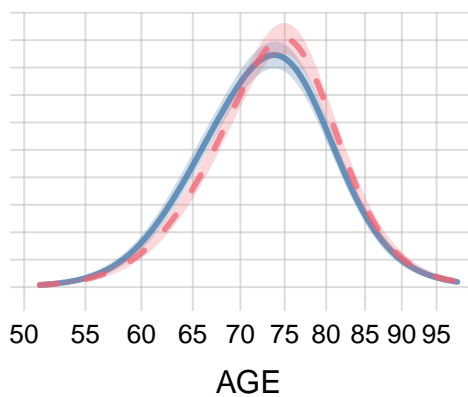
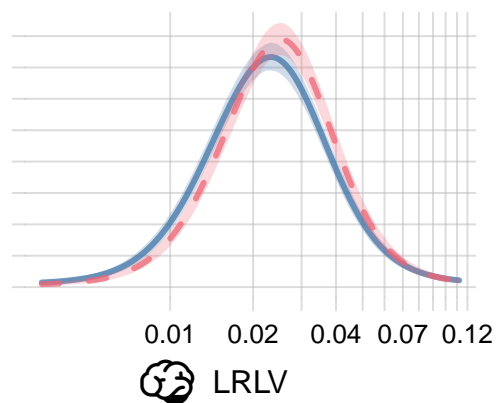
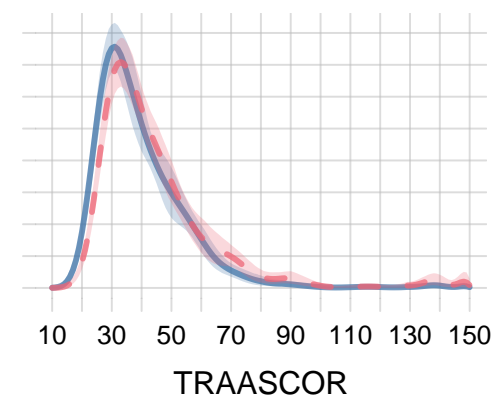
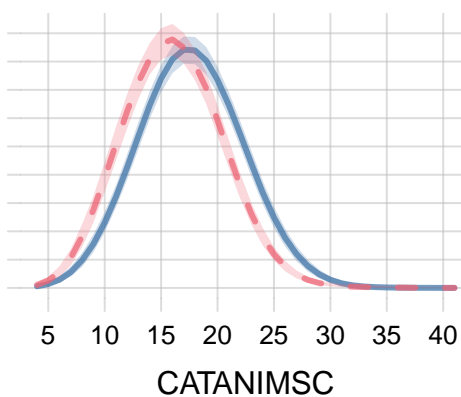
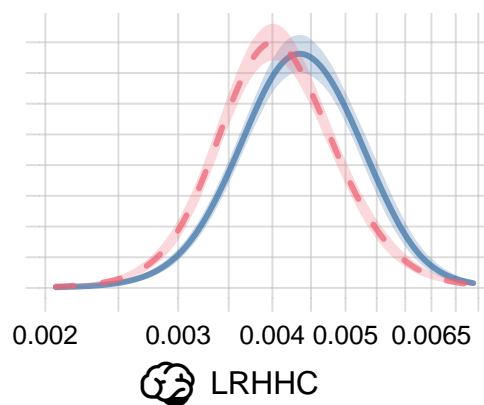
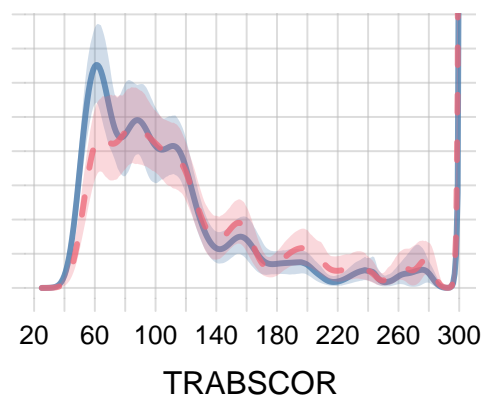
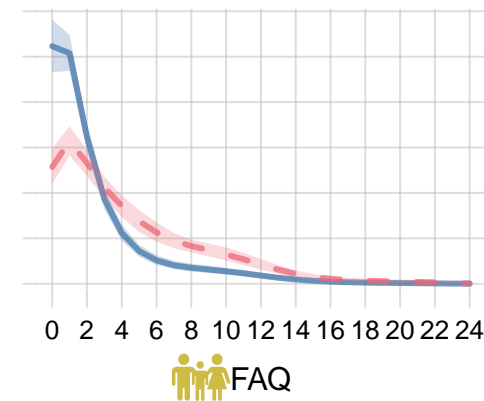
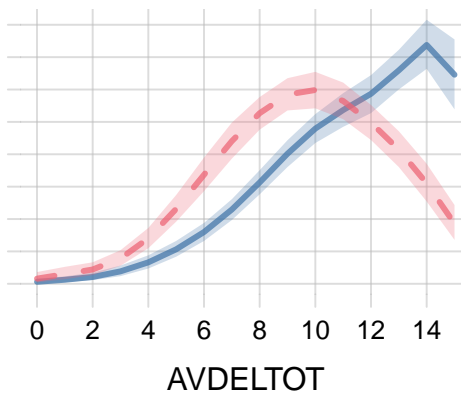
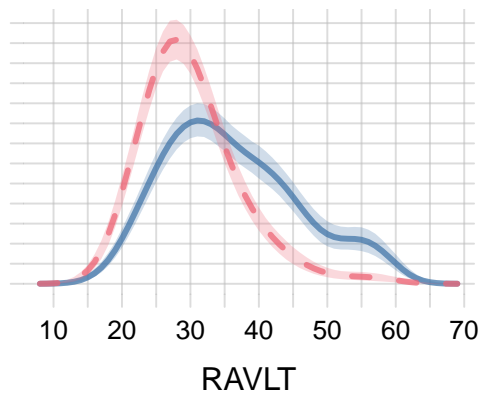
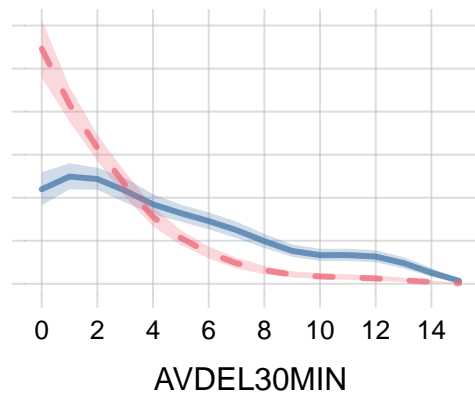


— MCI    - - - AD    87.5% credible interval

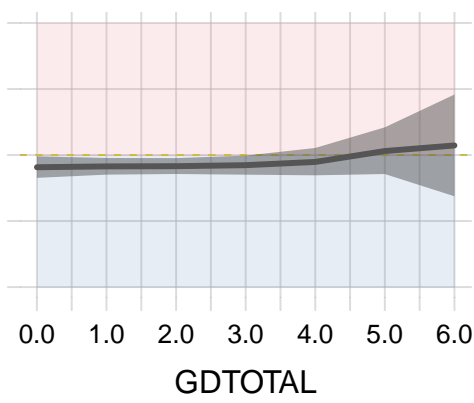
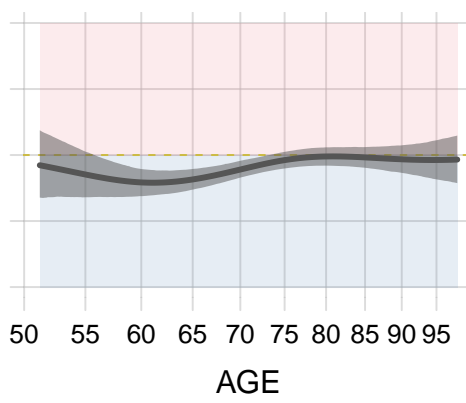
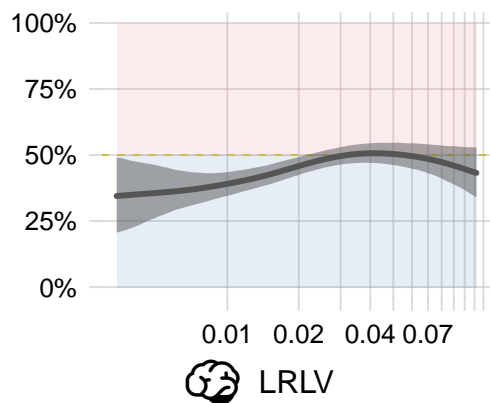
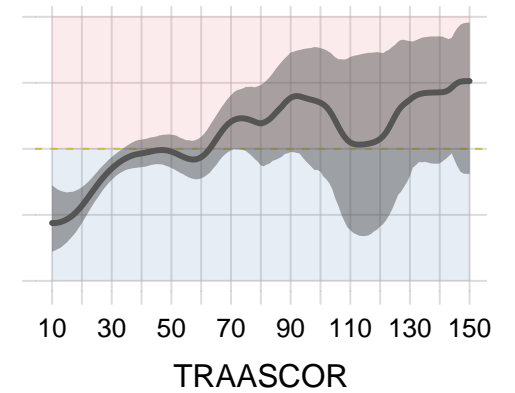
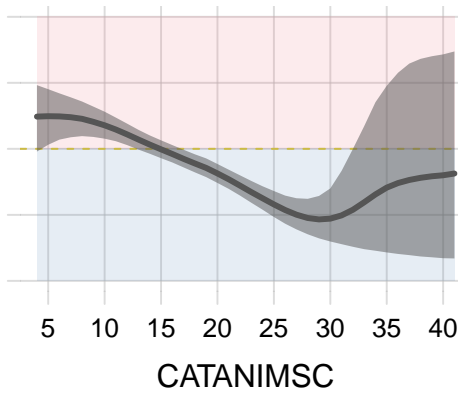
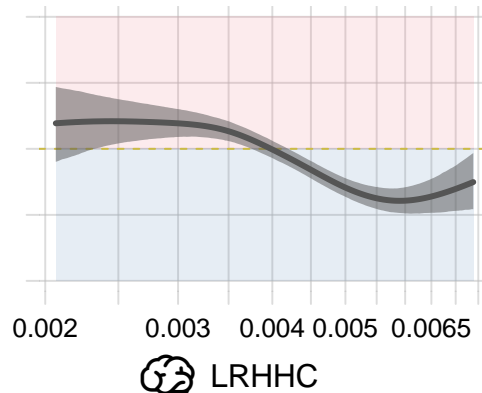
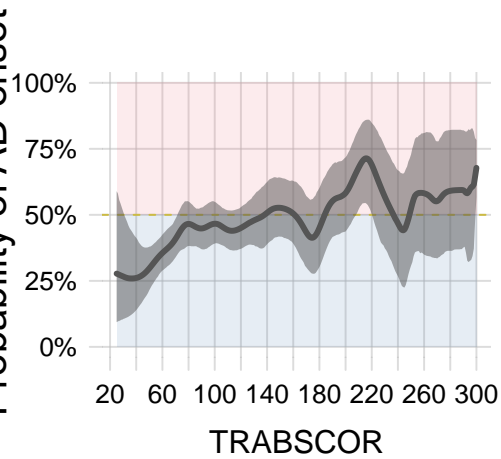
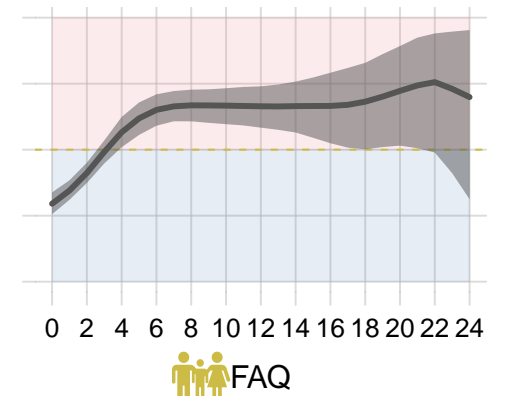
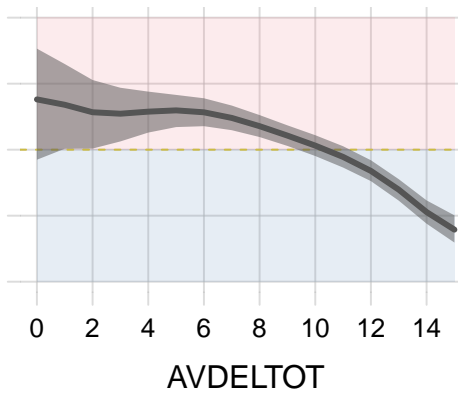
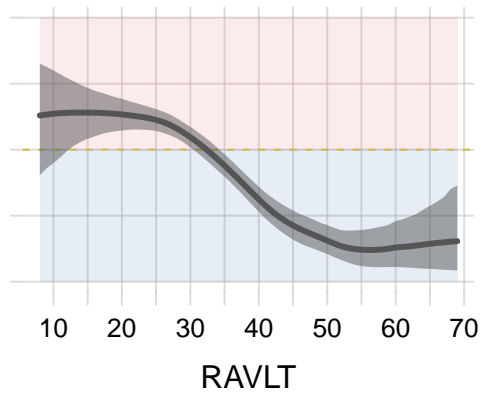
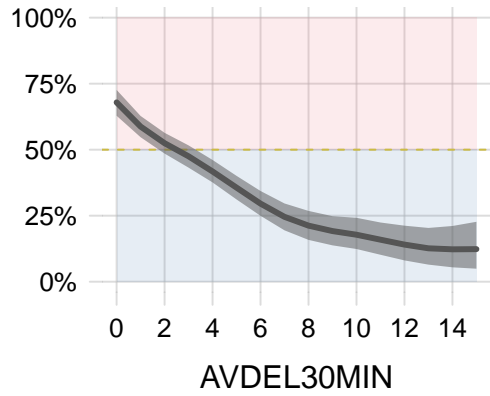


87.5% credible interval





87.5% credible interval





Interesting characteristics of  $F(Y, X)$  in Ingrid's & Alexandra's studies:

- Several high-density regions in the 12D space
- Some features seem more robust if used in a 'discriminative' way:  $P(Y | X)$ , others in a 'generative' way:  $P(X | Y)$

$$P(Y | X_d, X_g) \propto P(X_g | Y) P(Y | X_d)$$



How to quantify the ‘importance’ or ‘prognostic power’ of a set of features?

*“Language is a product of, and reflects, thinking.  
Sloppy usage reflects sloppy thinking, a kind of thinking  
incompatible with good scientific habits of mind”*  
(D. J. Helfand)

Prediction problem:

guess the six digits of the winning lottery ticket    ???????

Clue A:    ✓✓✓✓??

Clue B:    ✓✓✓?✓?

Clue C:    ???✓✓✓

*What is the ‘importance’ or ‘predictive power’ of each clue?*

## Scenario 1: we can use **only one** clue

Clue A: ✓✓✓✓??

Clue B: ✓✓✓?✓?

Clue C: ???✓✓✓



Best: **A** or **B** (each gives  $1/81$  winning chance)

Worst: **C** (gives  $1/729$  winning chance)

Scenario 2: we can use **all** clues

Clue A: ✓✓✓✓??

Clue B: ✓✓✓?✓?

Clue C: ???✓✓✓

→ We fully know the winning number! 💰

Scenario 2: what happens if we **discard** clues?

Clue A: ✓✓✓✓??

Clue B: ✓✓✓?✓?

Clue C: ???✓✓✓

## Scenario 2: what happens if we **discard** clues?

Clue A: ✓✓✓✓??

Clue B: ✓✓✓?✓?

Clue C: ???✓✓✓

- Discard A: still 100% win  $\Rightarrow$  A has 'importance=0'



## Scenario 2: what happens if we **discard** clues?

Clue A: ✓✓✓✓??

Clue B: ✓✓✓?✓?

Clue C: ???✓✓✓

- Discard **A**: still 100% win  $\Rightarrow$  **A** has 'importance=0'
- Discard **B**: still 100% win  $\Rightarrow$  **B** has 'importance= 0'

## Scenario 2: what happens if we **discard** clues?

Clue A: ✓✓✓✓??

Clue B: ✓✓✓?✓?

