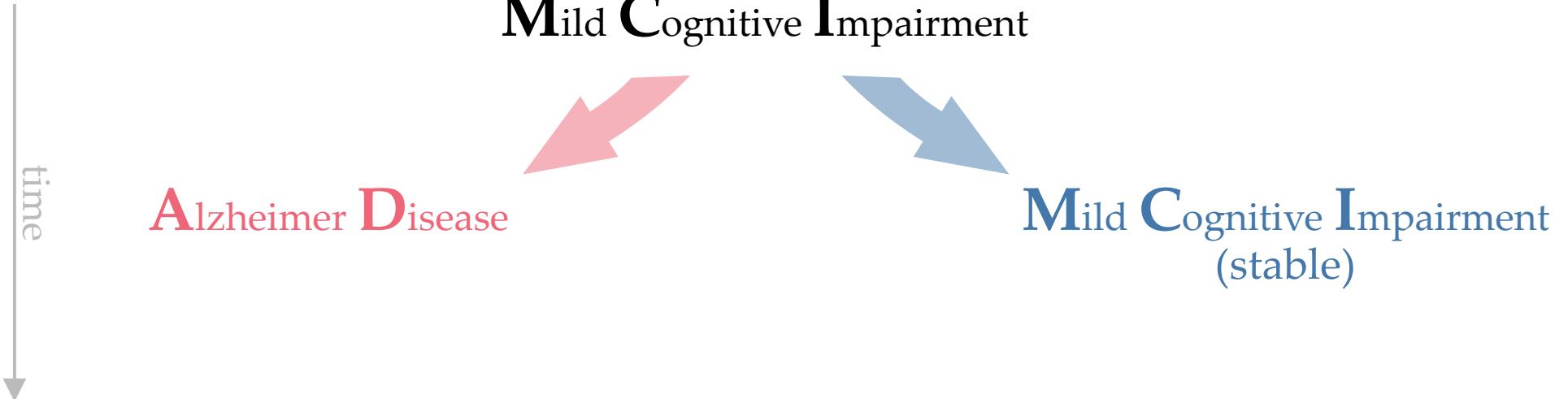


Analysis of some features
for prognosis of Alzheimer onset:
Probability theory & Information theory

Mild Cognitive Impairment



↓
time

Mild Cognitive Impairment



Alzheimer Disease

Mild Cognitive Impairment
(stable)



♀ ♂ Gender

♀ ♂ AGE

⌚ ANARTERR

⌚ GDTOTAL

⌚ RAVLT

⌚ TRABSCOR

⌚ CATANIMSC

⌚ TRAASCOR

⌚ AVDELTOT

⌚ AVDEL30MIN

⌚ LRHHC

⌚ LRLV

.ribbon Apoe4

people FAQ

♀ Gender

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⌚ RAVLT

⌚ TRABSCOR

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.ribbon Apoe4

people FAQ

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



♀ Gender

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⌚ ANARTERR

⌚ GDTOTAL

⌚ CATANIMSC

⌚ AVDELTOT

⌚ AVDEL30MIN

⌚ RAVLT

⌚ TRABSCOR

⌚ TRAASCOR

⌚ LRHHC

⌚ LRLV

🍬 Apoe4

👤 FAQ

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



⌚ ANAR

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

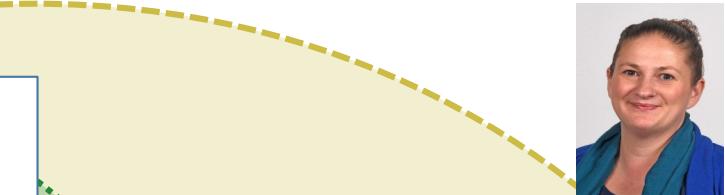
Evaluation

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 15th Street NW, Suite 250, Washington, DC 20005 via Copyright Clearance Center, Inc.

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ABSCOR

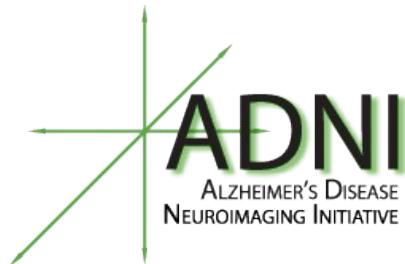
SCOR

HHC

⌚ LRLV



Data source:

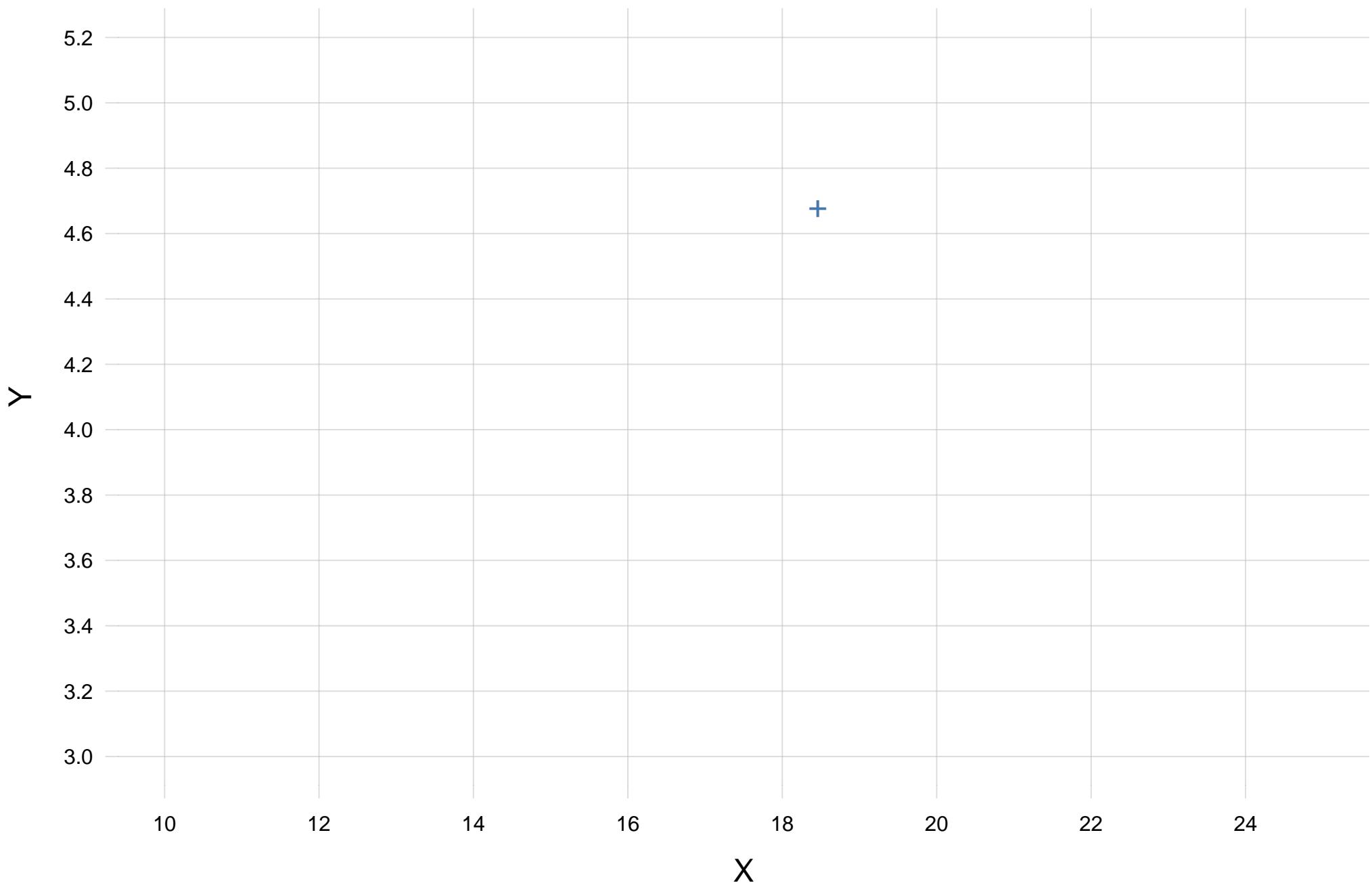


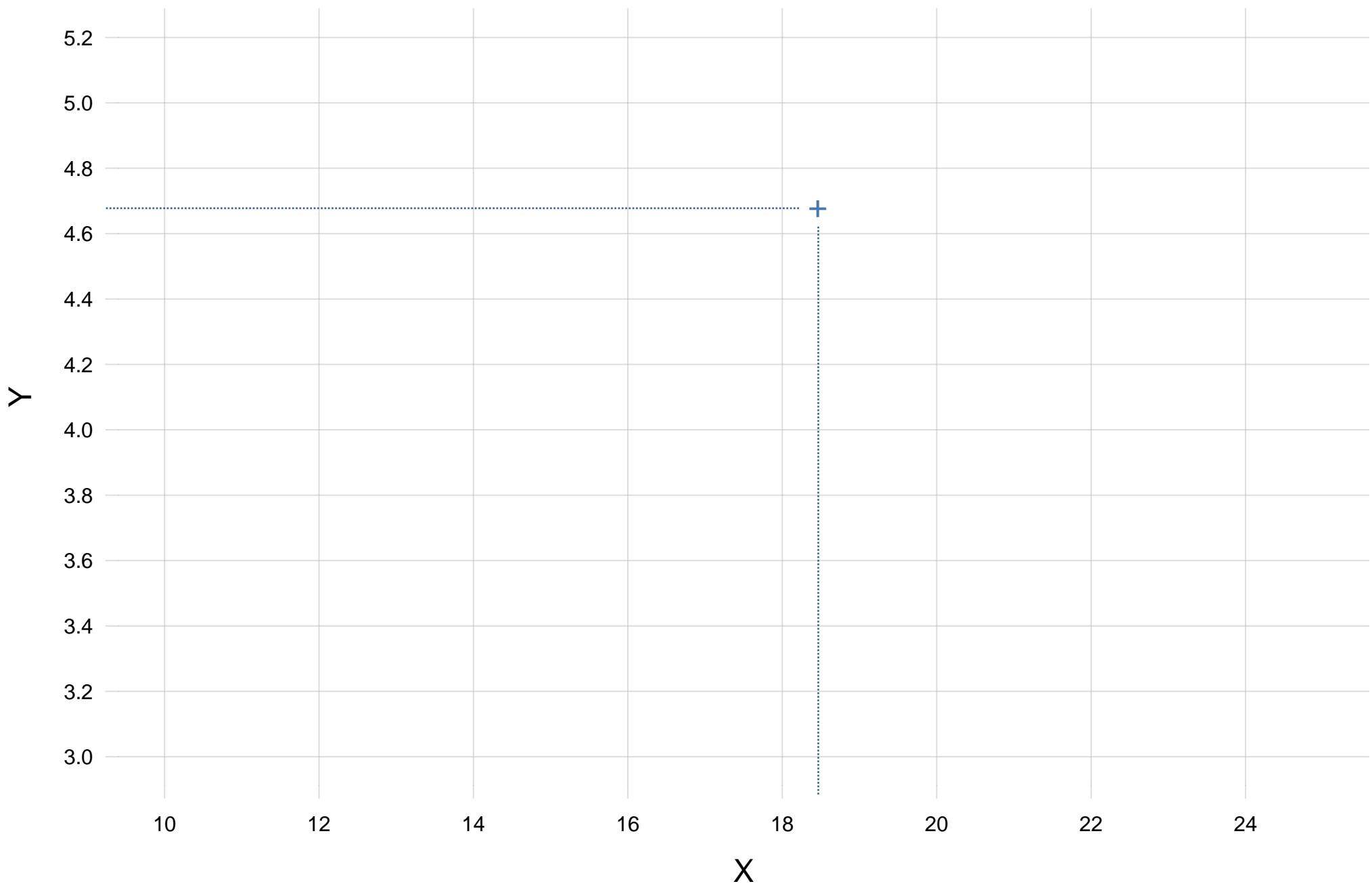
Ingrid's study: 12 + 1 variates, 678 datapoints

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

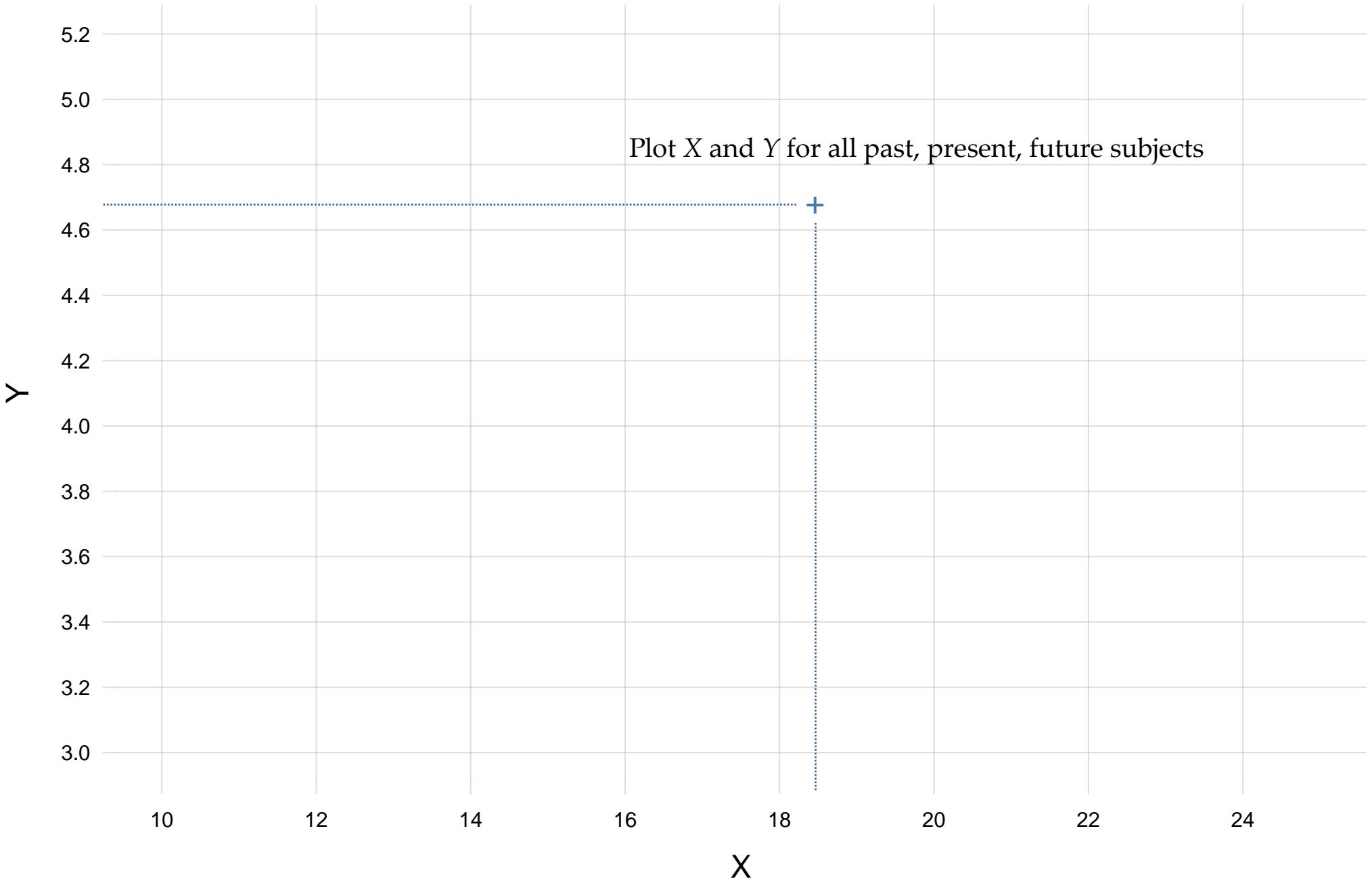
Computation time: ~65 h/study (3 parallel sessions to assess numeric convergence)