Clue C: ???✓✓✓

- Discard **A**: still 100% win  $\Rightarrow$  **A** has 'importance=0'
- Discard **B**: still 100% win  $\Rightarrow$  **B** has 'importance= 0'
- Discard **A and B**: 1/9 winning chance

## Scenario 2: what happens if we **discard** clues?

Clue A: ✓✓✓✓??

Clue B: ✓✓✓?✓?

Clue C: ???✓✓✓

- Discard **A**: still 100% win  $\Rightarrow$  **A** has 'importance=0'
- Discard **B**: still 100% win  $\Rightarrow$  **B** has 'importance=0'
- Discard **A and B**: 1/9 winning chance  
 $\Rightarrow$  **A and B** together have 'importance>0'

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 $\Rightarrow$  **A and B** together have 'importance>0'

$$'0 + 0 \neq 0'$$

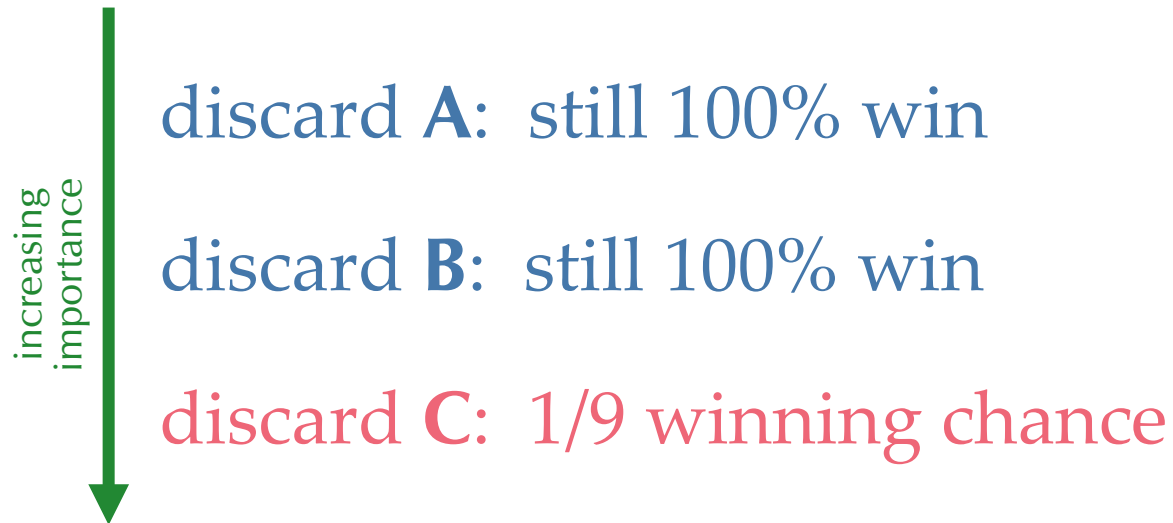
‘Importance’ or ‘predictive power’ is *not* an *additive* property

Scenario 3: we have to **discard one** clue. Which?

Clue A: ✓✓✓✓??

Clue B: ✓✓✓?✓?

Clue C: ???✓✓✓



→ If we have to discard one clue, it's most important that we keep **C**

increasing importance →

Scenario 1:  
choose one clue

C

A  
B

---

Scenario 3:  
discard one clue

A  
B

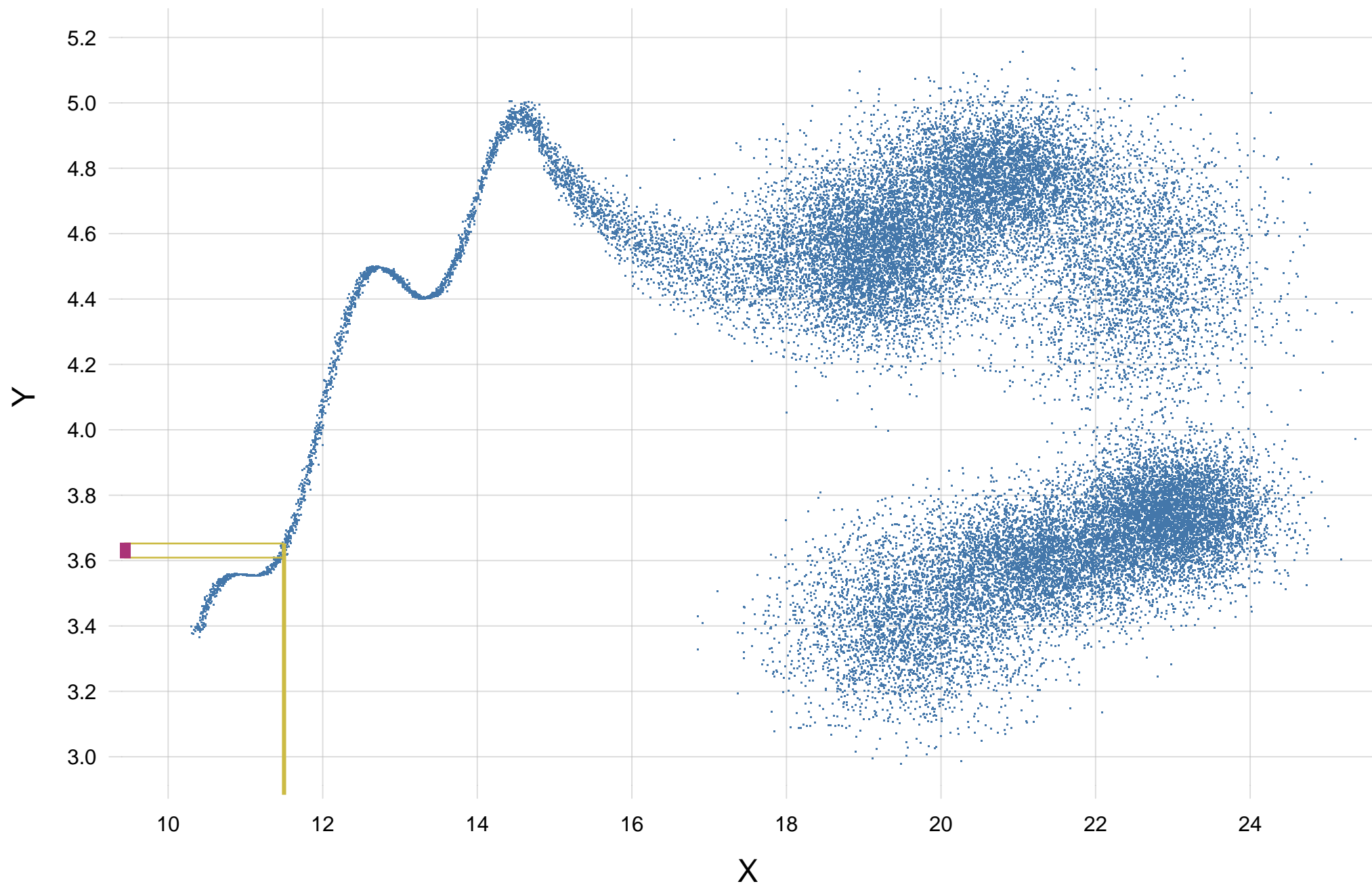
C

increasing importance →

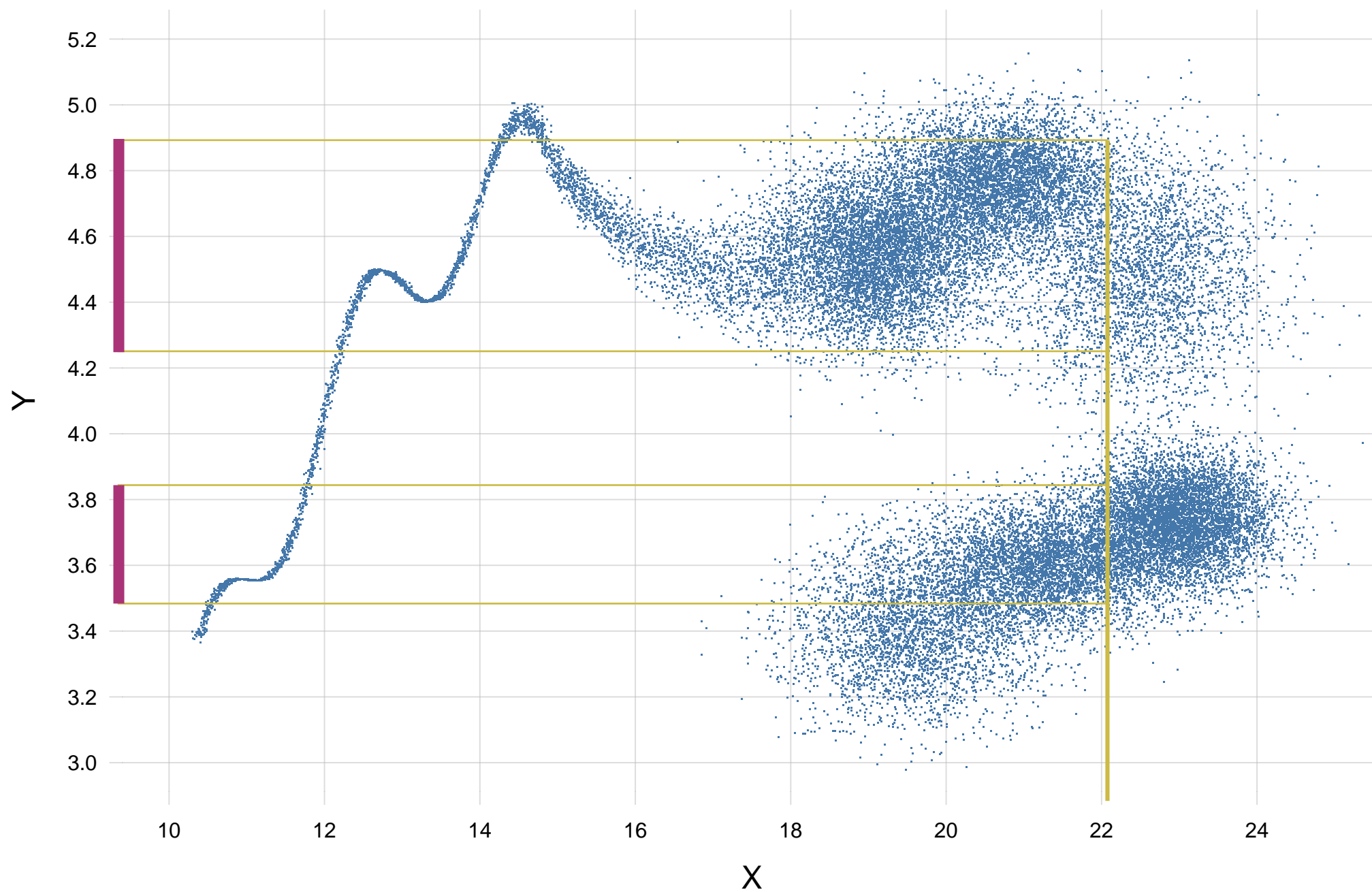
‘Importance’ or ‘predictive power’ of  $X$  is *context-dependent*  
(which other features are we considering?)



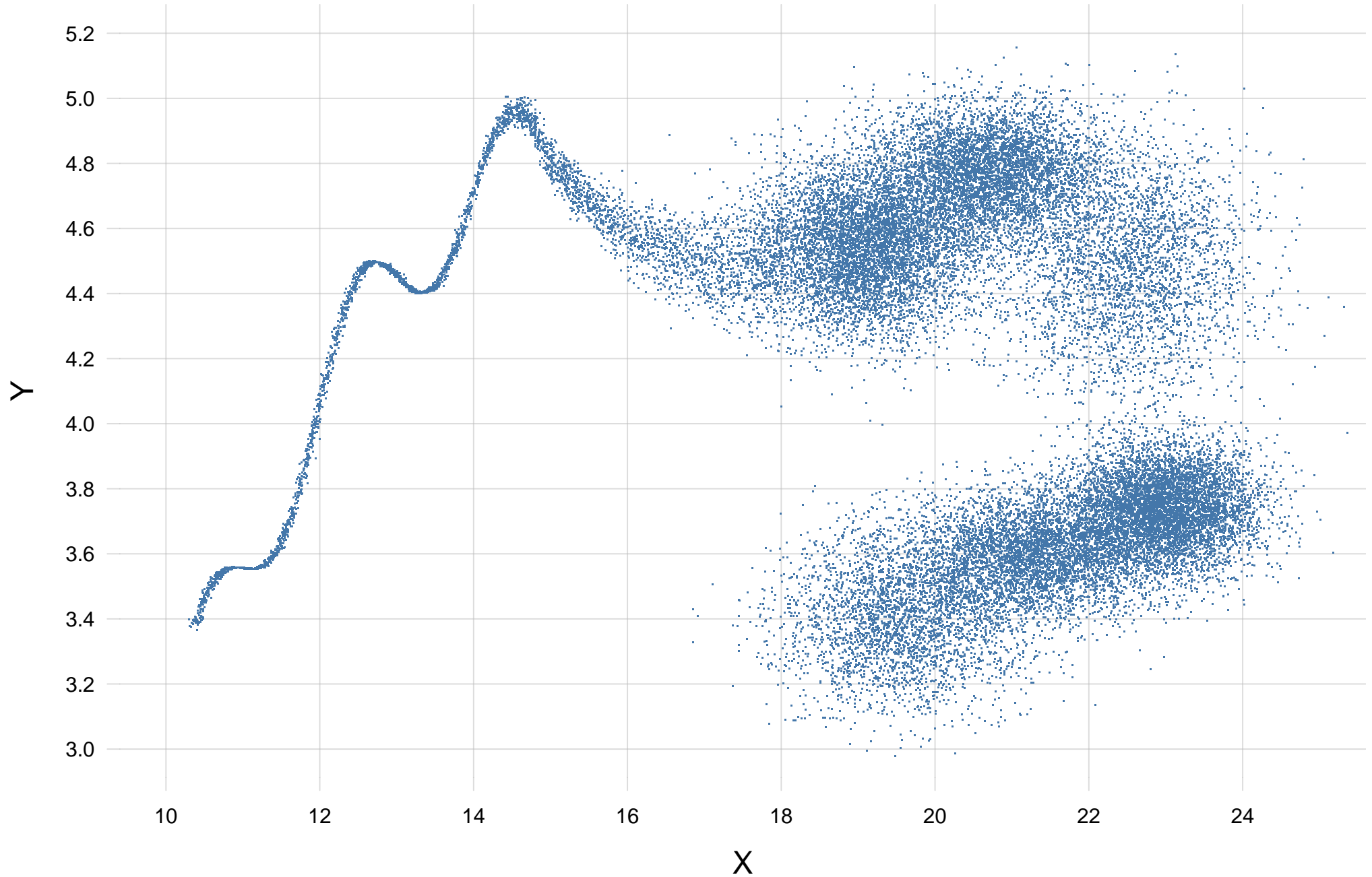
$$x = 11.5 \Rightarrow y \approx 3.60-3.65$$