HPC **UNINETT** sigma2

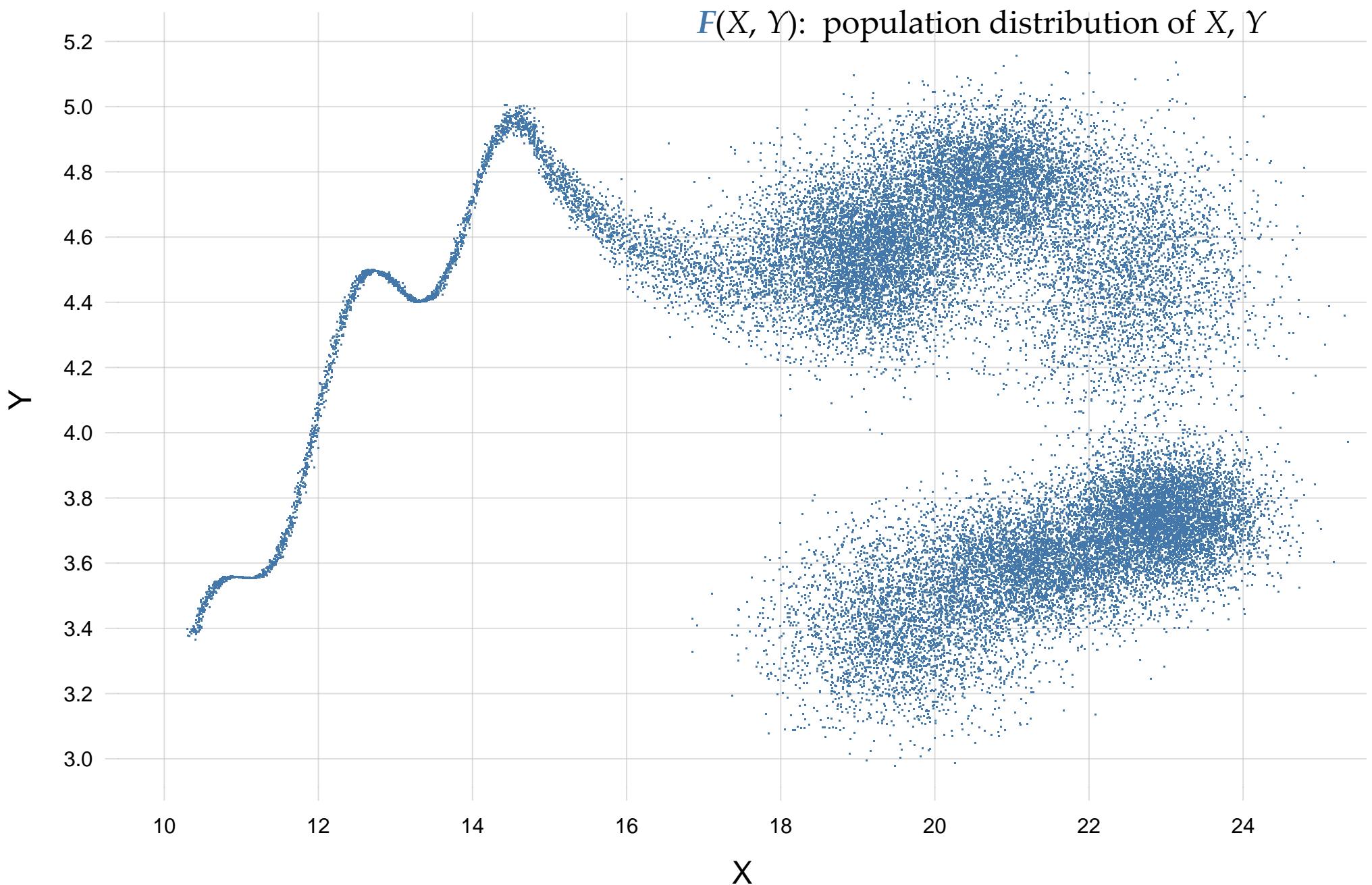




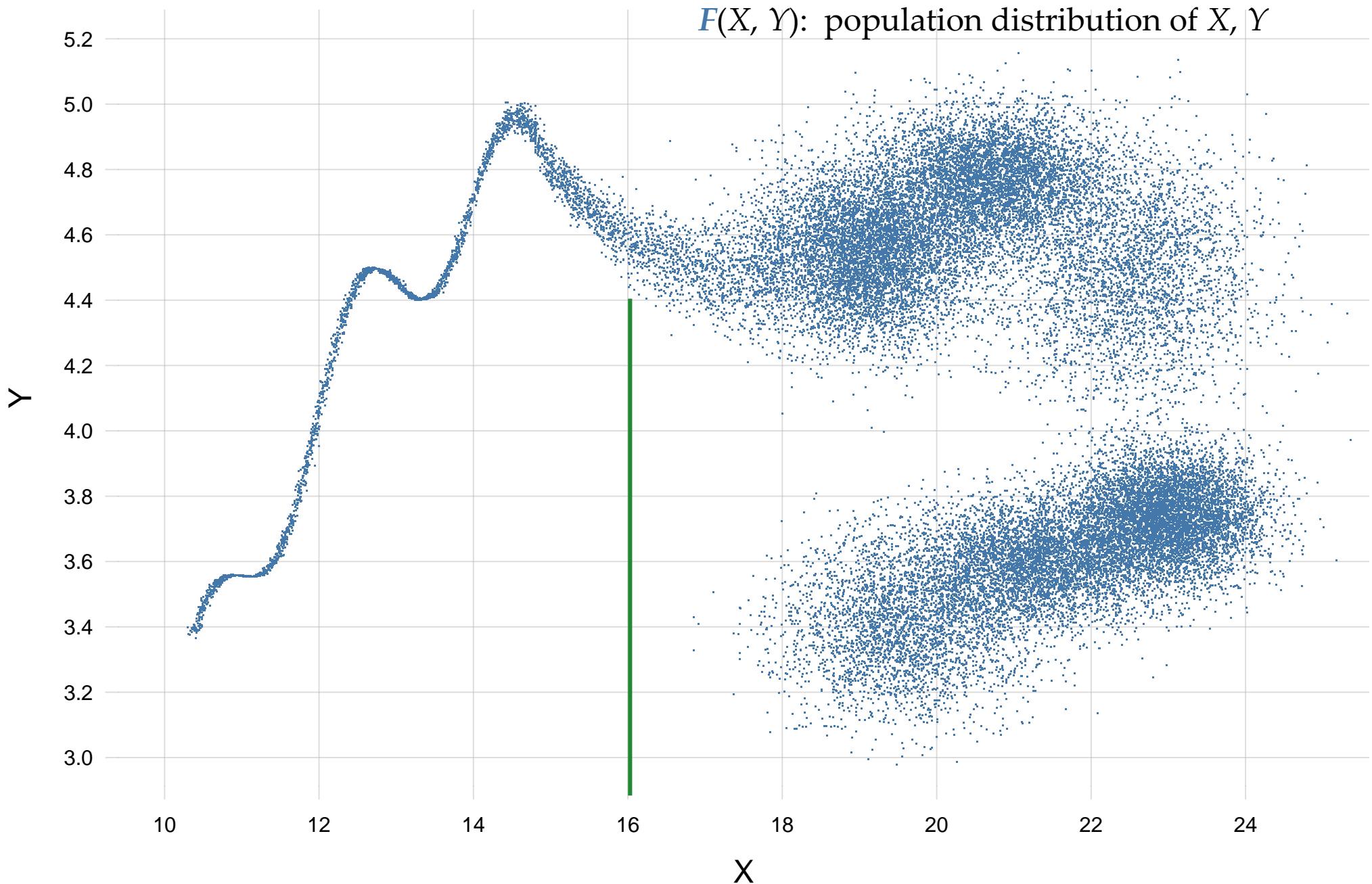
Plot X and Y for all past, present, future subjects