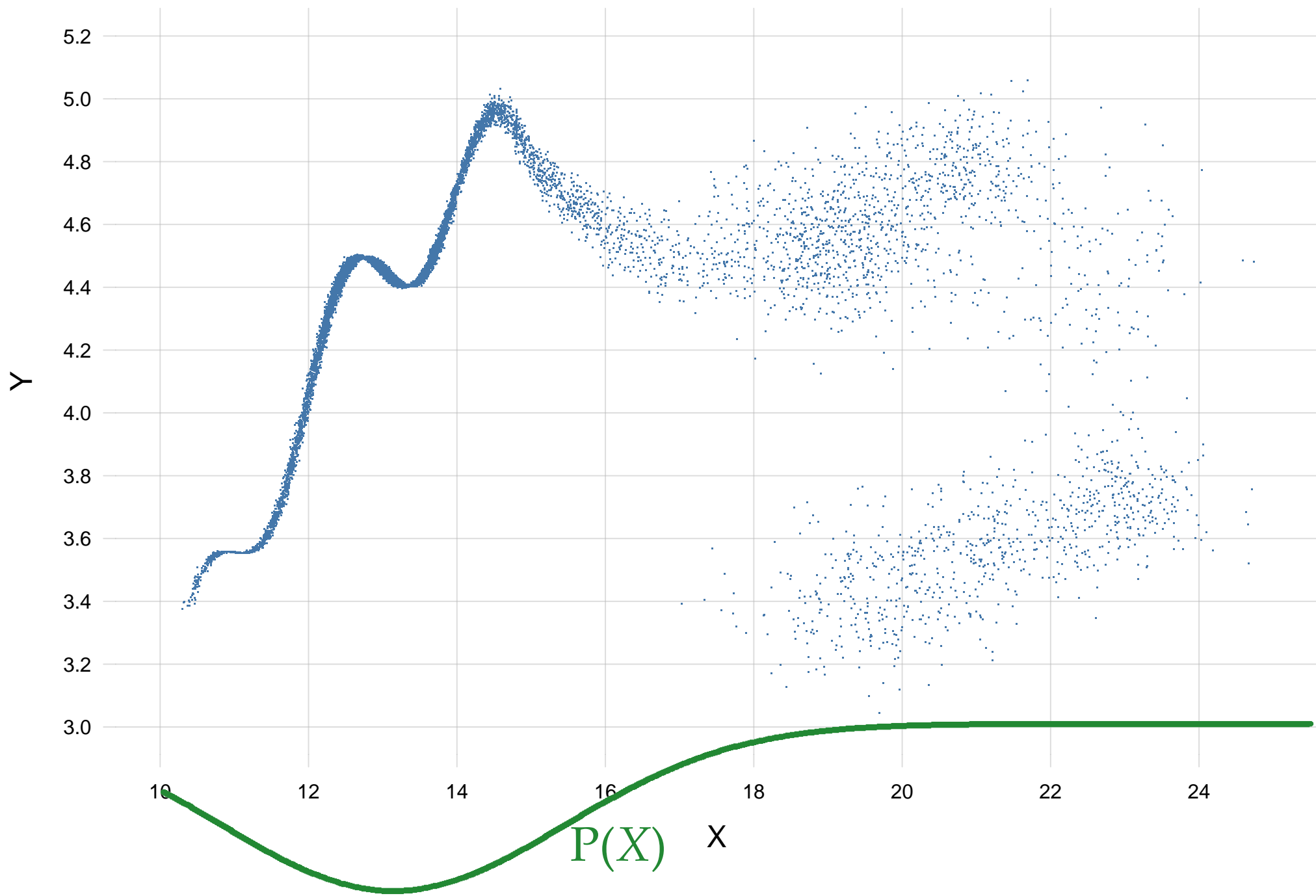


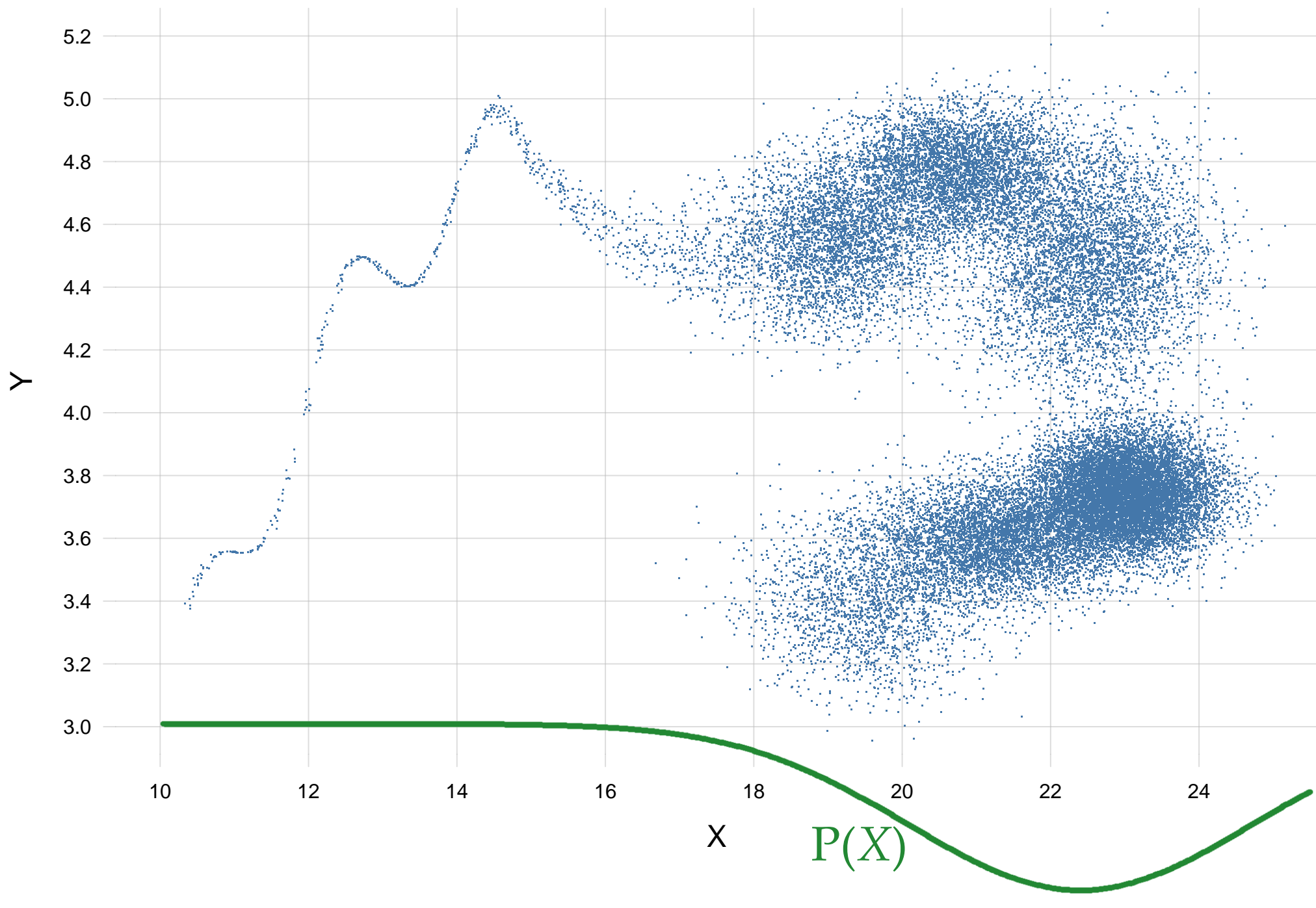
$x = 22 \Rightarrow y \approx 3.50\text{--}3.85 \text{ or } 4.25\text{--}4.90$



What is the 'overall predictive power' of  $X$ ?







The ‘importance’ or ‘predictive power’ of  $X$  depends on  $P(X)$

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⚠ Careful with ‘data balancing’! ⚠

$$P(Y|X) P(X) \equiv P(X|Y) P(Y)$$



$$P(Y|X) P(X) \stackrel{!}{=} P(X|Y) \textcolor{red}{P^*(Y)}$$

$$P^*(Y|X) P^*(X) \equiv P^*(X|Y) P^*(Y)$$



## The Bell System Technical Journal

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### **A Mathematical Theory of Communication**

**By C. E. SHANNON**

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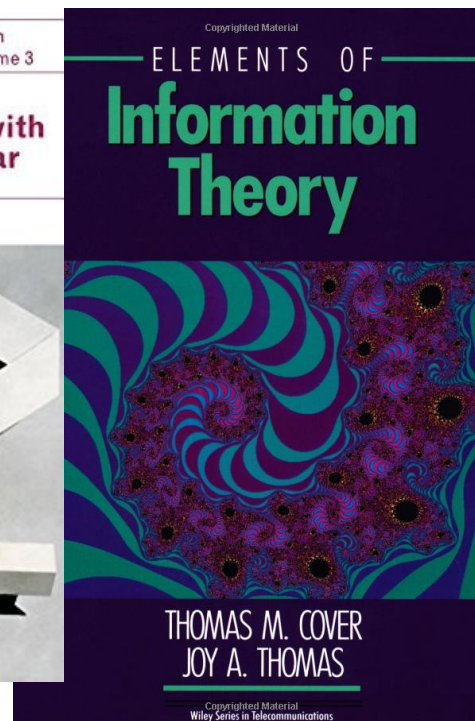
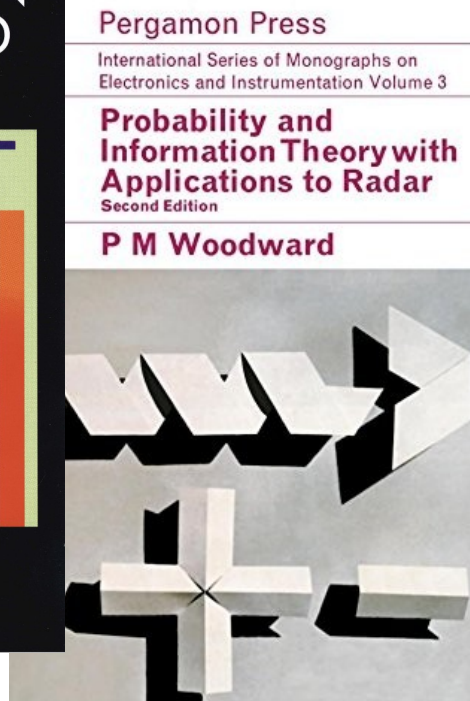
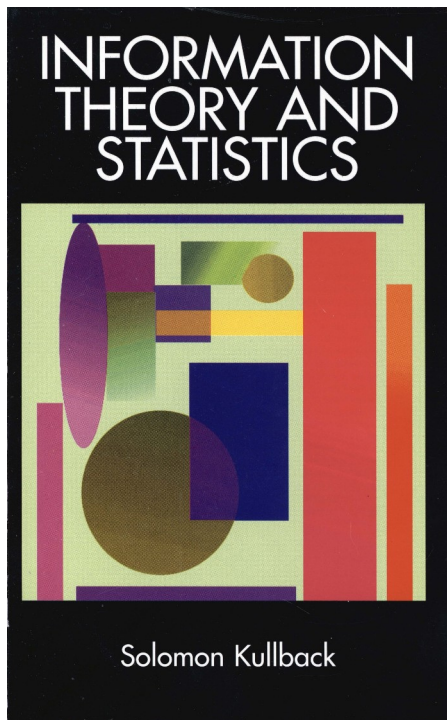
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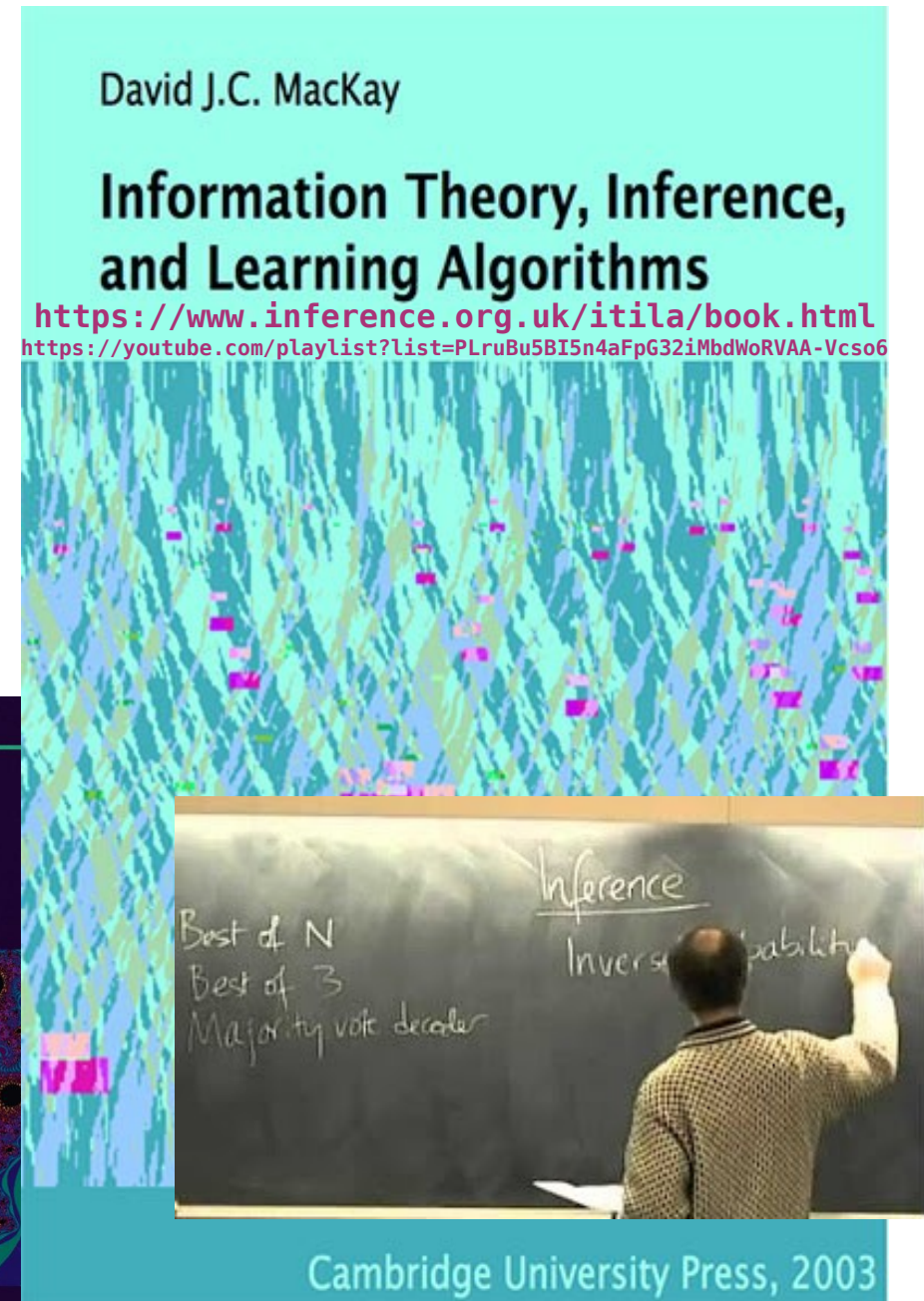
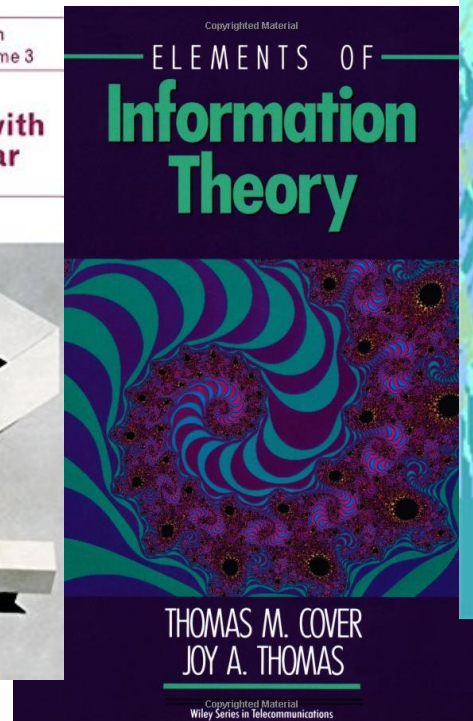
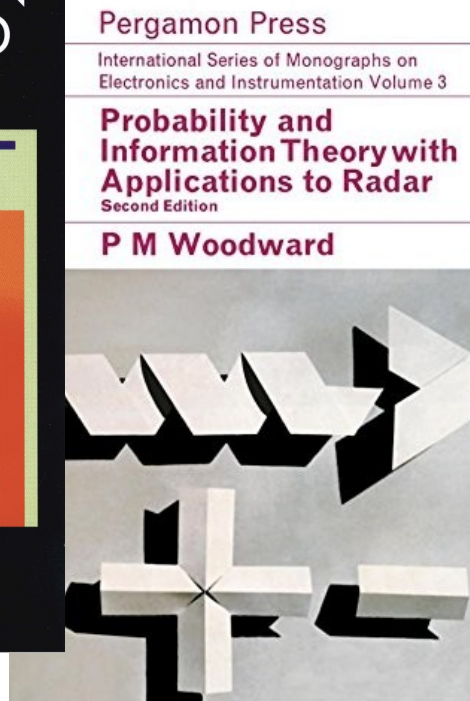
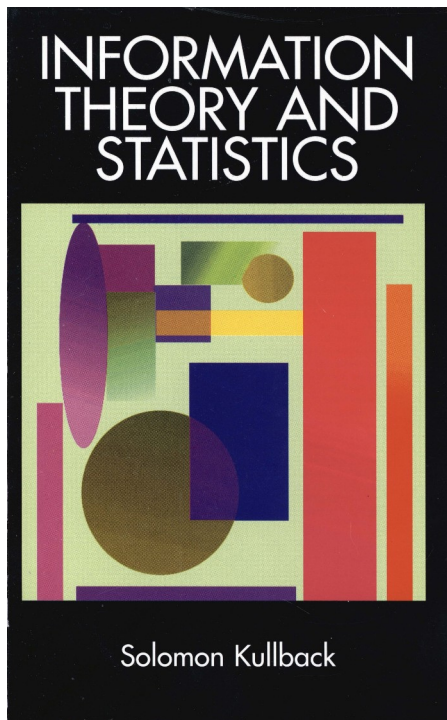
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‘predictive power’ of  $X$  for  $Y$   $\coloneqq$  **Mutual information** between  $Y$  and  $X$   
(mean transinformation content)

$$I(X; Y) := \int p(y|x) p(x) \log \left[ \frac{p(y|x)}{p(y)} \right] dy dx$$

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$$I(Y; X_1, X_2) \geq I(Y; X_2)$$

$$\text{but } I(Y; X_1, X_2) \neq I(Y; X_1) + I(Y; X_2)$$

# INTERNATIONAL STANDARD

## NORME INTERNATIONALE

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**Quantities and units –  
Part 13: Information science and technology**