$F(X, Y)$: population distribution of X, Y



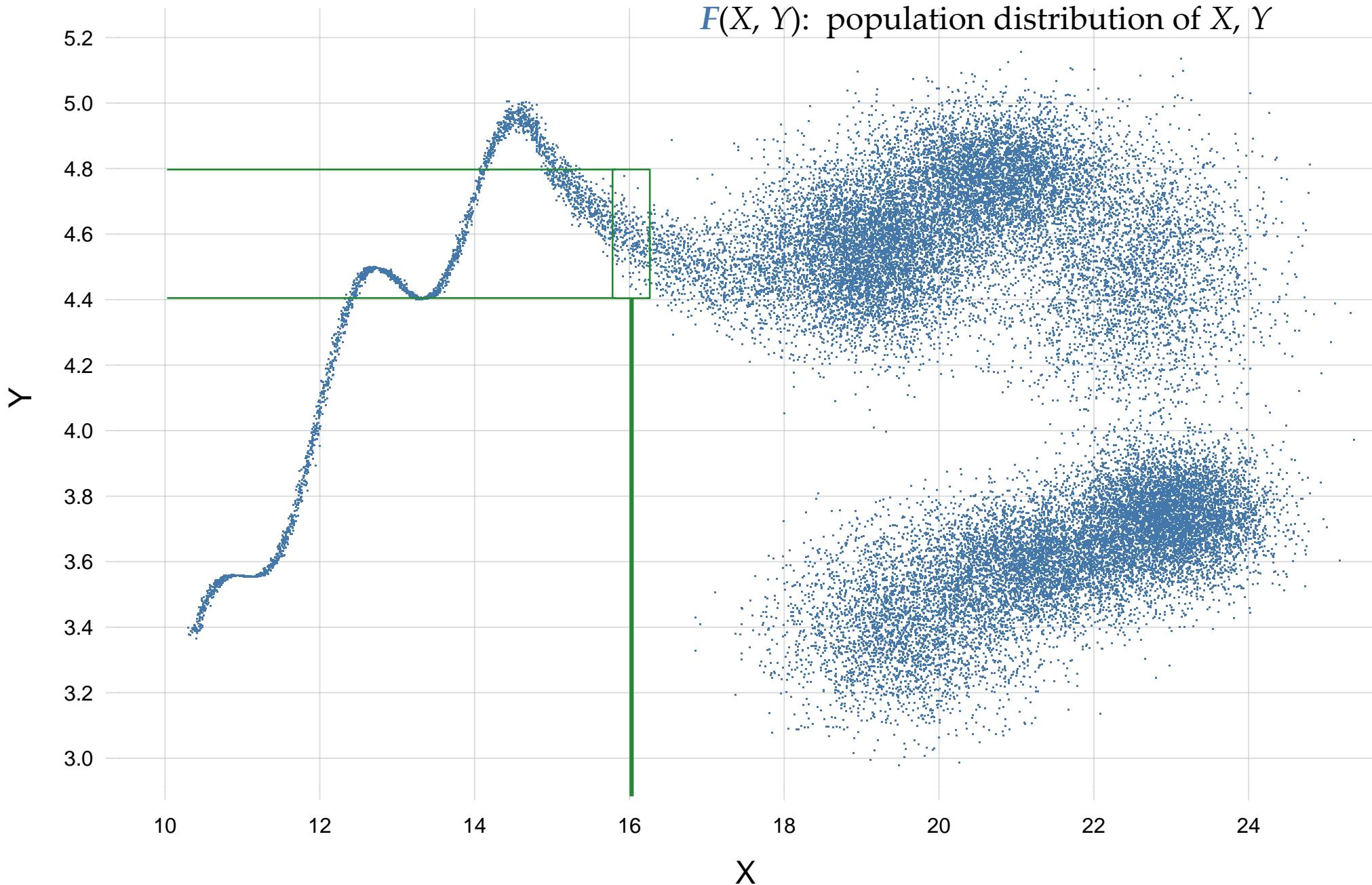
New patient: $X = 16$



New patient: $X = 16$

$\Rightarrow Y \approx 4.5\text{--}4.7$

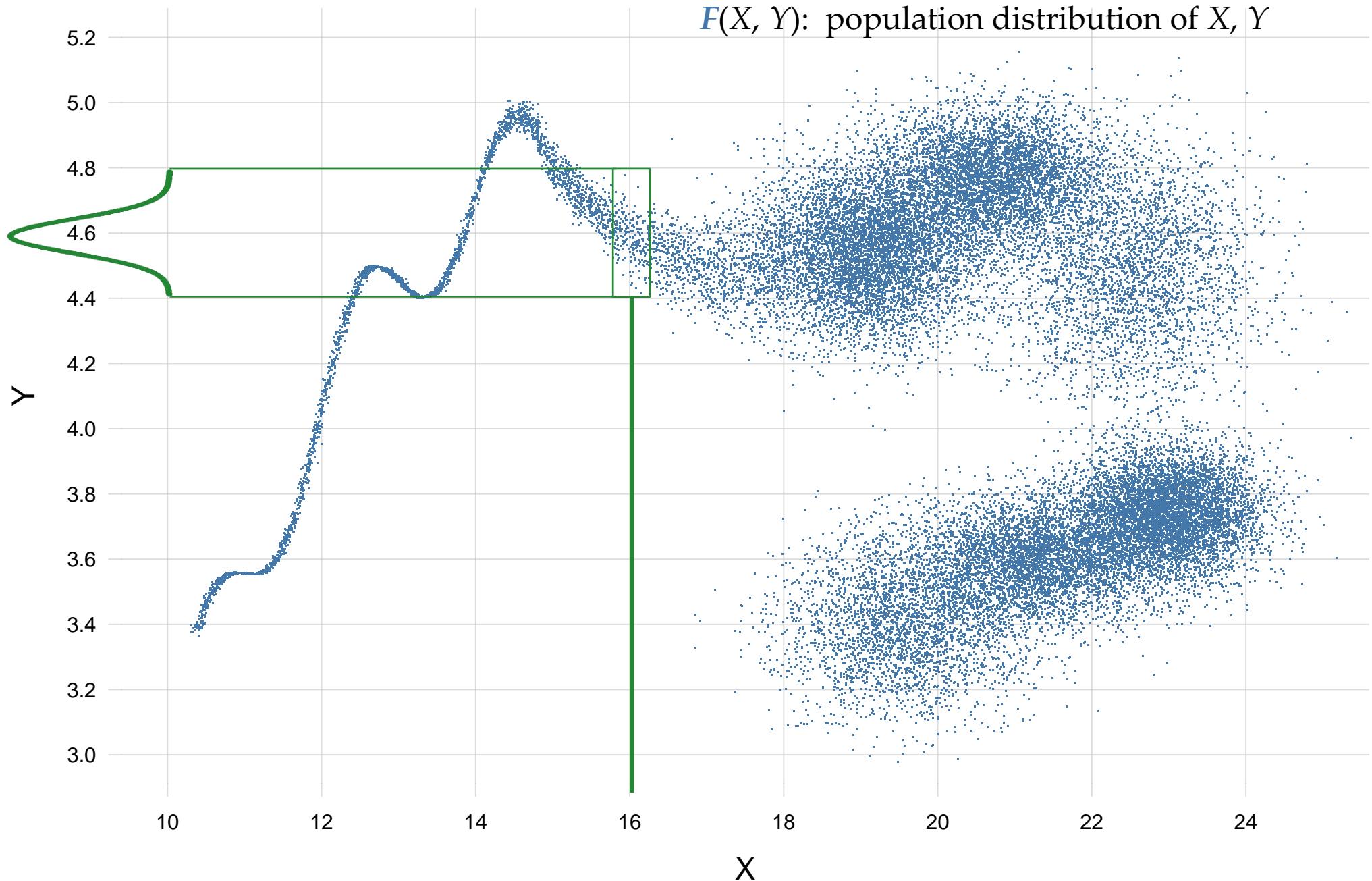
$F(X, Y)$: population distribution of X, Y



New patient: $X = 16$

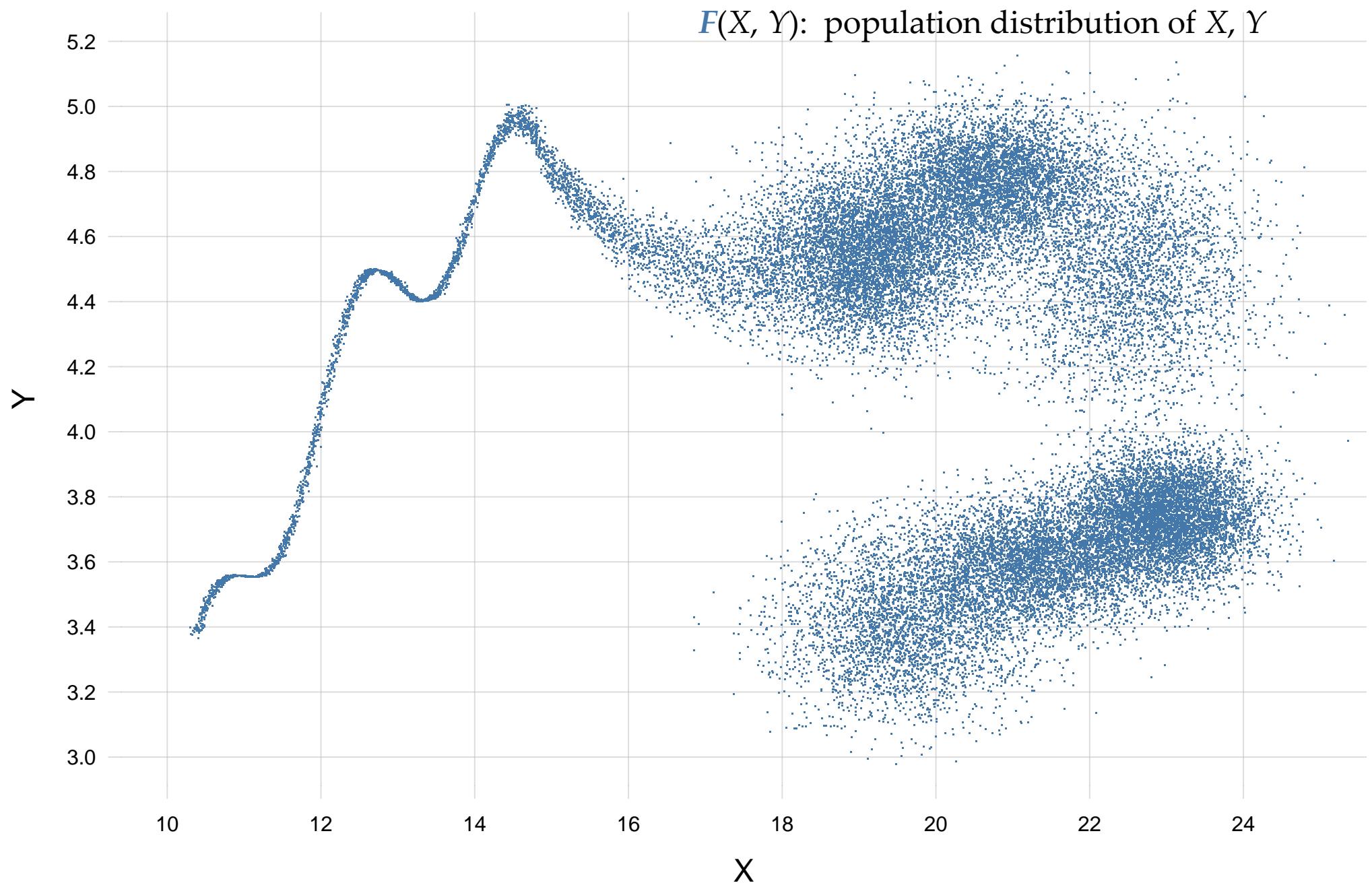
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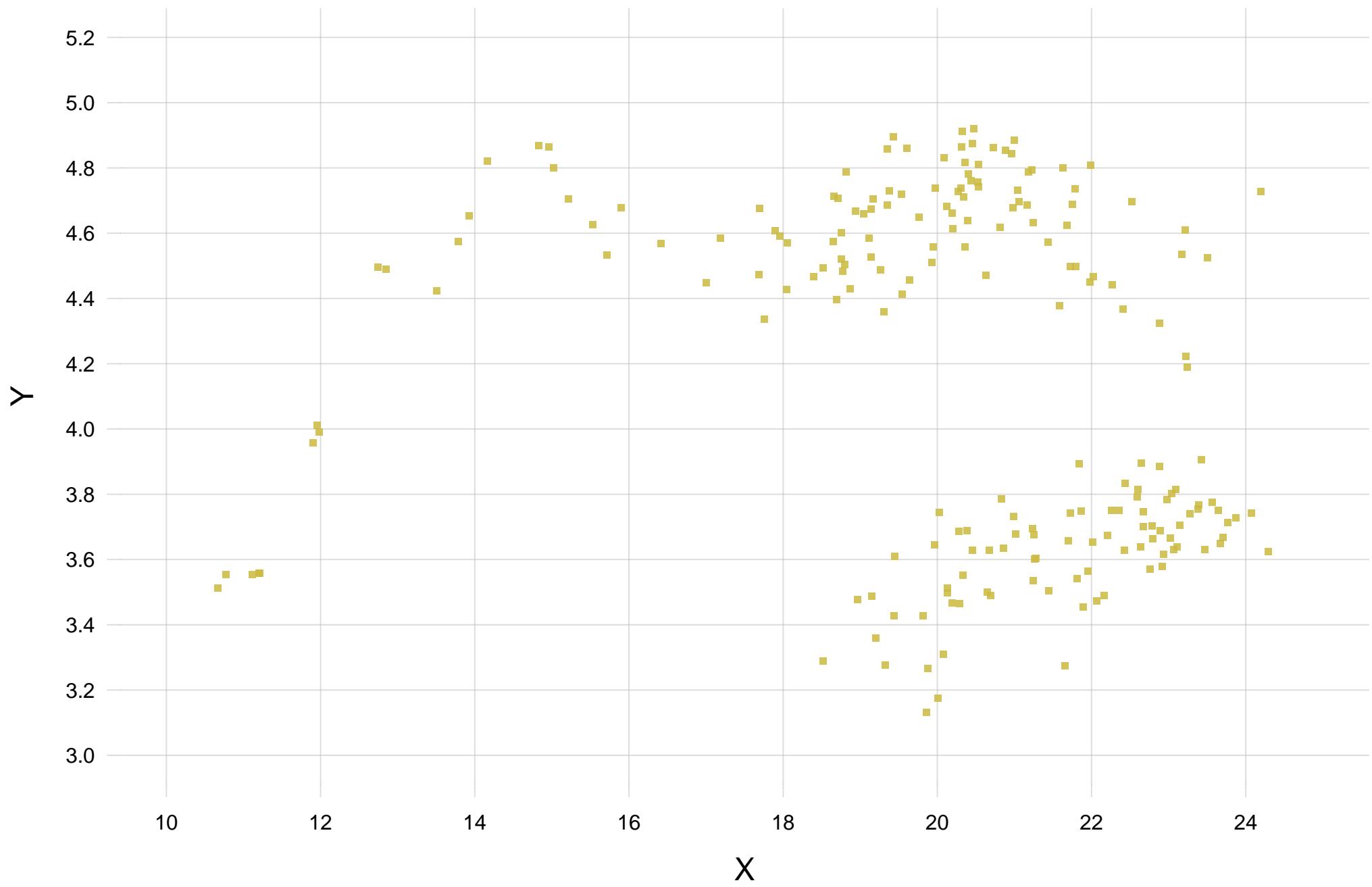
$F(X, Y)$: population distribution of X, Y



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

$F(X, Y)$: population distribution of X, Y





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

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

probability = average over all possible population distributions

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probability = average over all possible population distributions

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

how well the 'candidate' distribution fits the data

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probability = average over all possible population distributions

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

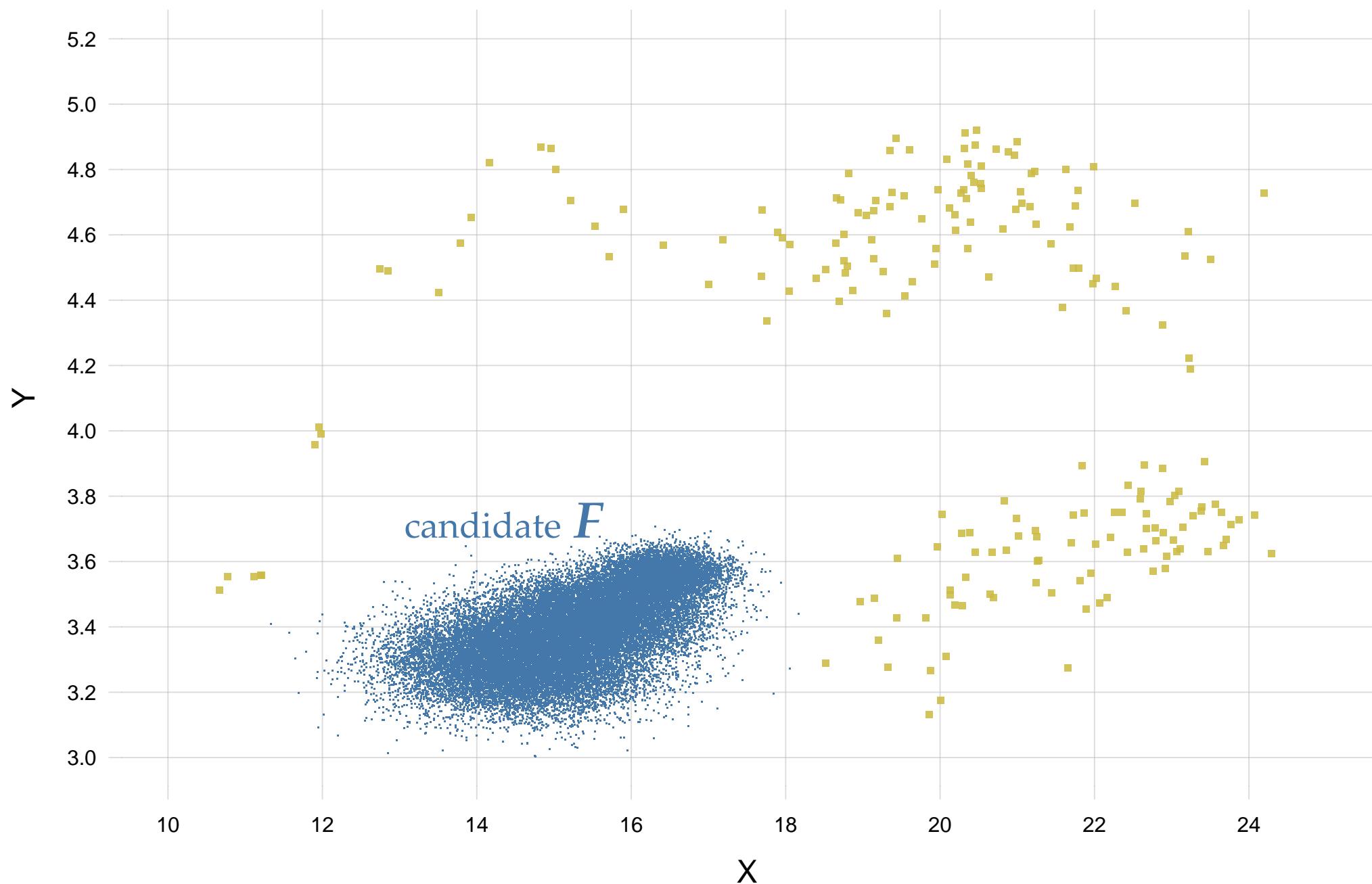
extra-data knowledge

poor candidate: doesn't fit the data

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

low

high

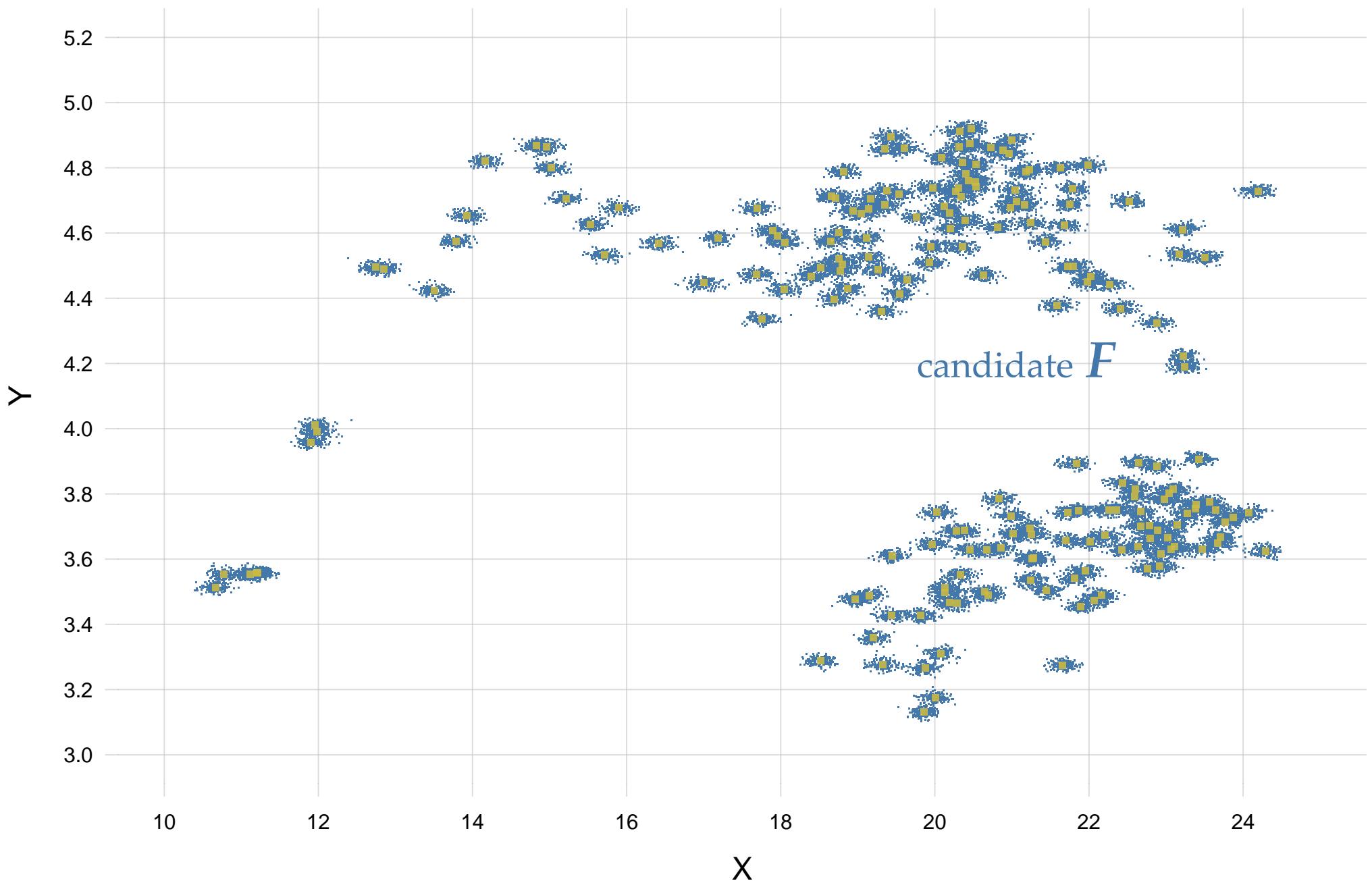


poor candidate: biologically implausible

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

high

low

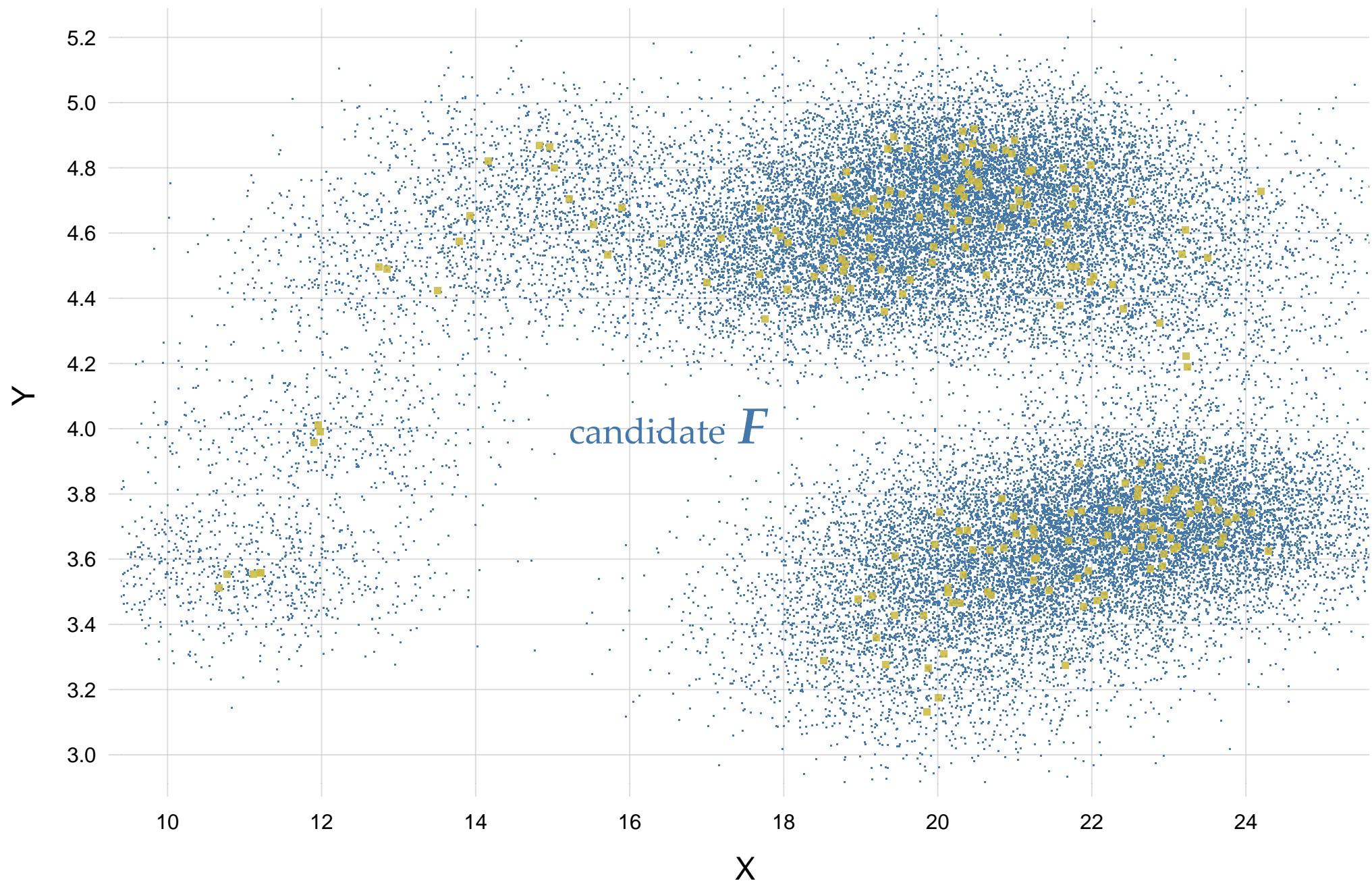


reasonable candidate

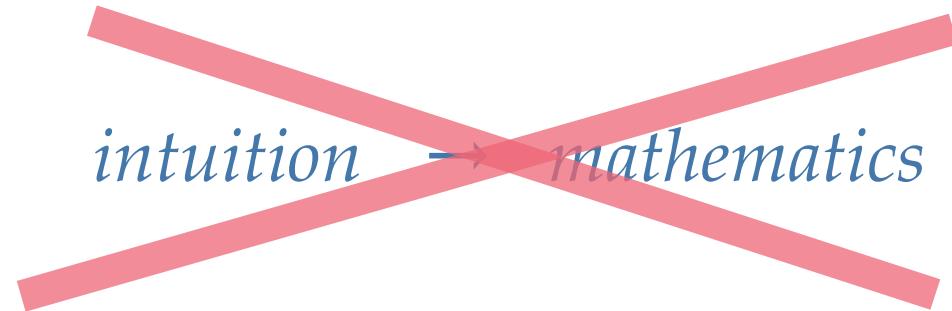
$F(y_1, x_1) \times F(y_2, x_2) \times F(y_3, x_3) \times \dots \times p(F \mid \text{prior info})$