**Grandeurs et unités –  
Partie 13: Science et technologies de l'information**

## INTERNATIONAL STANDARD

INFORMATION SCIENCE AND TECHNOLOGY			QUANTITIES	
Item No.	Name	Symbol	Definition	Remarks
13-24 (902)	information content <i>fr</i> quantité (f) d'information	$I(x)$	$I(x) = \lg \frac{1}{p(x)} \text{ Sh} = \lg \frac{1}{p(x)} \text{ Hart} =$ $\ln \frac{1}{p(x)} \text{ nat}$ <p>where <math>p(x)</math> is the probability of event <math>x</math></p>	See ISO/IEC 2382-16, item 16.03.02. See also IEC 60027-3.
13-25 (903)	entropy <i>fr</i> entropie (f)	$H$	$H(X) = -\sum_{i=1}^n p(x_i) \lg p(x_i)$ <p>for the set <math>X = \{x_1, \dots, x_n\}</math> where <math>p(x_i)</math> is the probability and <math>I(x_i)</math> is the information content of event <math>x_i</math></p>	See ISO/IEC 2382-16, item 16.03.03.
13-30 (908)	joint information content <i>fr</i> quantité (f) d'information conjointe	$I(x, y)$	$I(x, y) = \lg \frac{1}{p(x, y)} \text{ Sh} = \lg \frac{1}{p(x, y)} \text{ Hart} =$ $\ln \frac{1}{p(x, y)} \text{ nat}$ <p>where <math>p(x, y)</math> is the joint probability of events <math>x</math> and <math>y</math></p>	
13-35 (912)	transinformation content <i>fr</i> transinformation (f)	$T(x, y)$	$T(x, y) = I(x) + I(y) - I(x, y)$ <p>where <math>I(x)</math> and <math>I(y)</math> are the information contents (13-24) of events <math>x</math> and <math>y</math>, respectively, and <math>I(x, y)</math> is their joint information content (13-30)</p>	See ISO/IEC 2382-16, item 16.04.07.
13-36 (913)	mean transinformation content <i>fr</i> transinformation (f) moyenne	$T$	$T(X, Y) = \sum_{i=1}^n \sum_{j=1}^m p(x_i, y_j) T(x_i, y_j)$ <p>for the sets <math>X = \{x_1, \dots, x_n\}</math>, <math>Y = \{y_1, \dots, y_m\}</math>, where <math>p(x_i, y_j)</math> is the joint probability of events <math>x_i</math> and <math>y_j</math>, and <math>T(x_i, y_j)</math> is their transinformation content (item 13-35)</p>	See ISO/IEC 2382-16, item 16.04.08.

UNITS					INFORMATION SCIENCE AND TECHNOLOGY	
Item No.	Name	Symbol	Definition	Conversion factors and remarks		
13-24.a	shannon	Sh	value of the quantity when the argument is equal to 2	1 Sh $\approx$ 0,693 nat $\approx$ 0,301 Hart		
13-24.b	hartley	Hart	value of the quantity when the argument is equal to 10	1 Hart $\approx$ 3,322 Sh $\approx$ 2,303 nat		
13-24.c	natural unit of information	nat	value of the quantity when the argument is equal to e	1 nat $\approx$ 1,433 Sh $\approx$ 0,434 Hart		
13-25.a	shannon	Sh				
13-25.b	hartley	Hart				
13-25.c	natural unit of information	nat				
13-30.a	shannon	Sh				
13-30.b	hartley	Hart				
13-30.c	natural unit of information	nat				
13-35.a	shannon	Sh				
13-35.b	hartley	Hart				
13-35.c	natural unit of information	nat				
13-36.a	shannon	Sh			In practice, the unit "shannon per character" is generally used, and sometimes the units "hartley per character" and "natural unit per character".	
13-36.b	hartley	Hart				
13-36.c	natural unit of information	nat				

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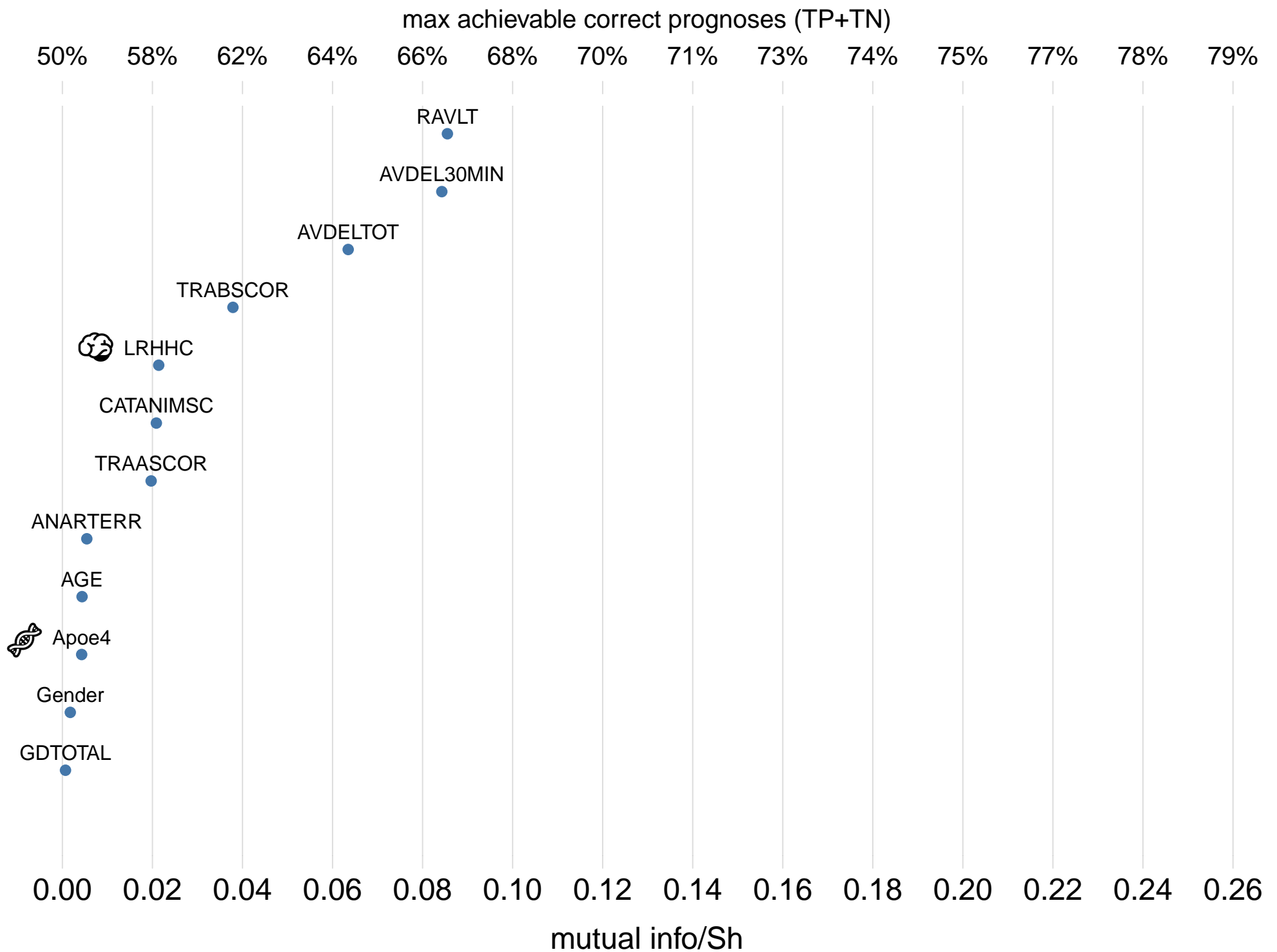
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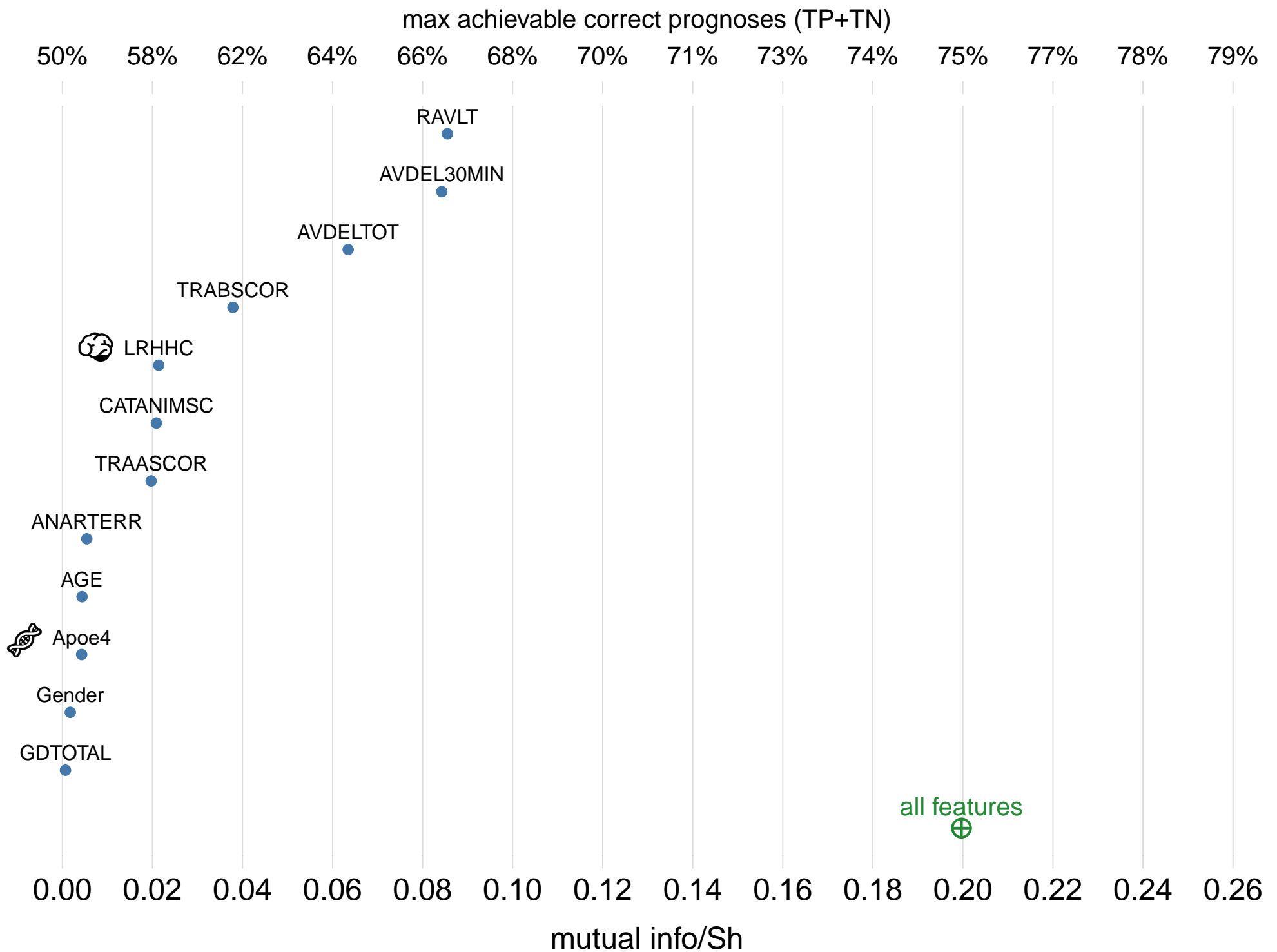
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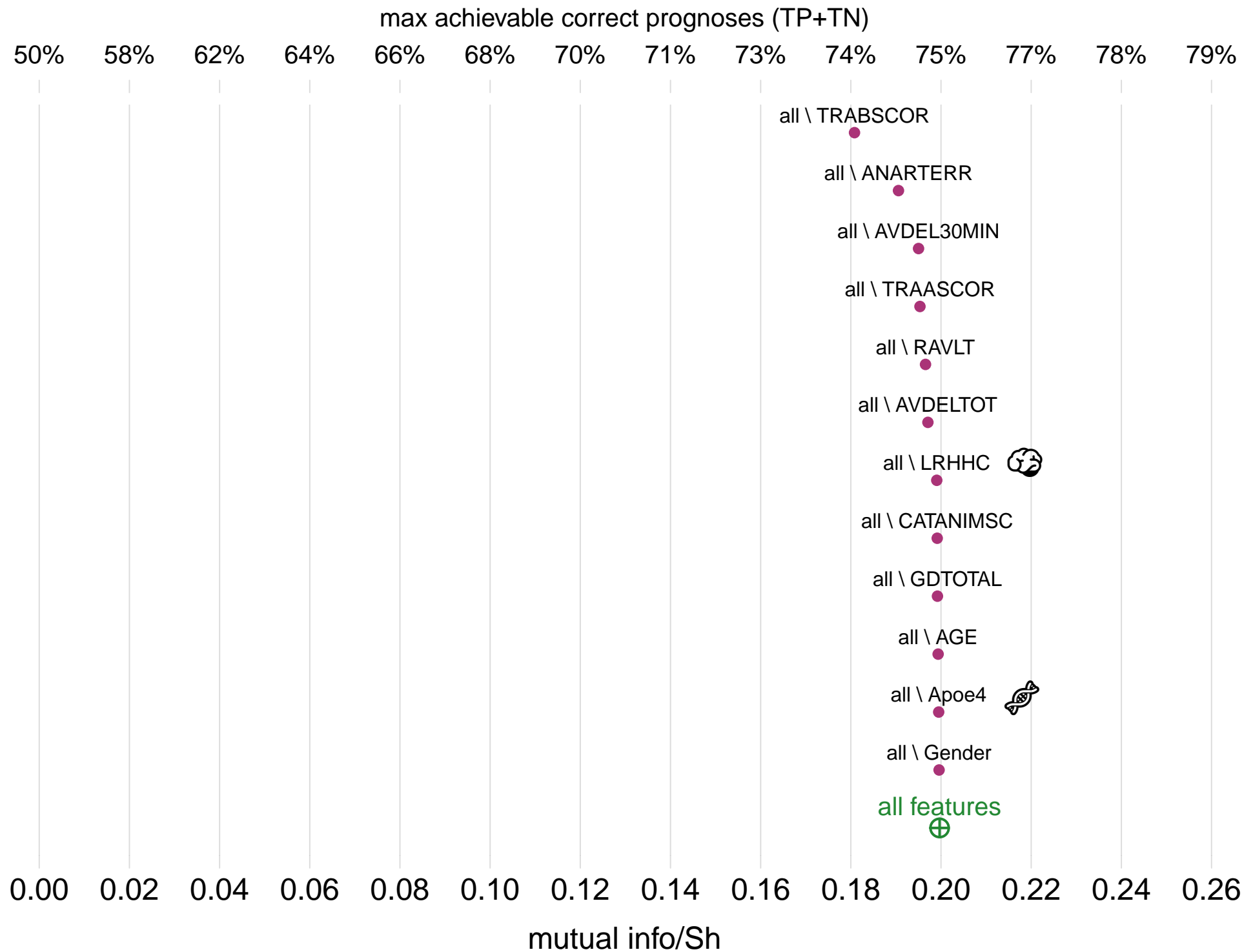
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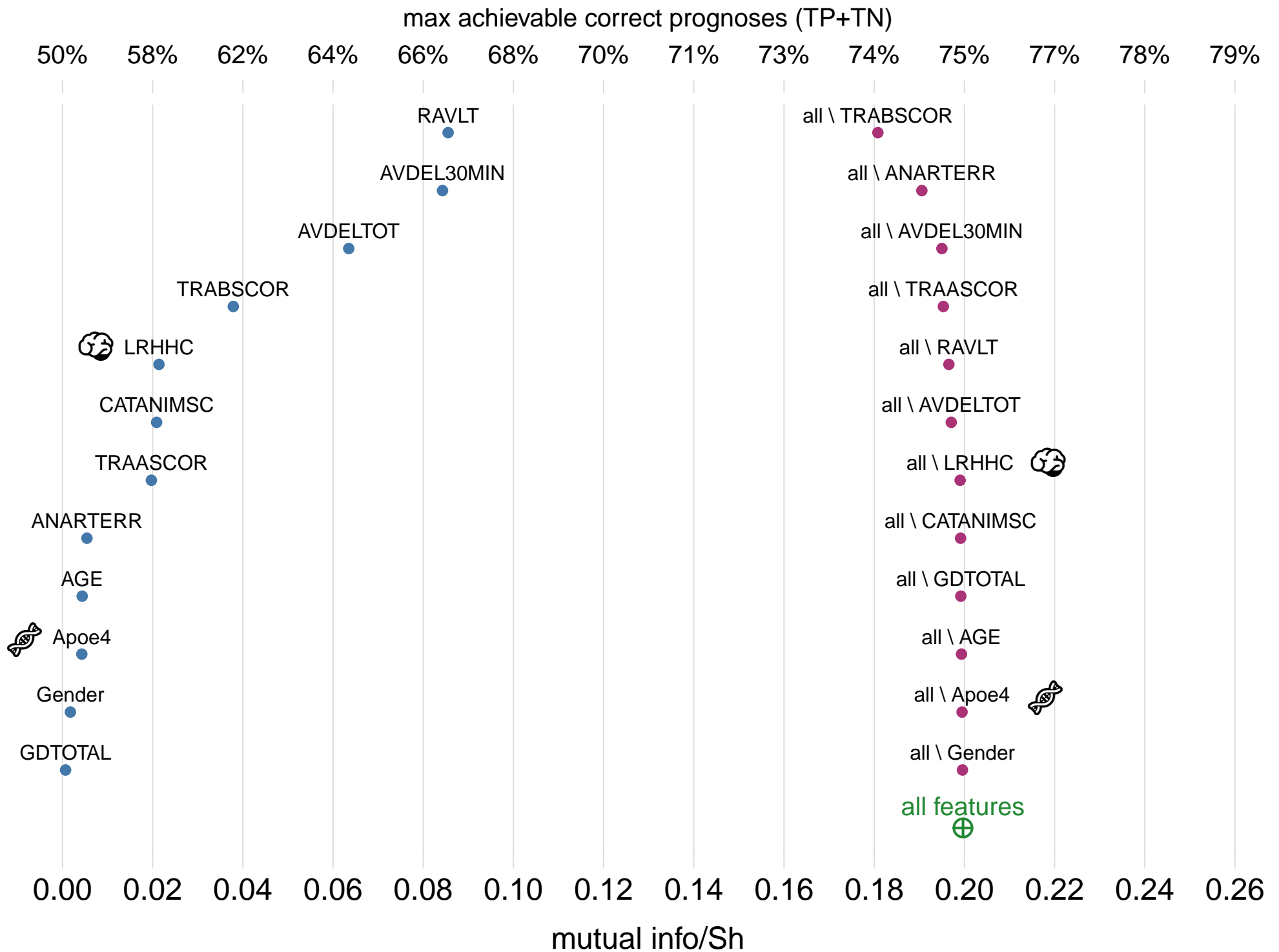
Maximum accuracy attainable  
by *any* algorithm which uses only feature set  $X$