high

high

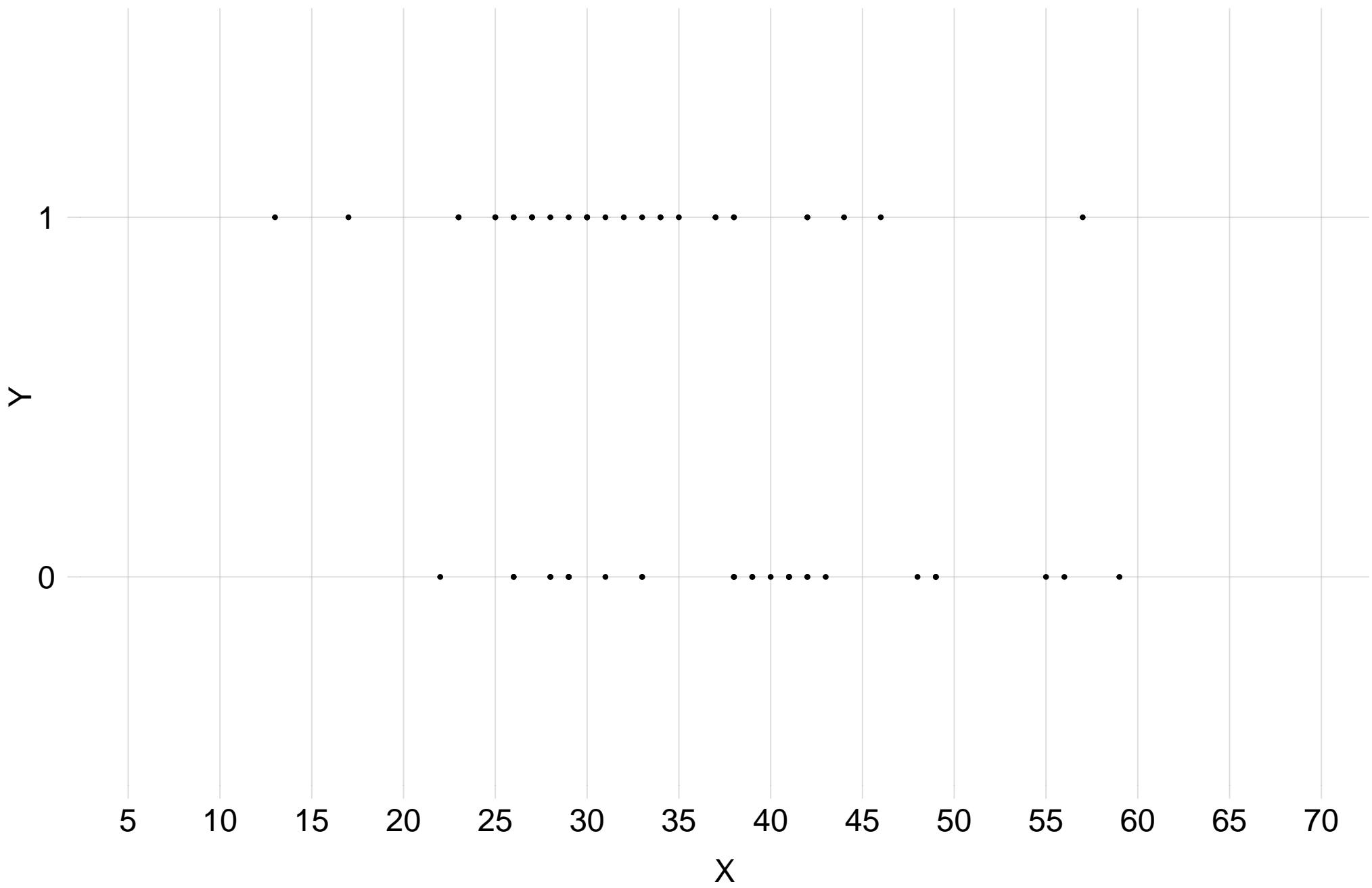


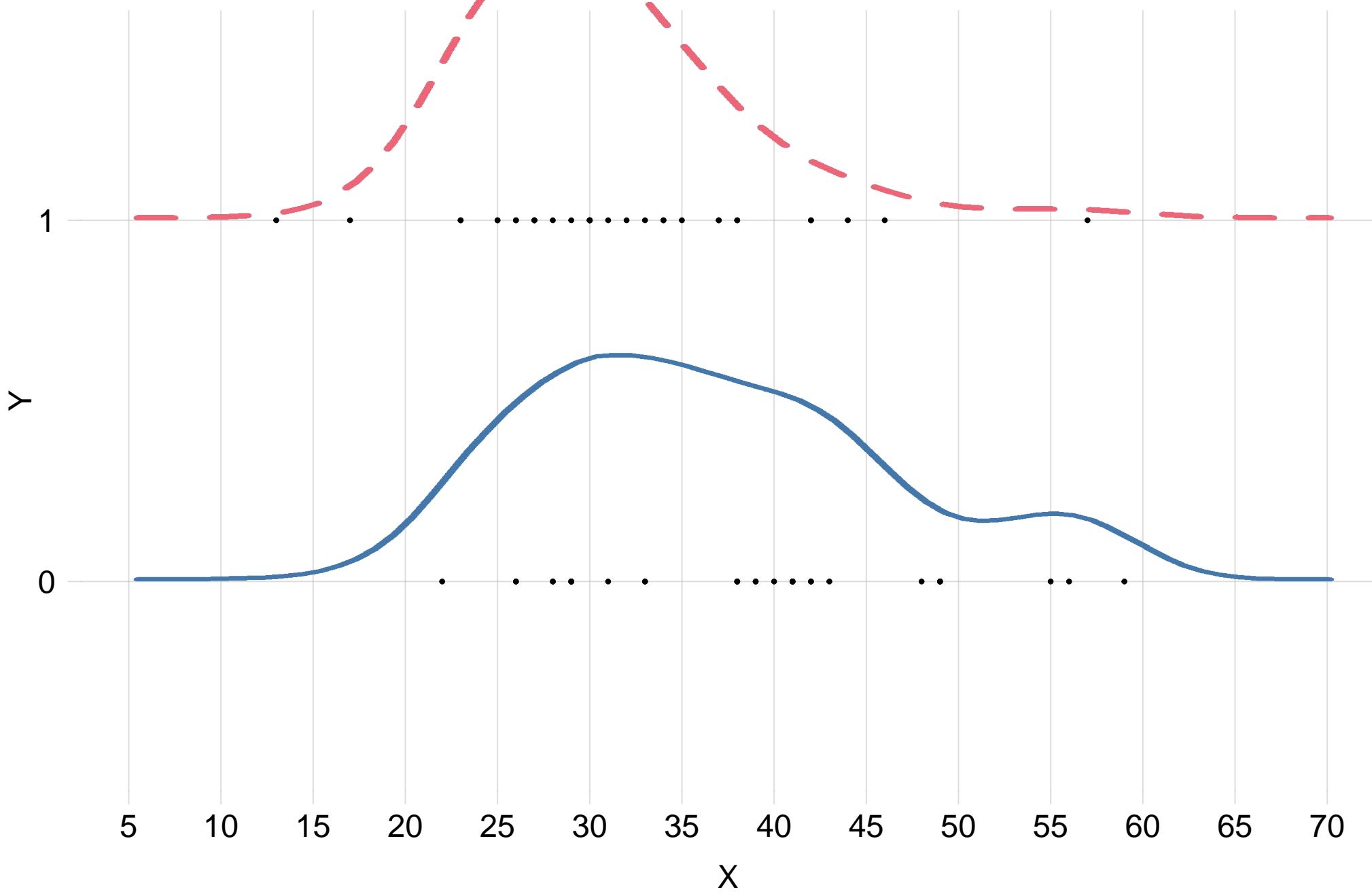
intuition → *mathematics*

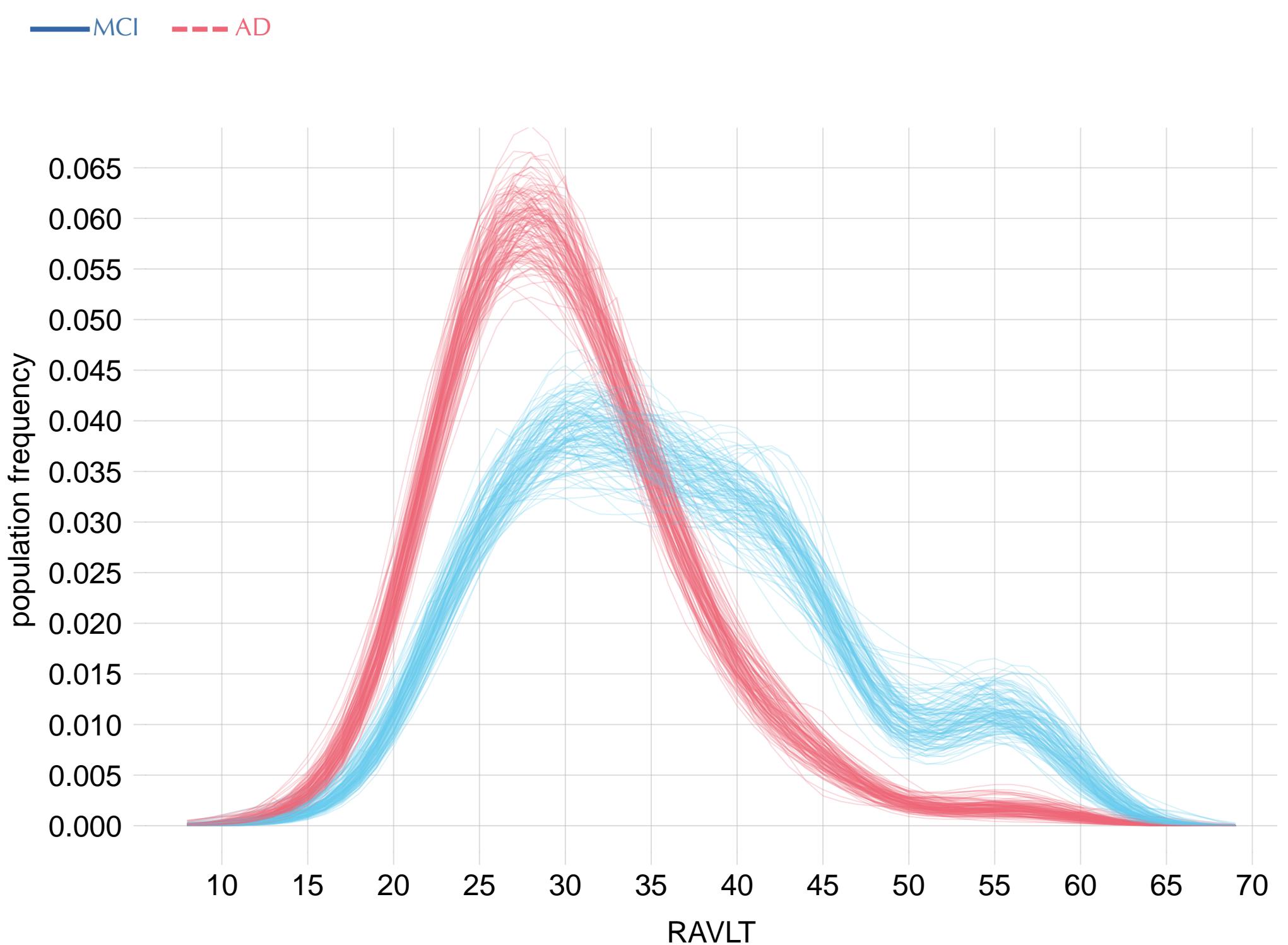


first principles → *mathematics* → *intuition*

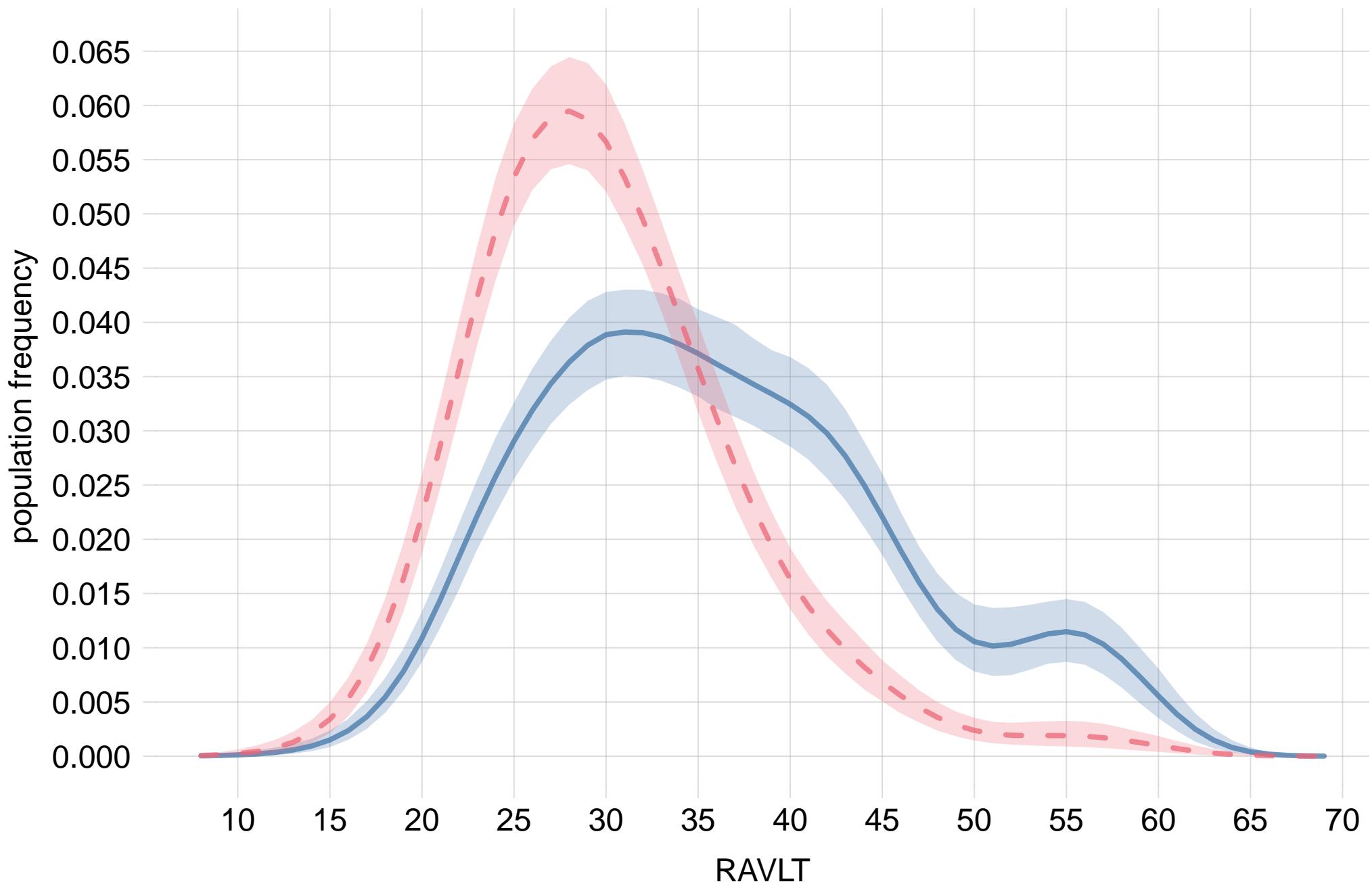
(‘*Bayesian*’)







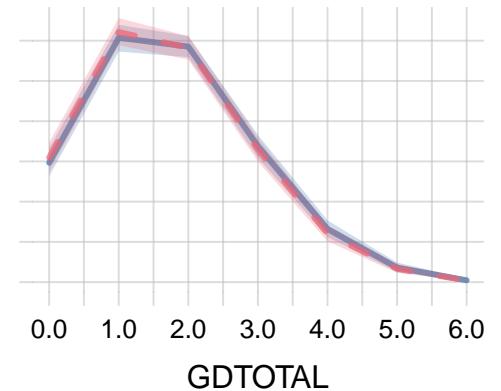
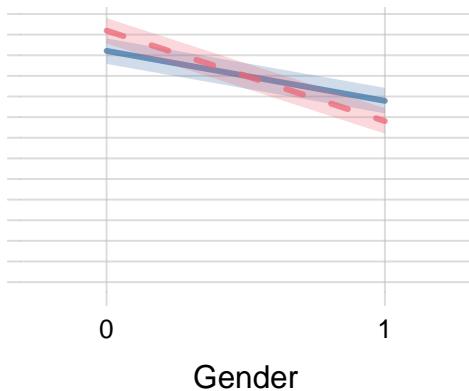
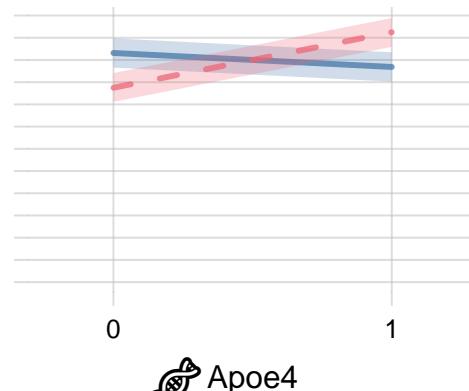
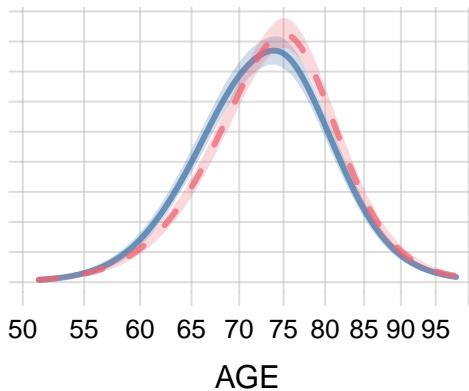
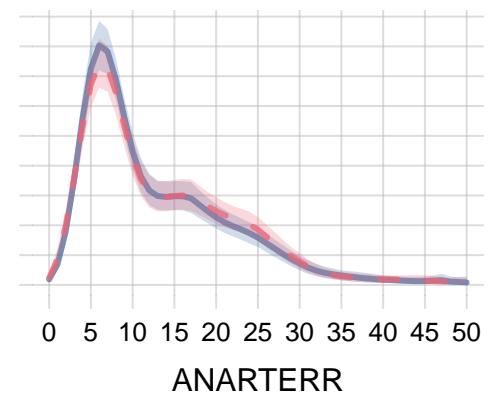
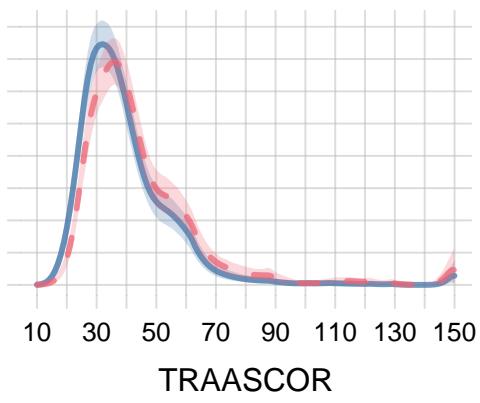
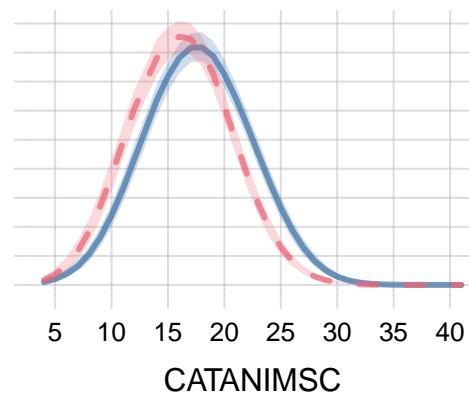
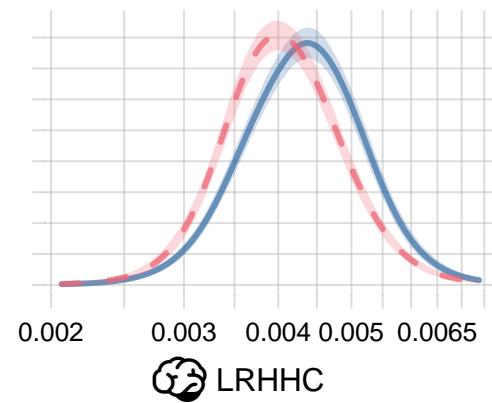
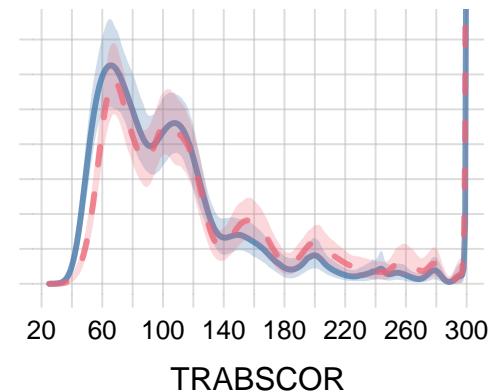
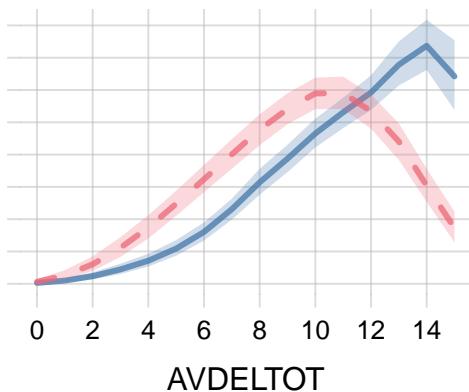
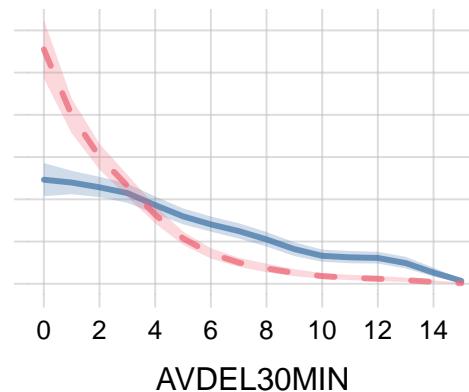
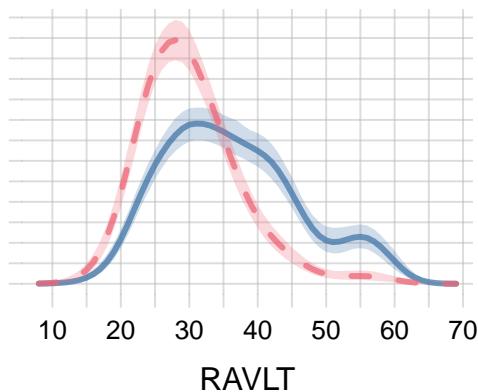
— MCI - - AD ■ 87.5% credible interval



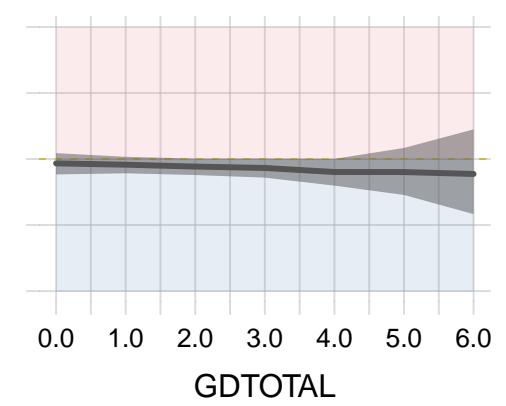
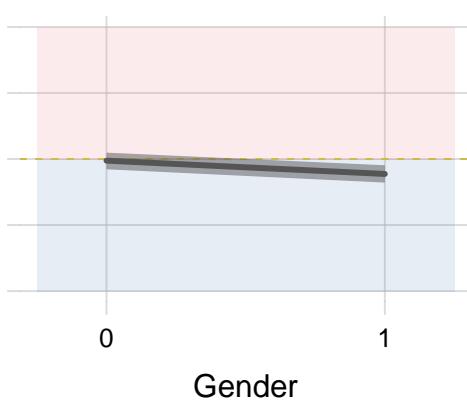
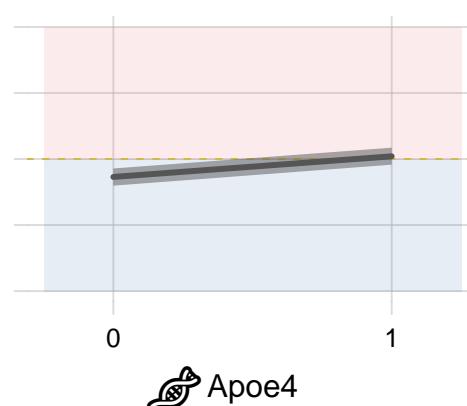
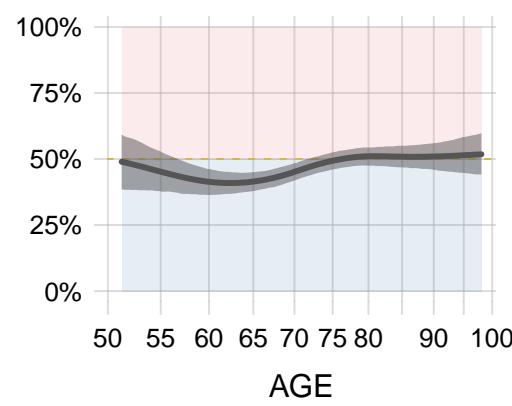
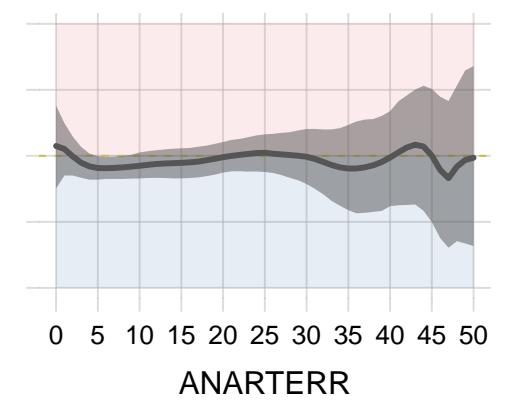
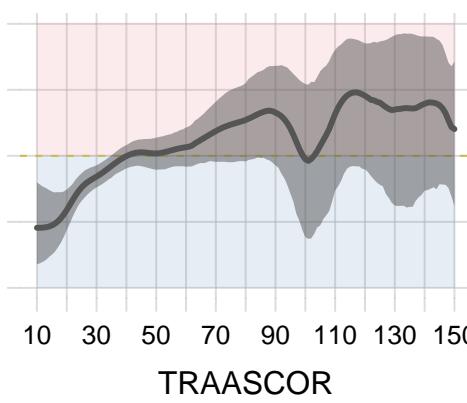
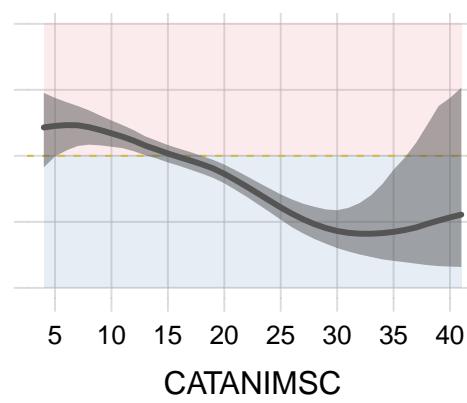
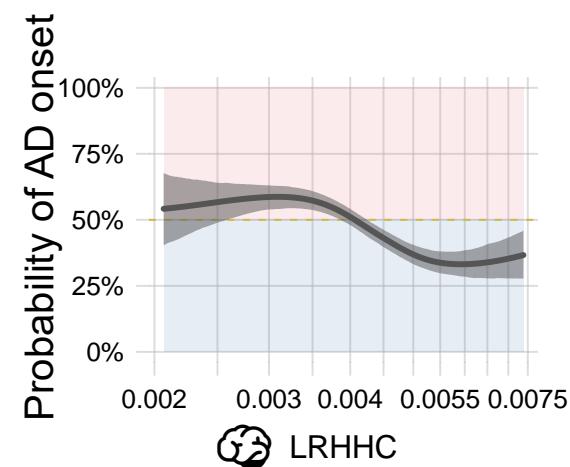
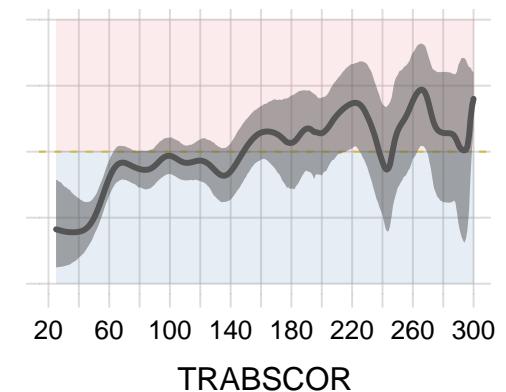
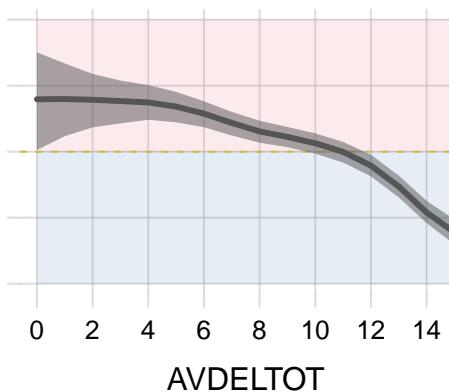
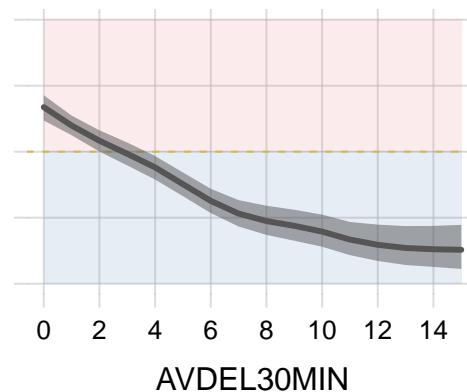
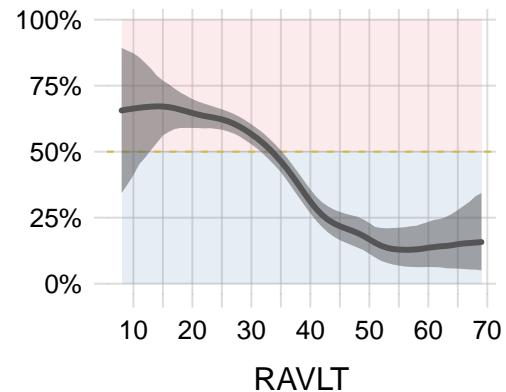
MCI