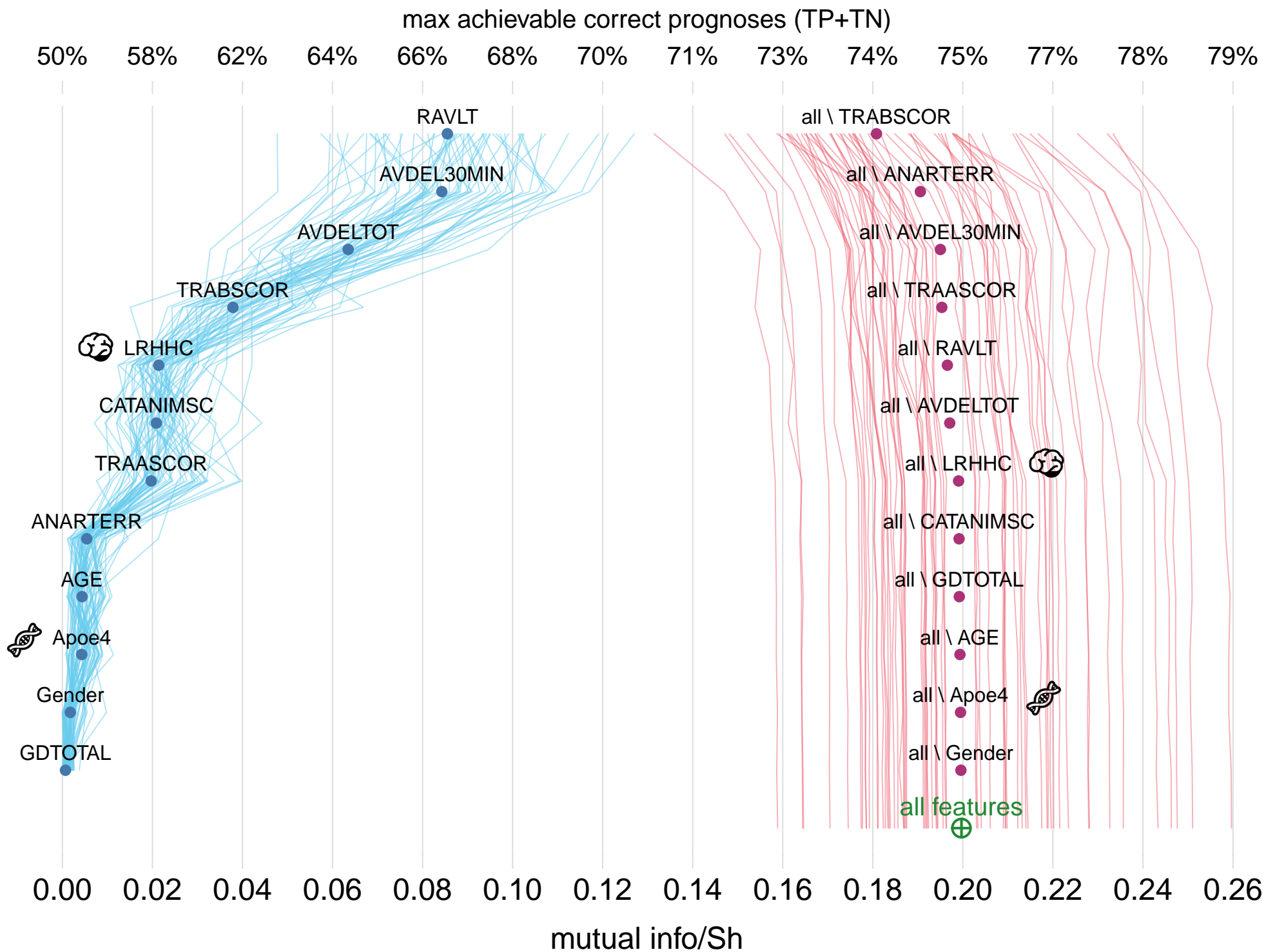


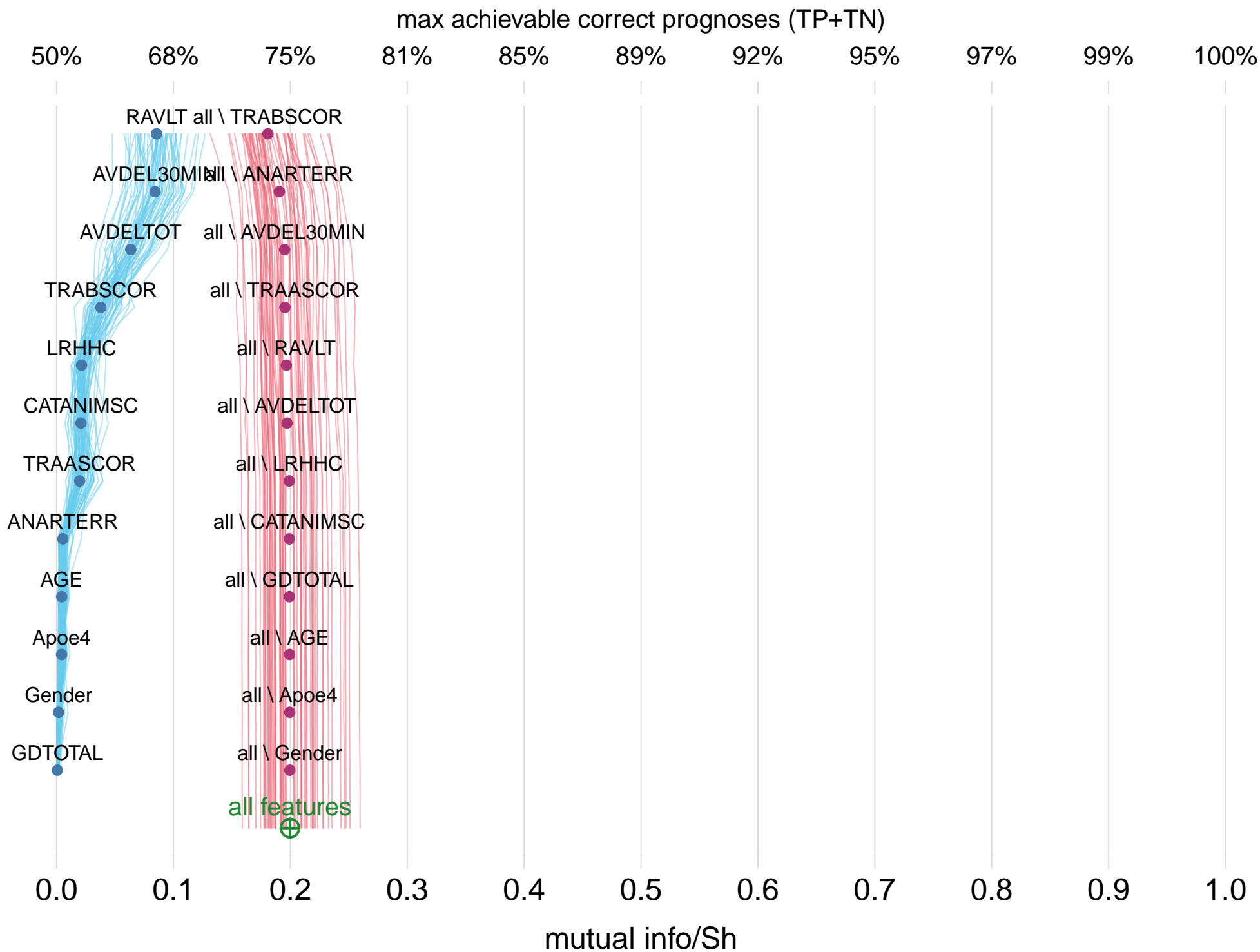


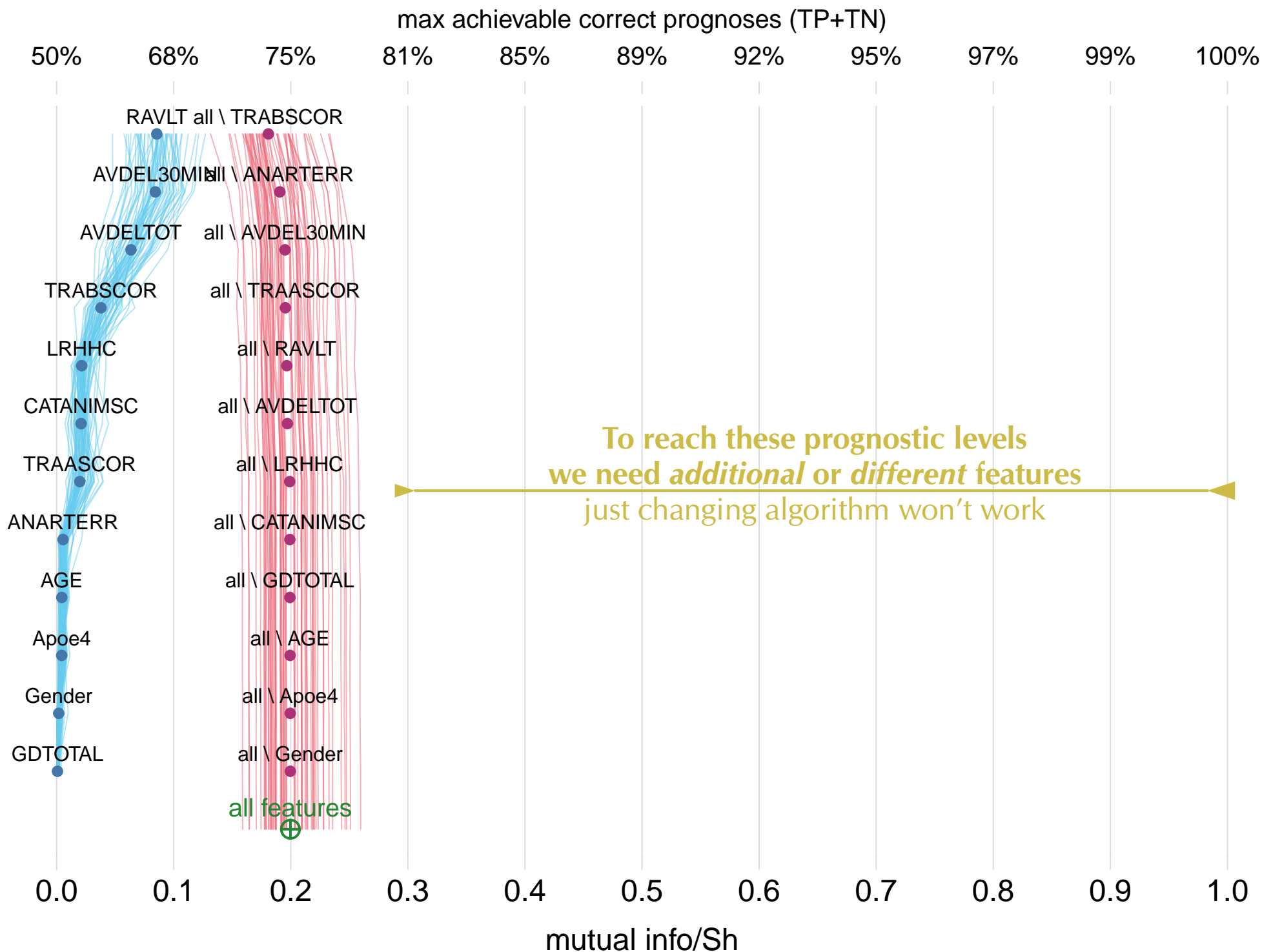


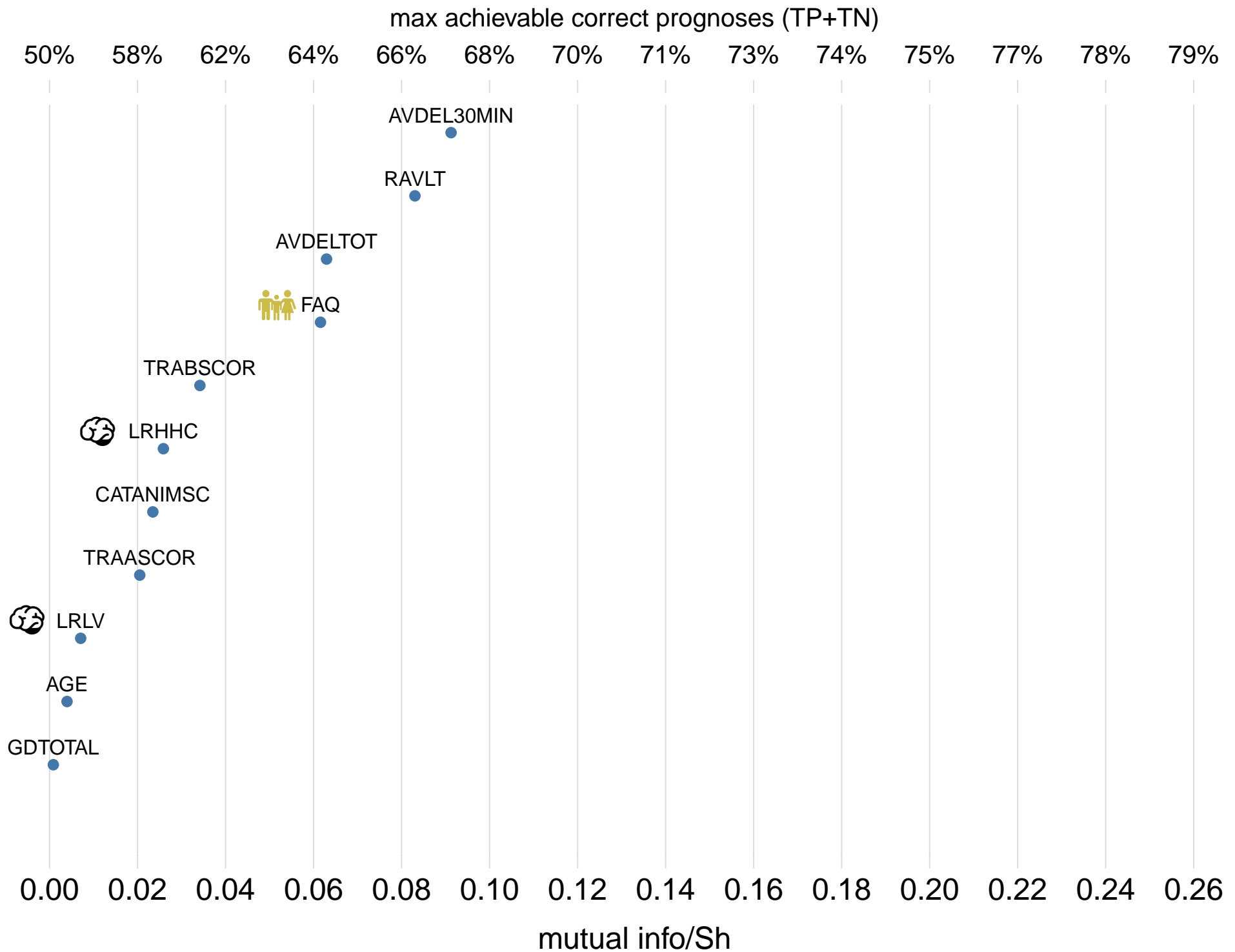


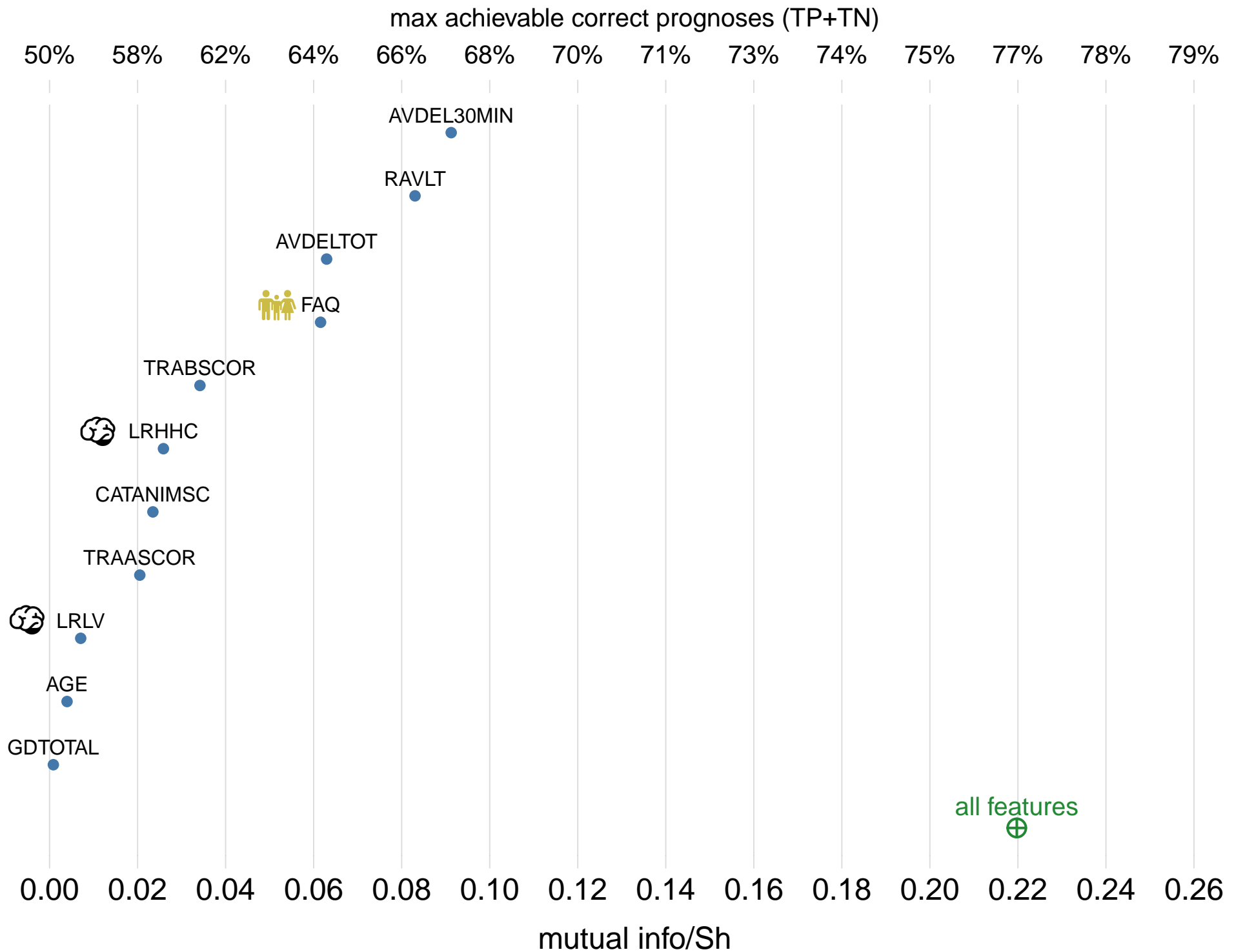


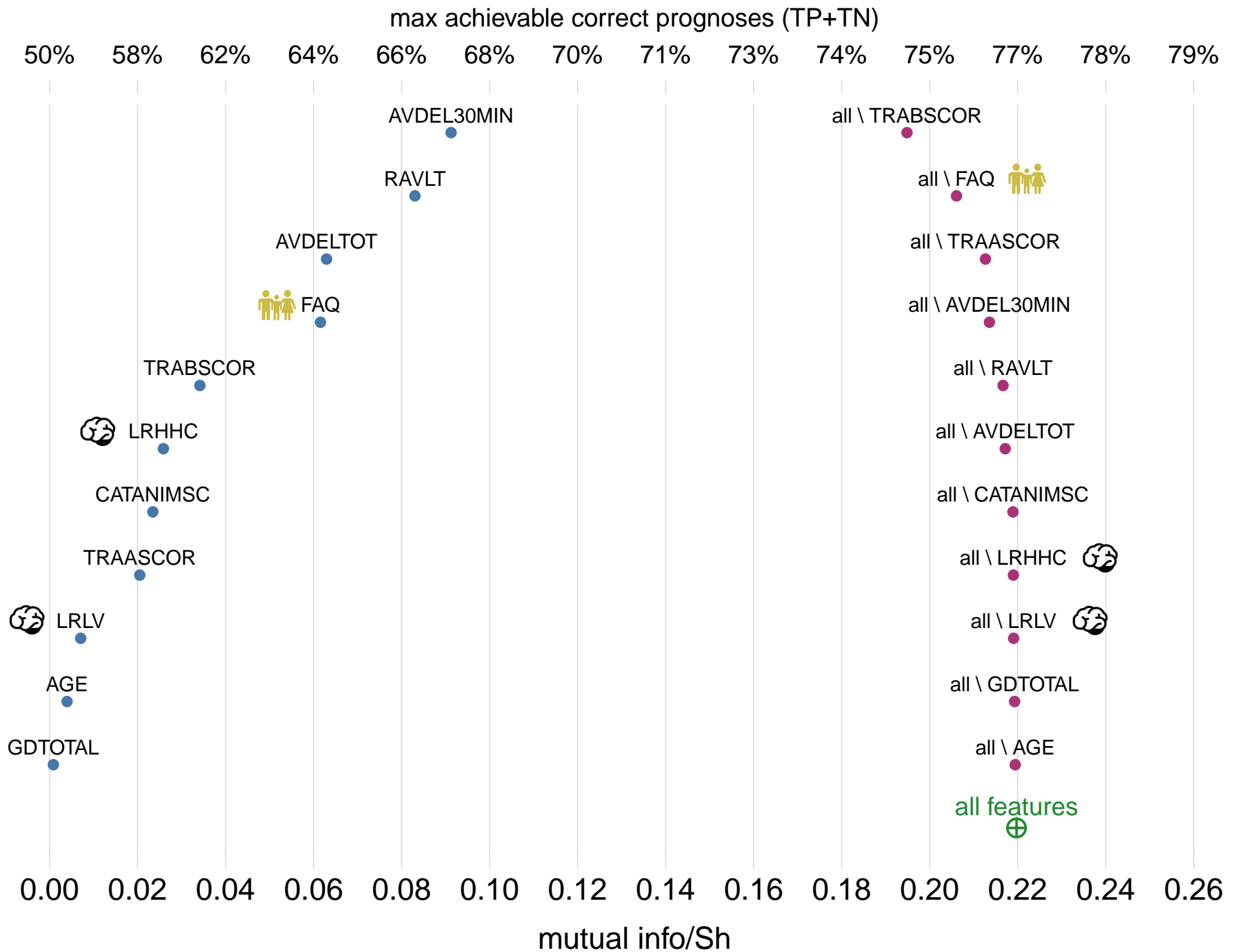


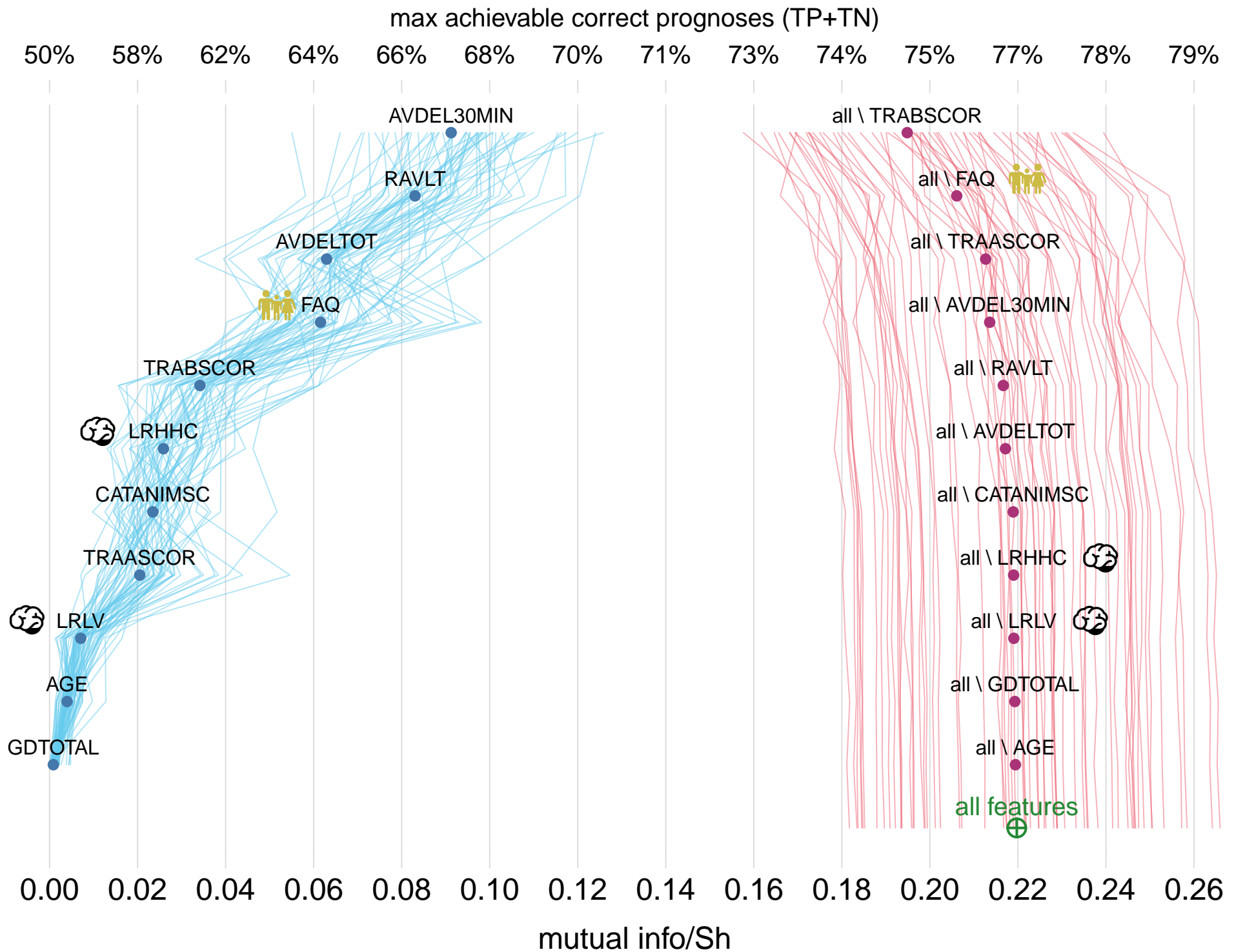






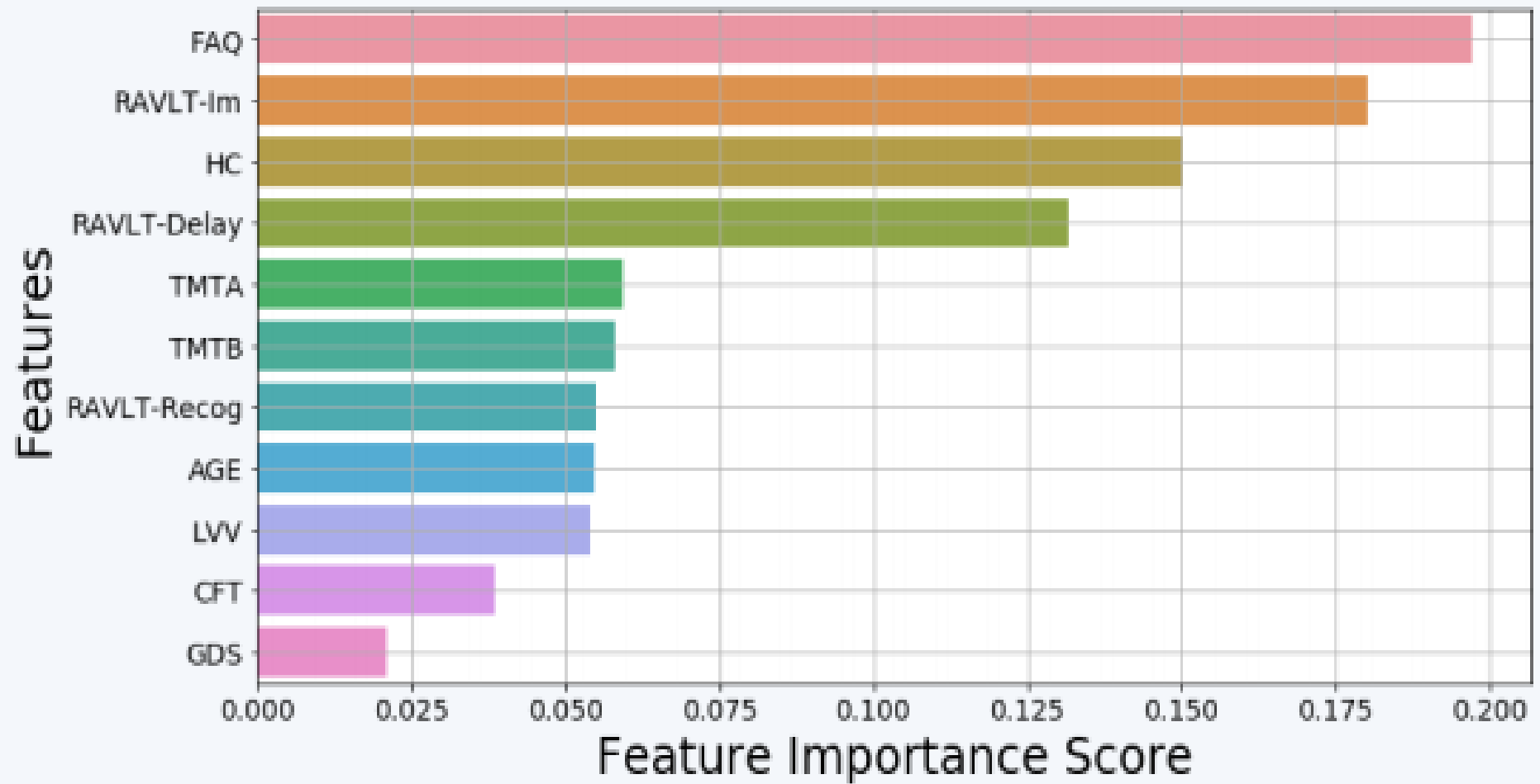




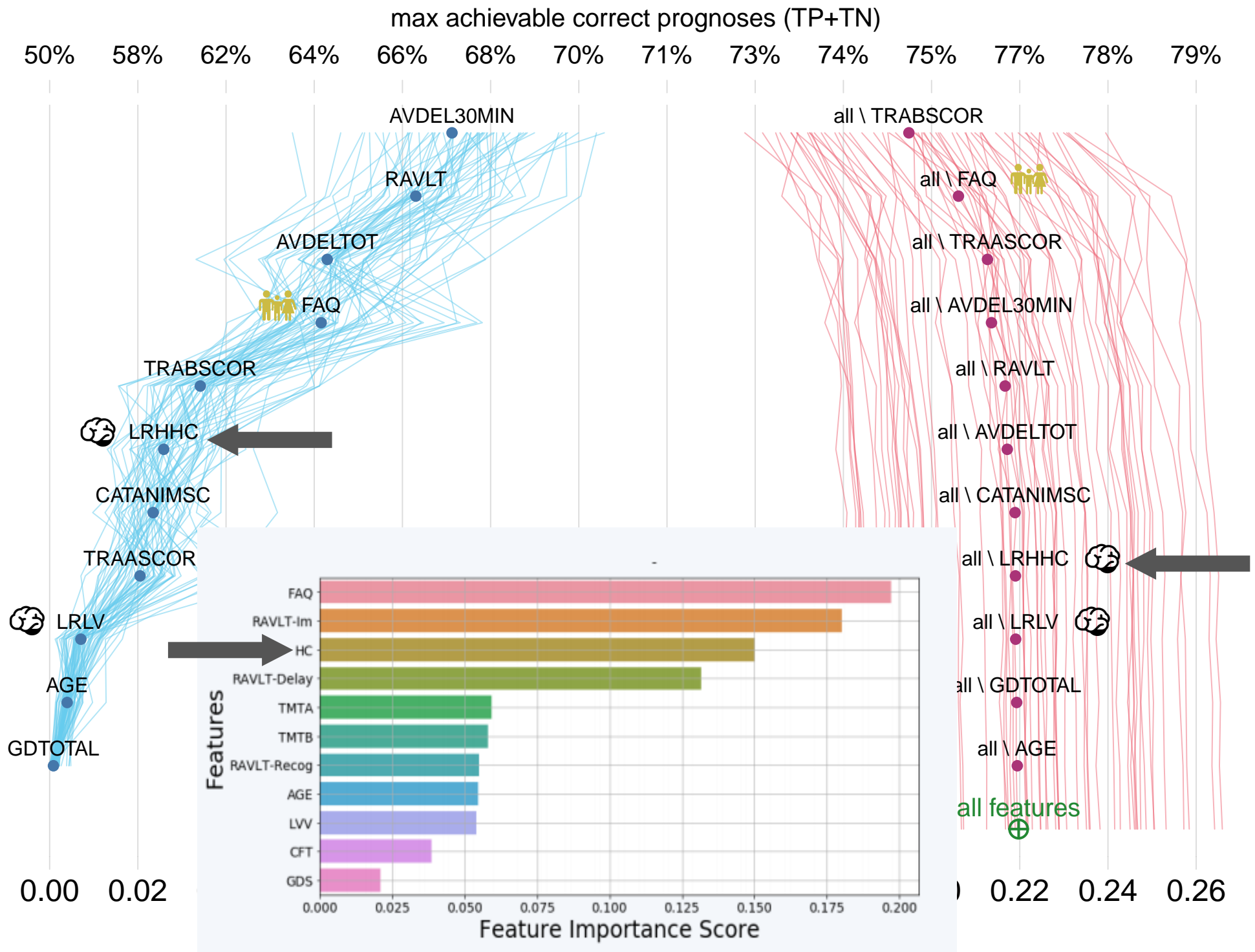