AD

87.5% credible interval



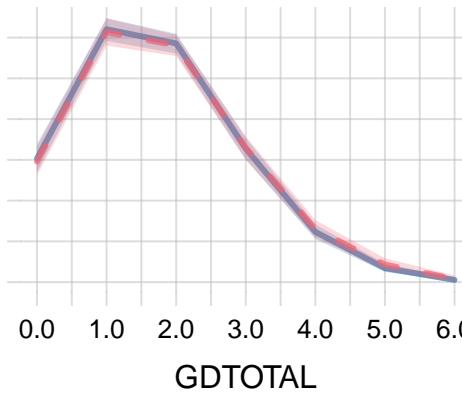
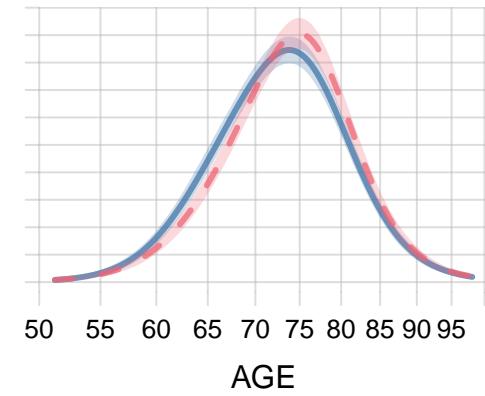
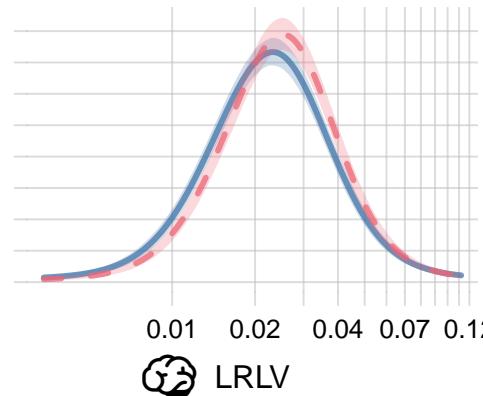
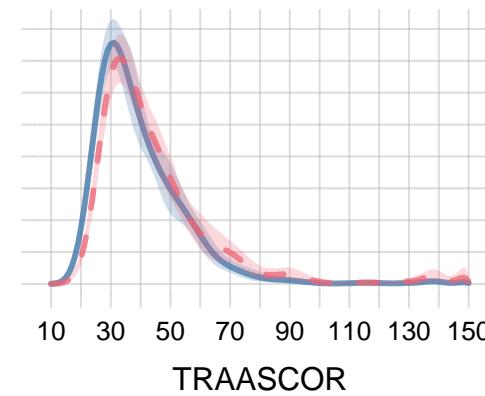
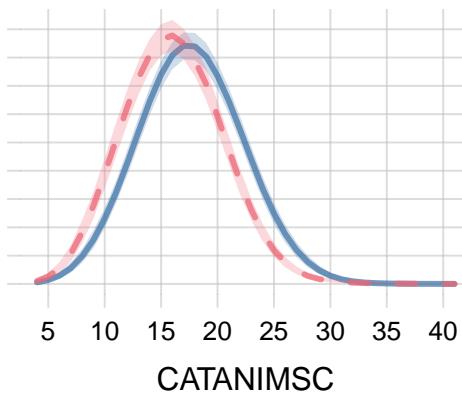
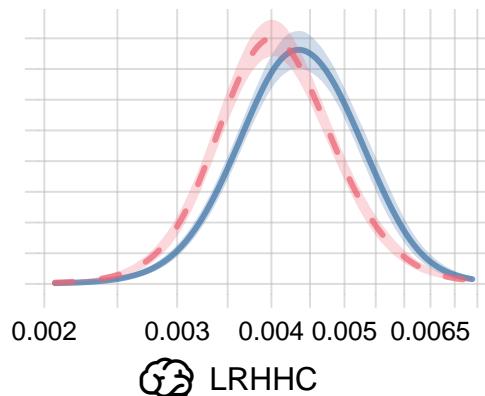
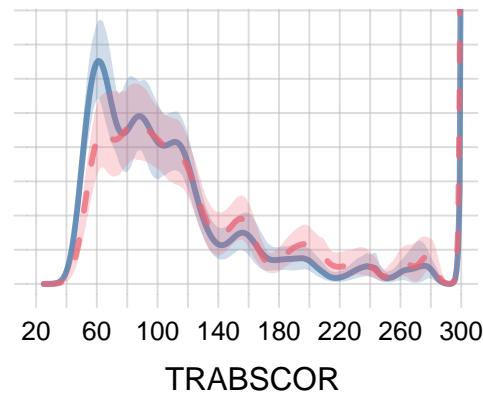
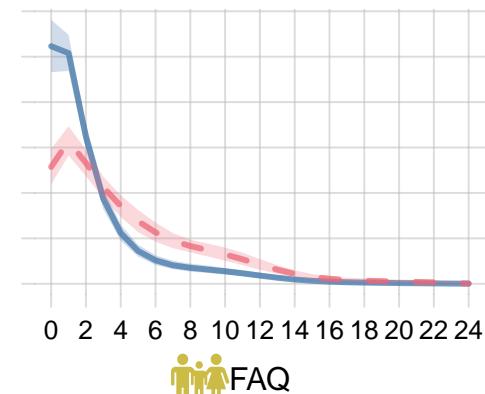
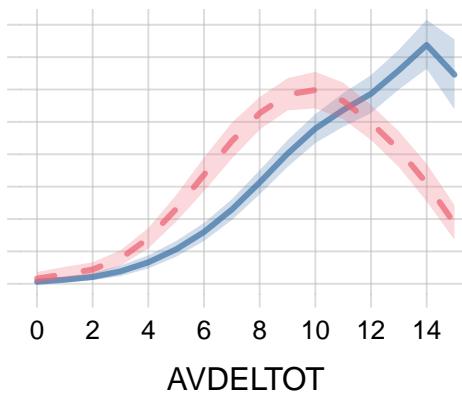
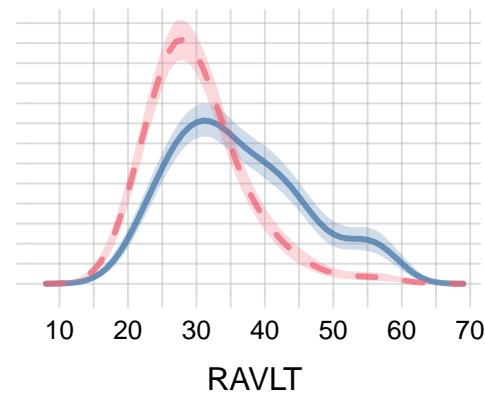
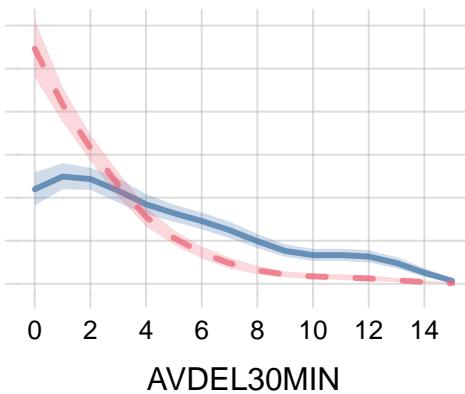
87.5% credible interval



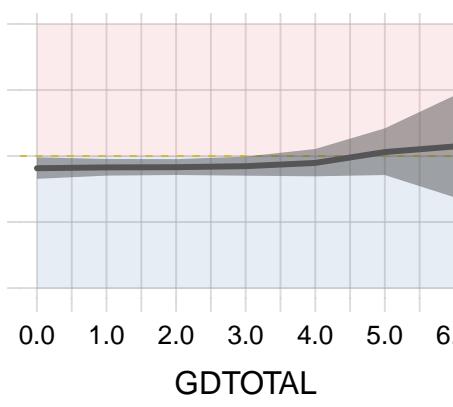
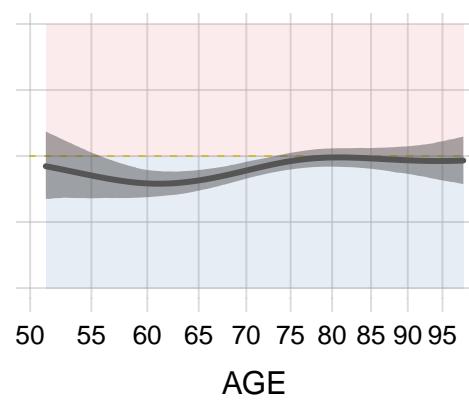
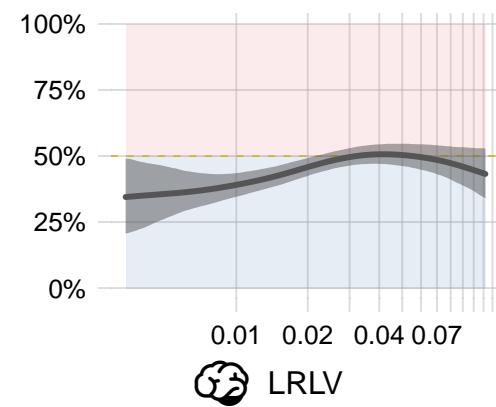
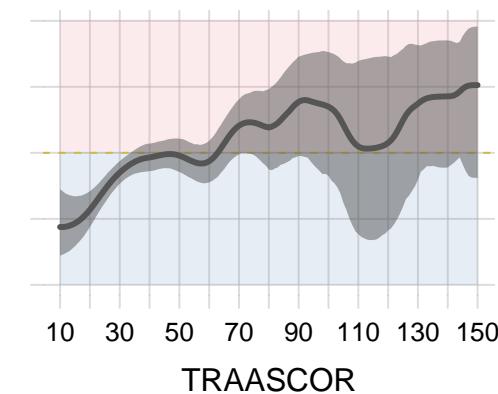
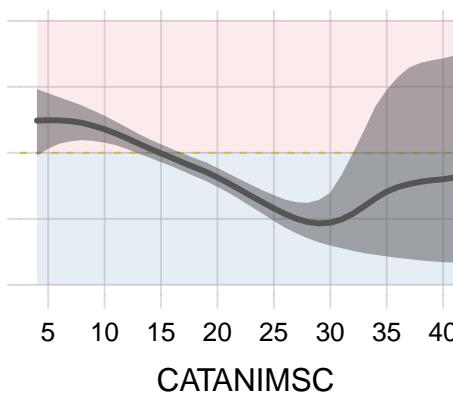
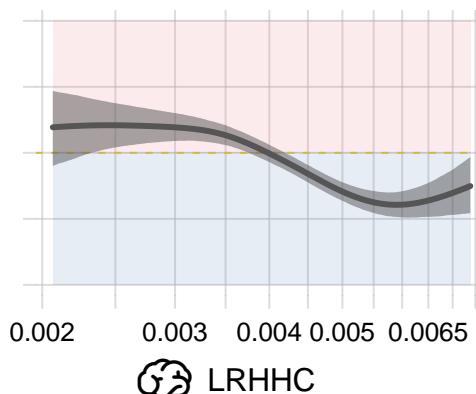
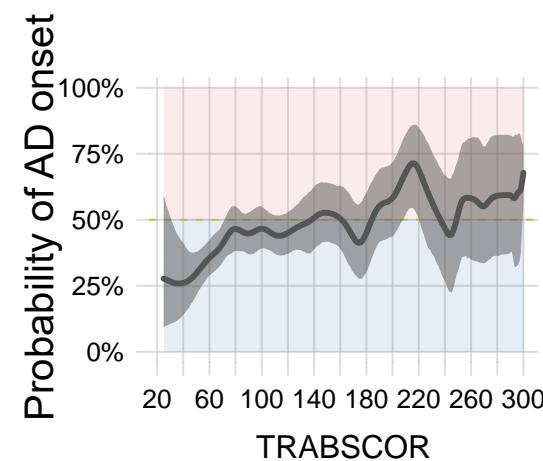
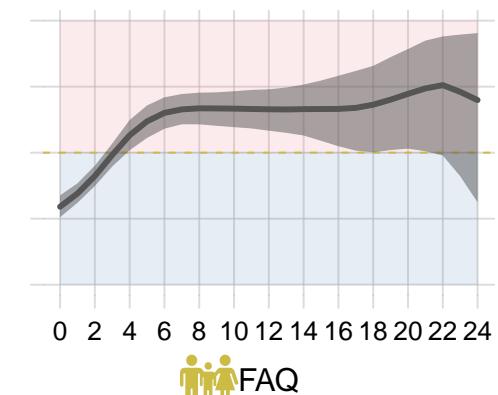
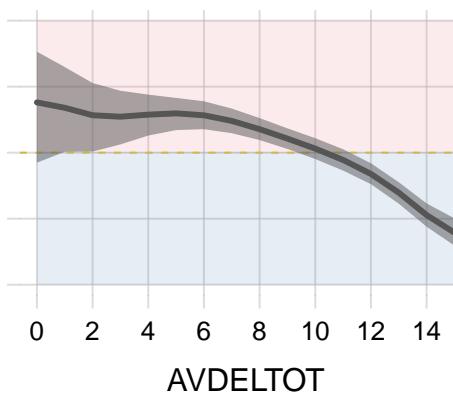
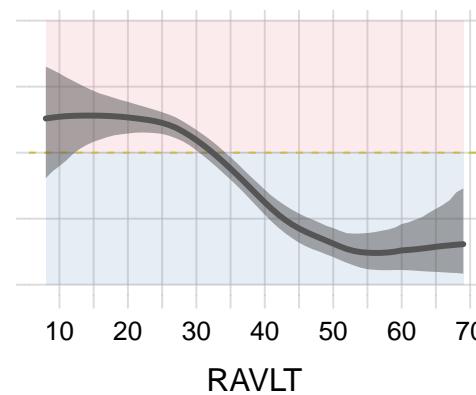
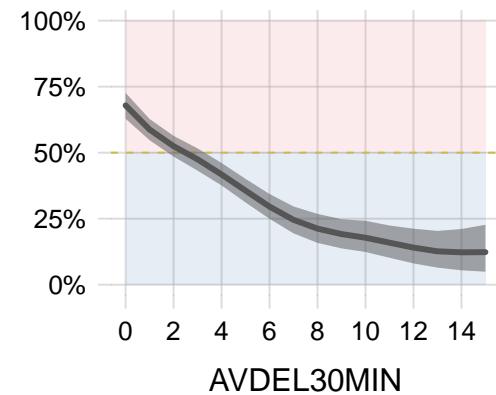
MCI

AD

87.5% credible interval



87.5% credible interval



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'

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’
- ‘0 + 0 ≠ 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: ???✓✓✓