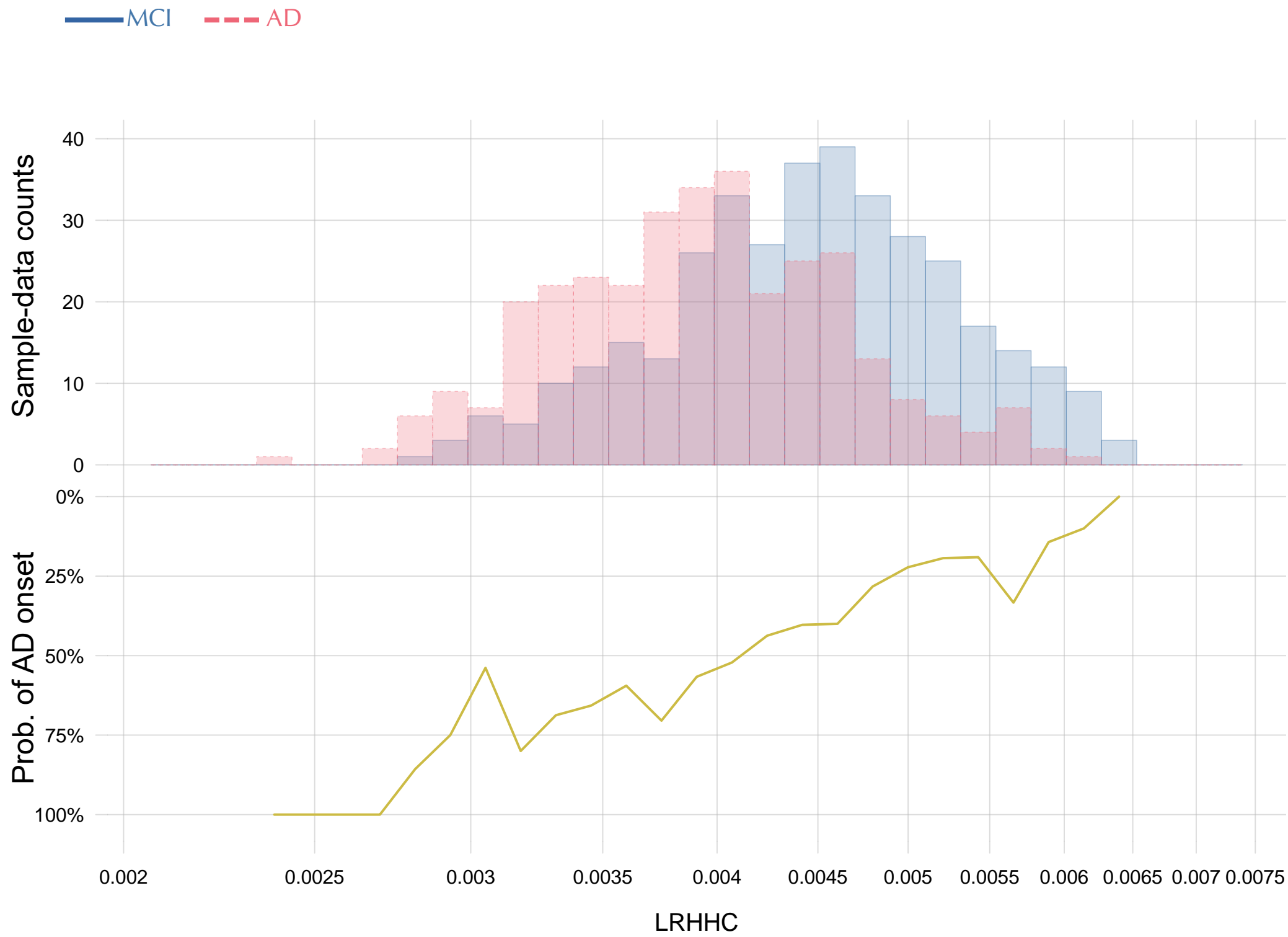


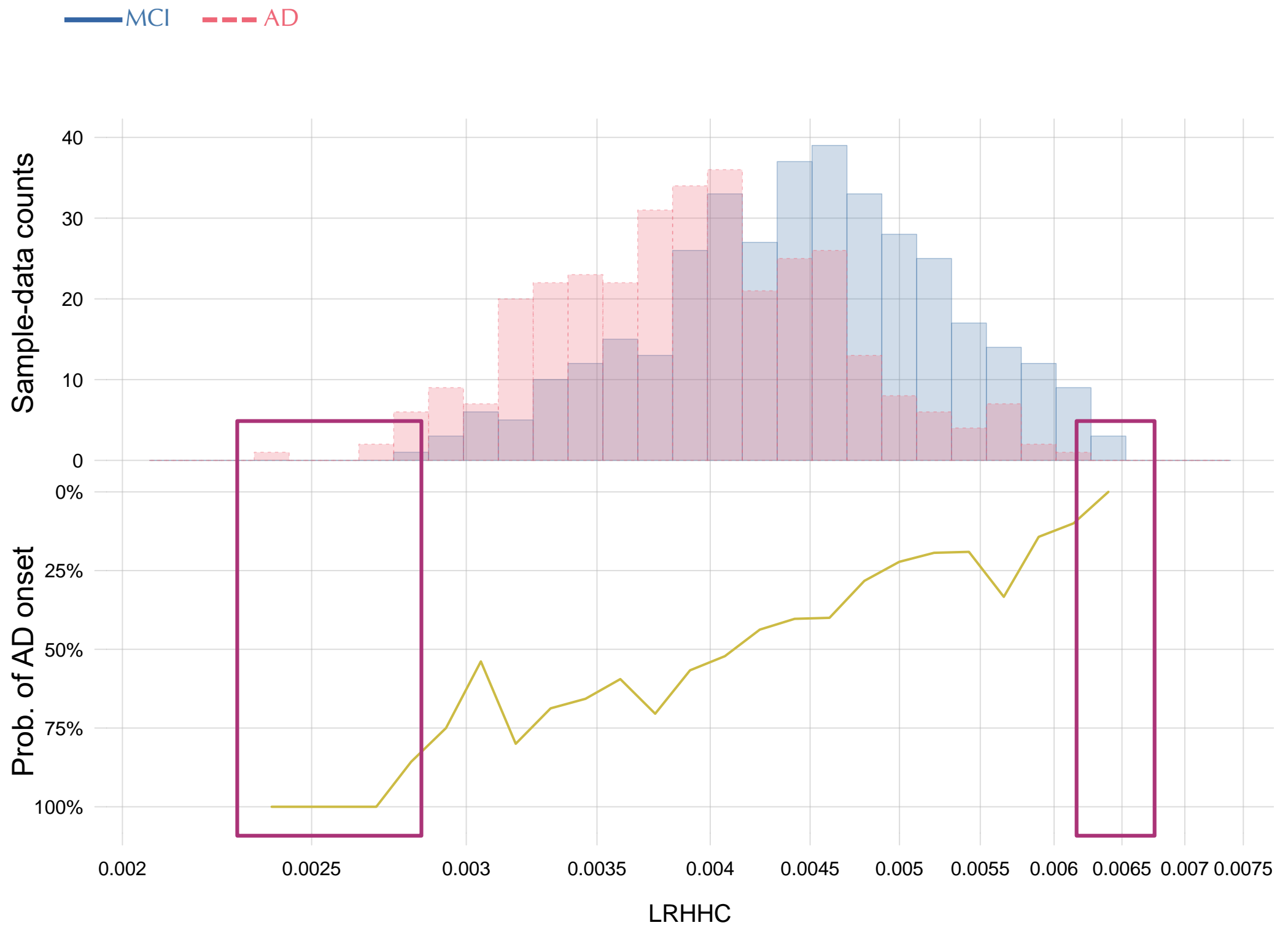
## Alexandra's results



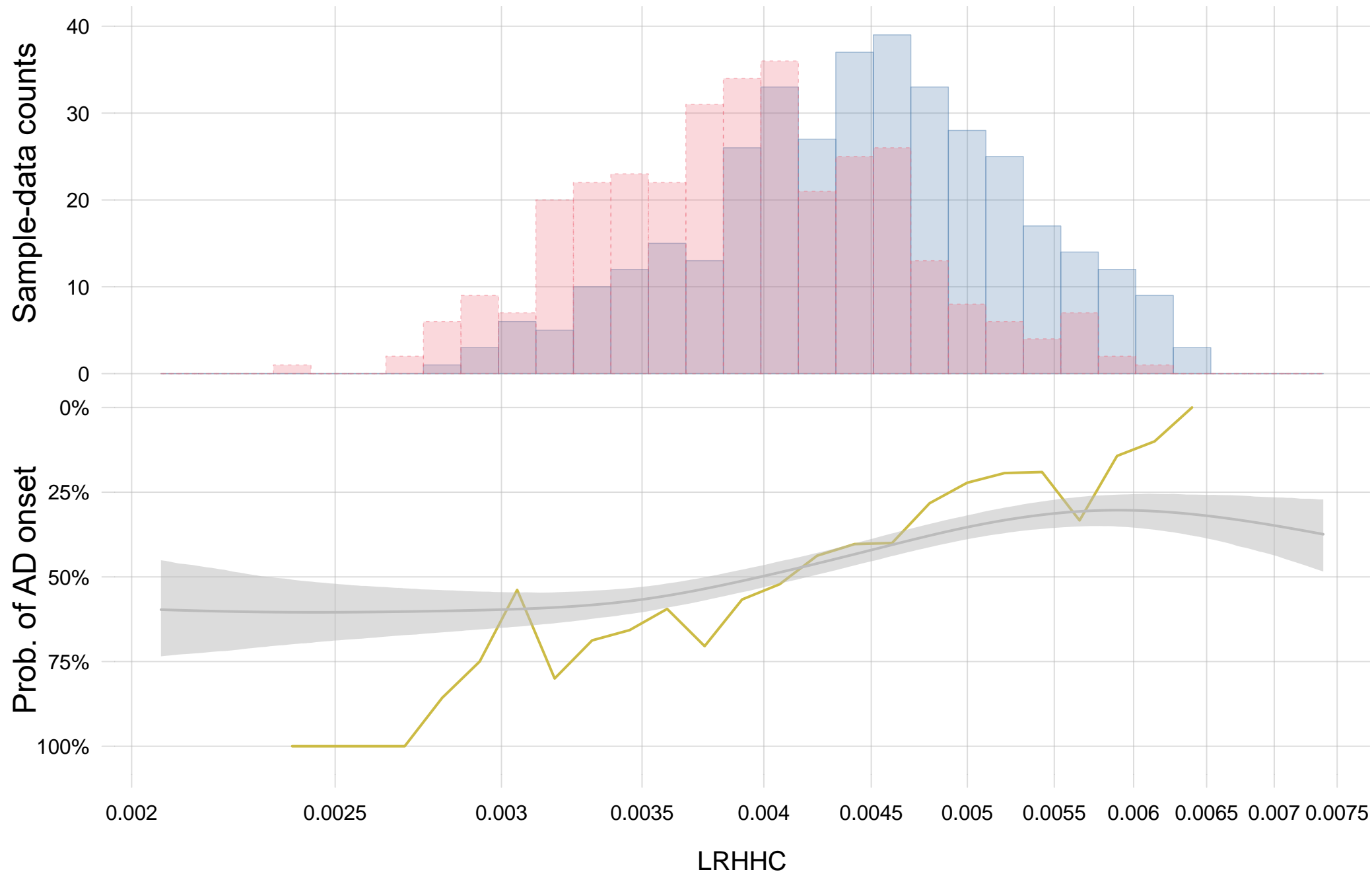


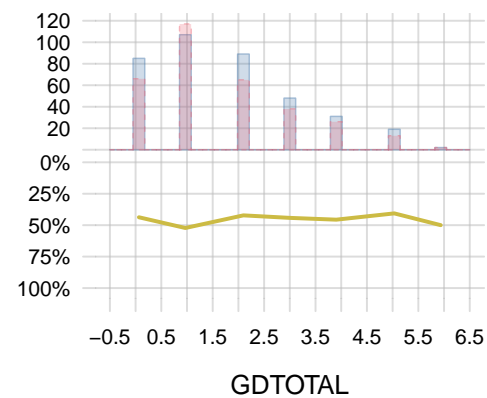
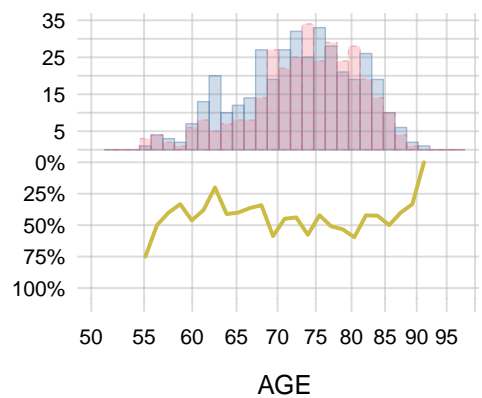
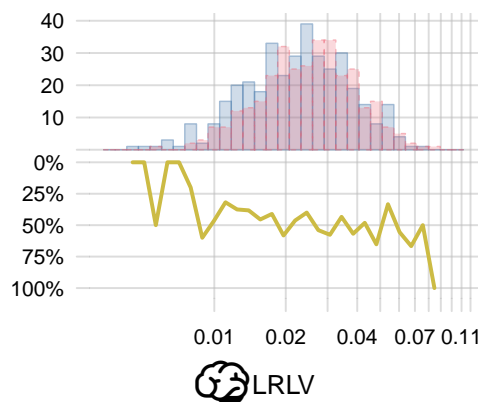
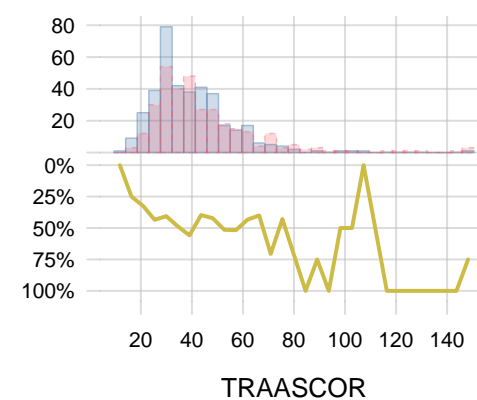
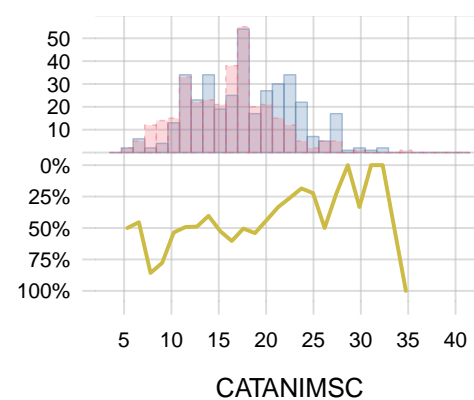
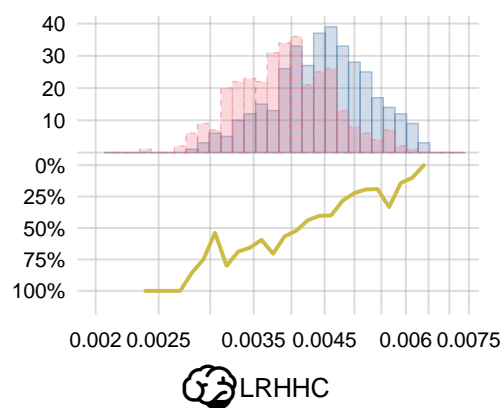
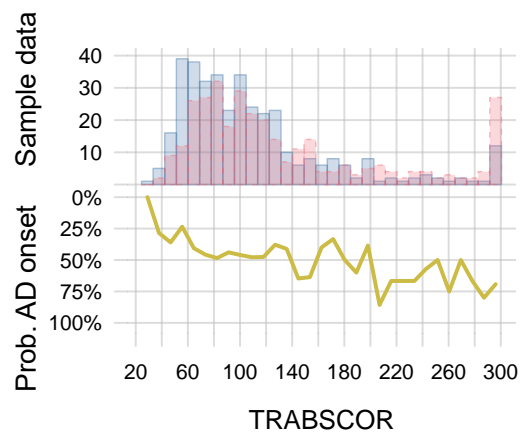
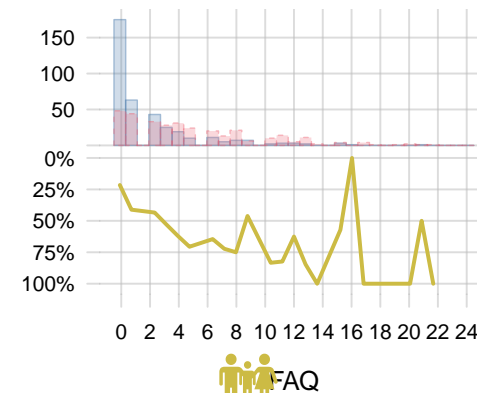
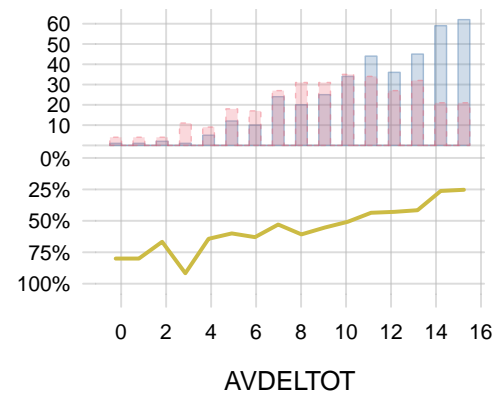
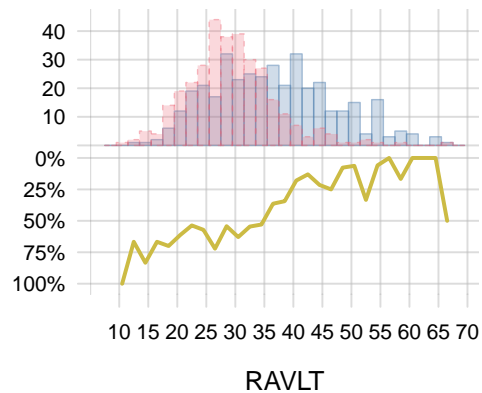
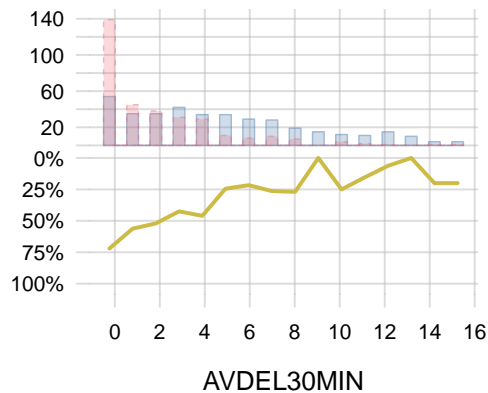


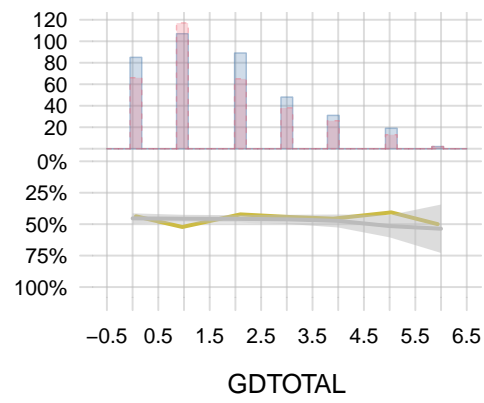
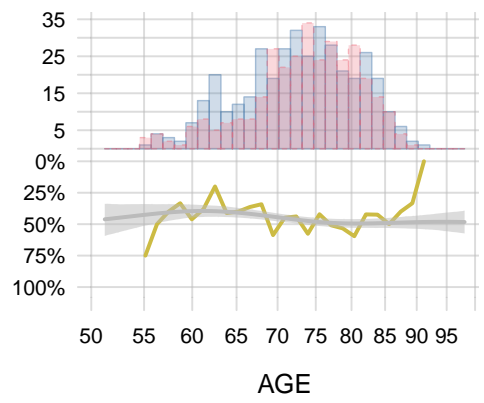
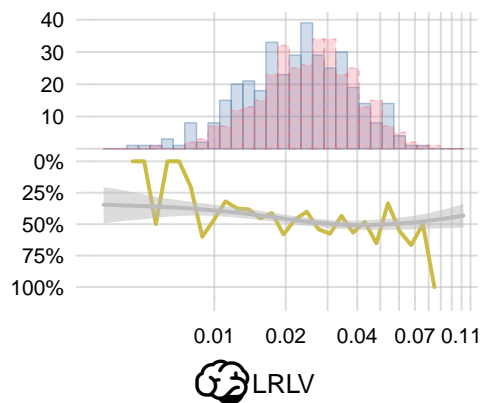
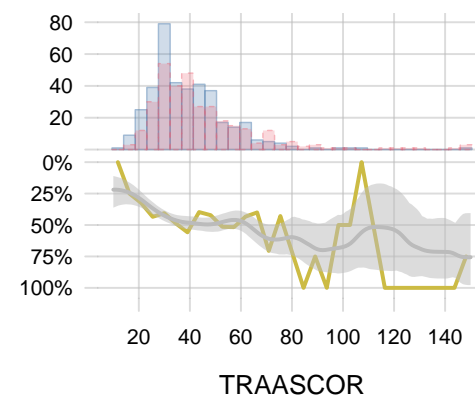
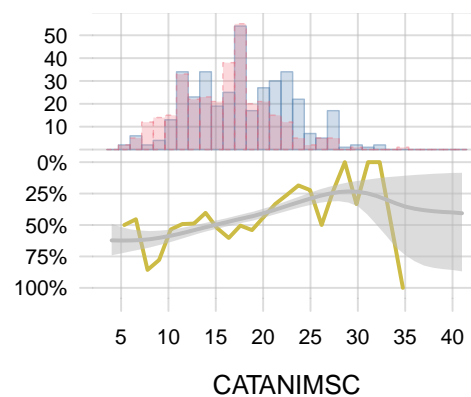
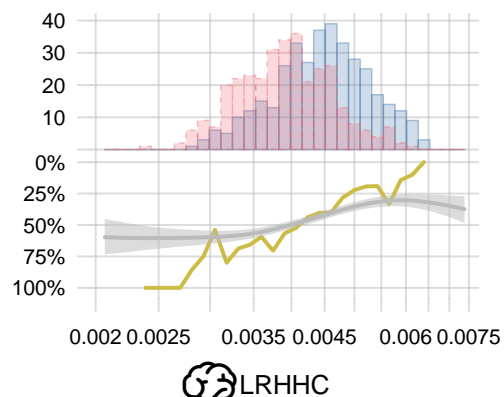
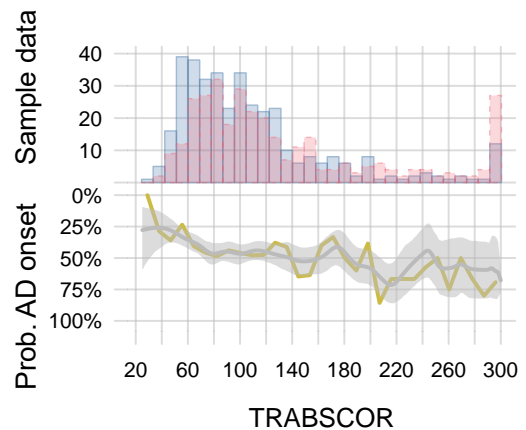
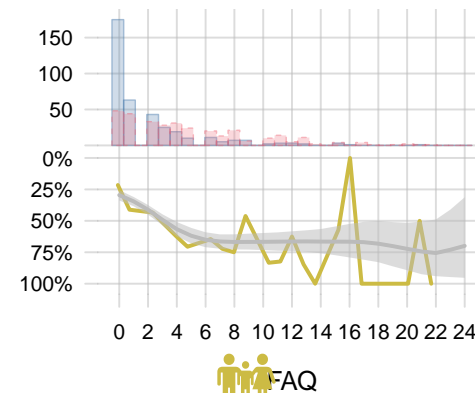
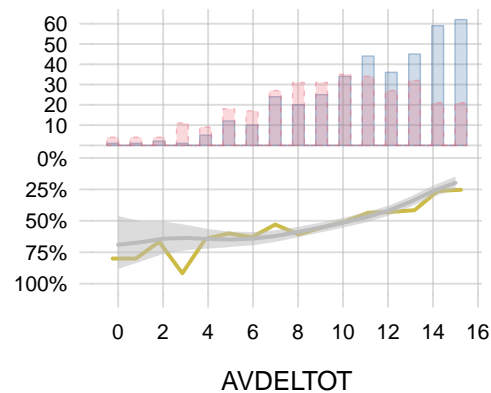
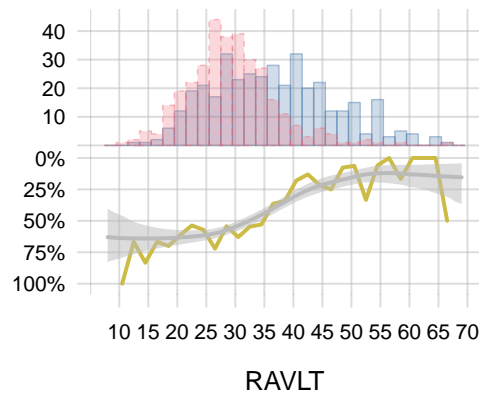
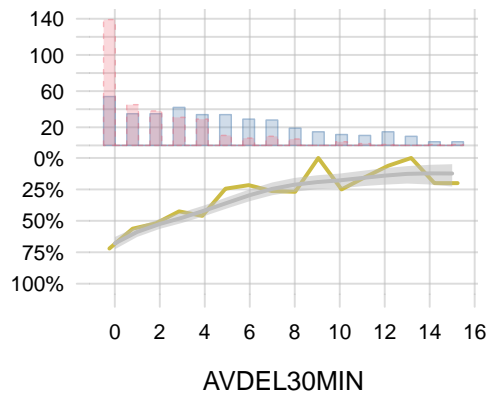




— MCI    - - - AD    ■ 87.5% credible interval







*Thank you!*