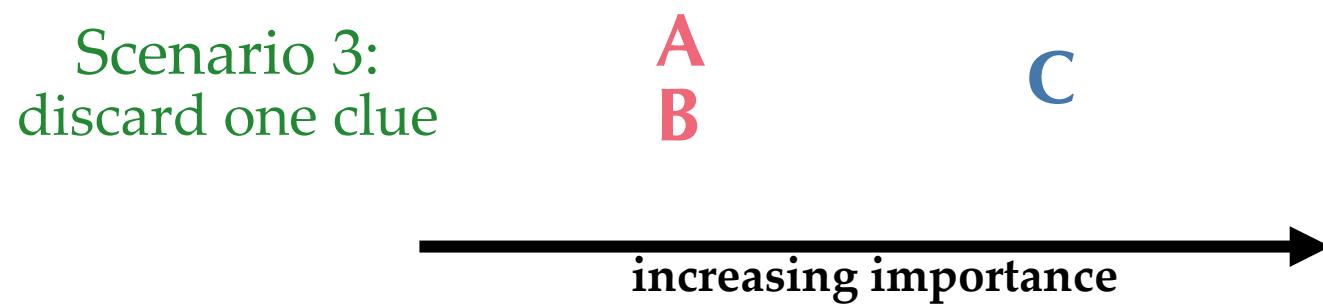
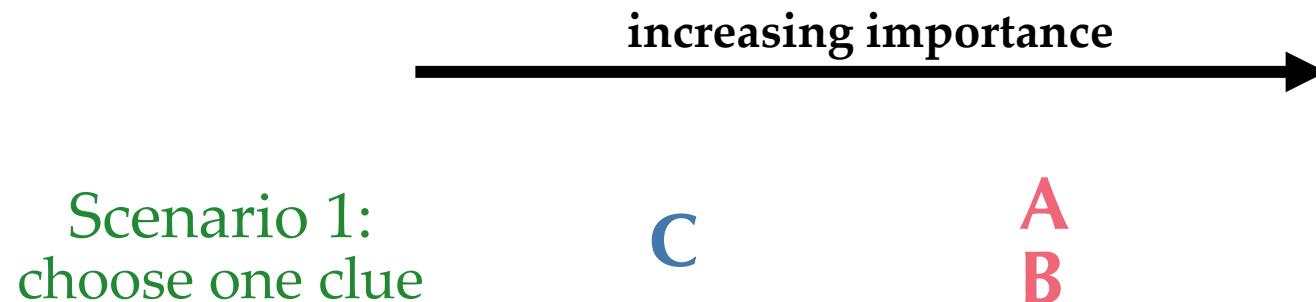


discard A: still 100% win

discard B: still 100% win

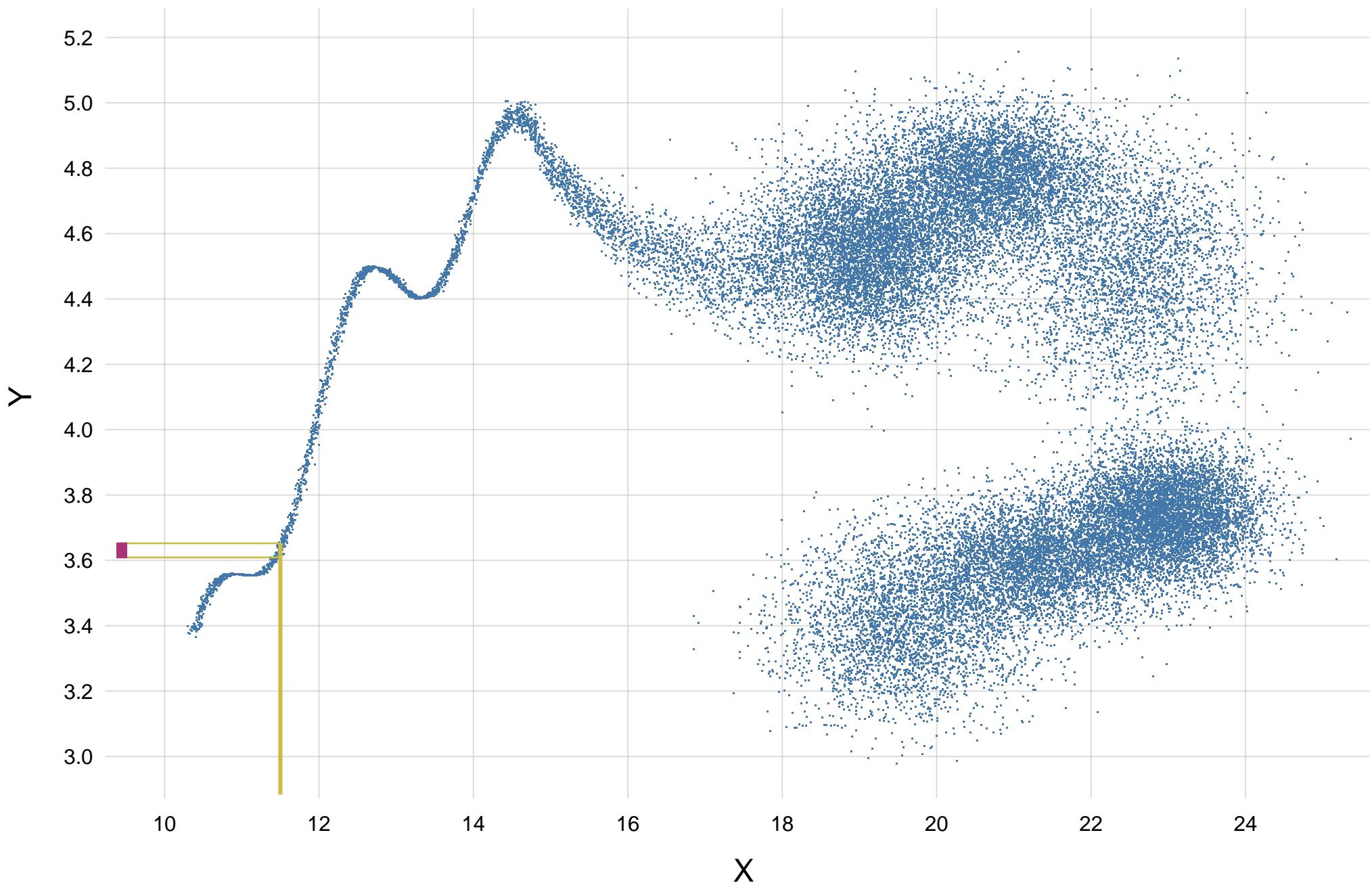
discard C: 1/9 winning chance

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

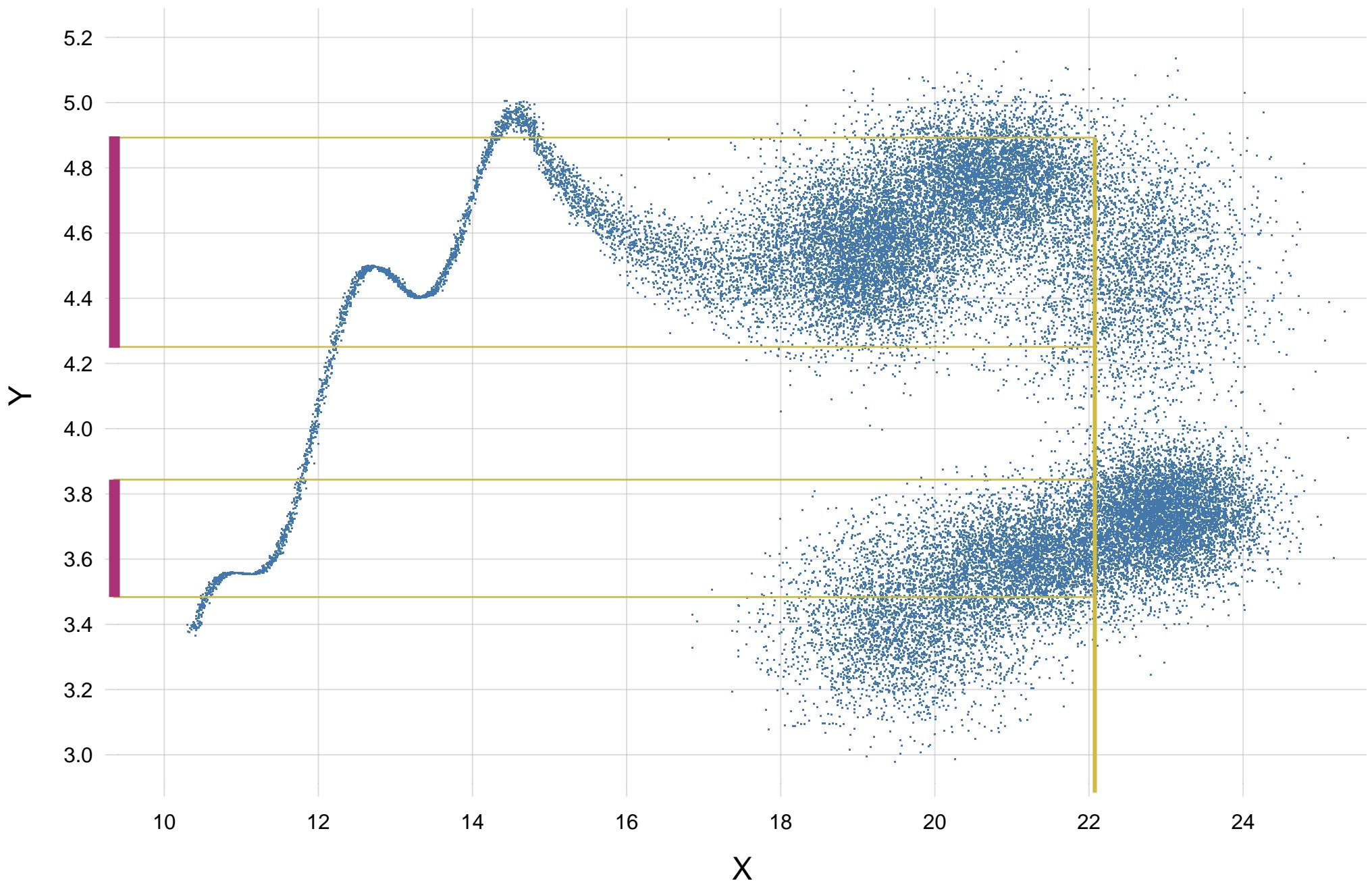


‘Importance’ or ‘predictive power’ of X is *context-dependent*
(which other features are we considering?)

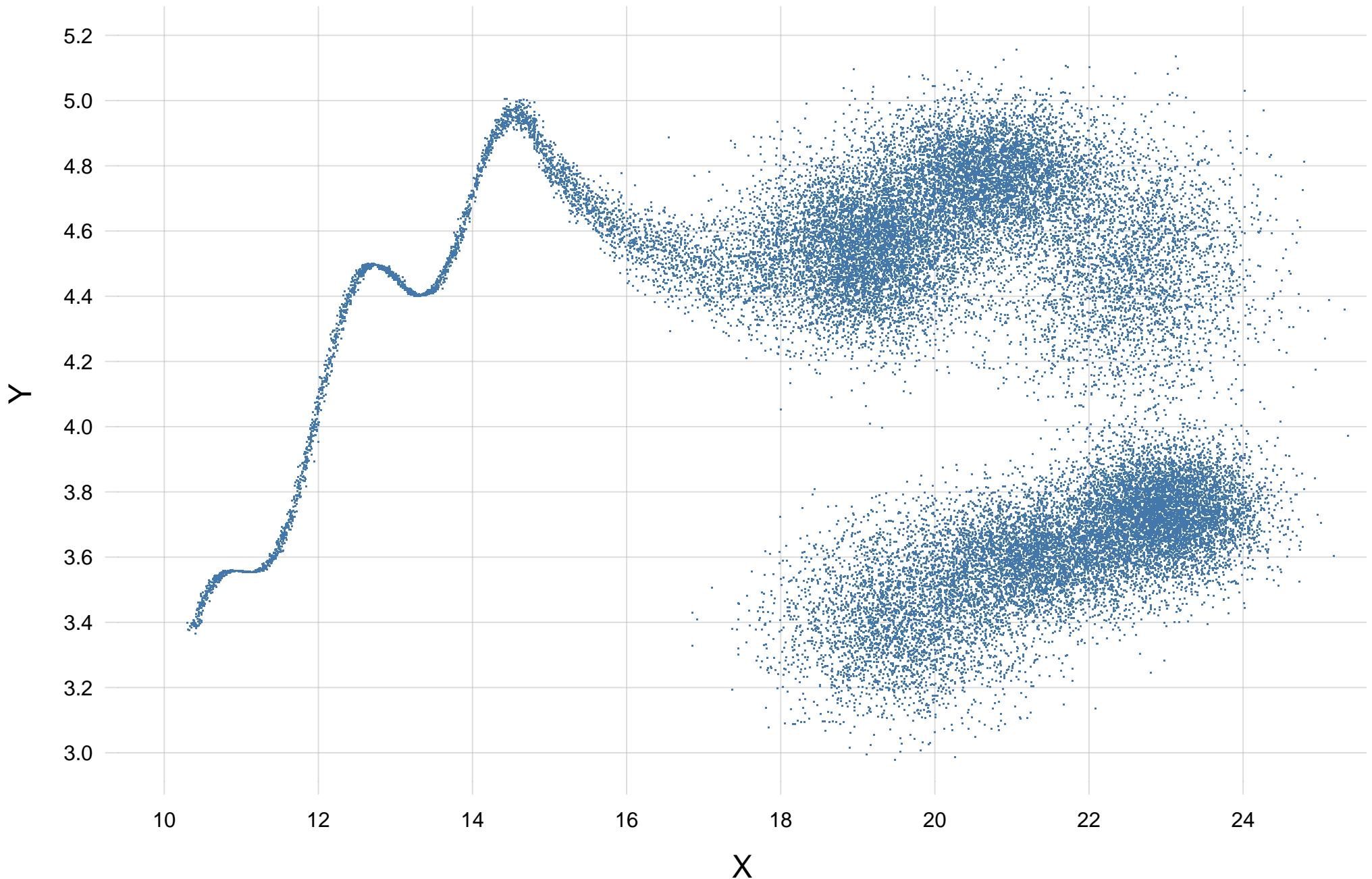
$$x = 11.5 \Rightarrow y \approx 3.60-3.65$$

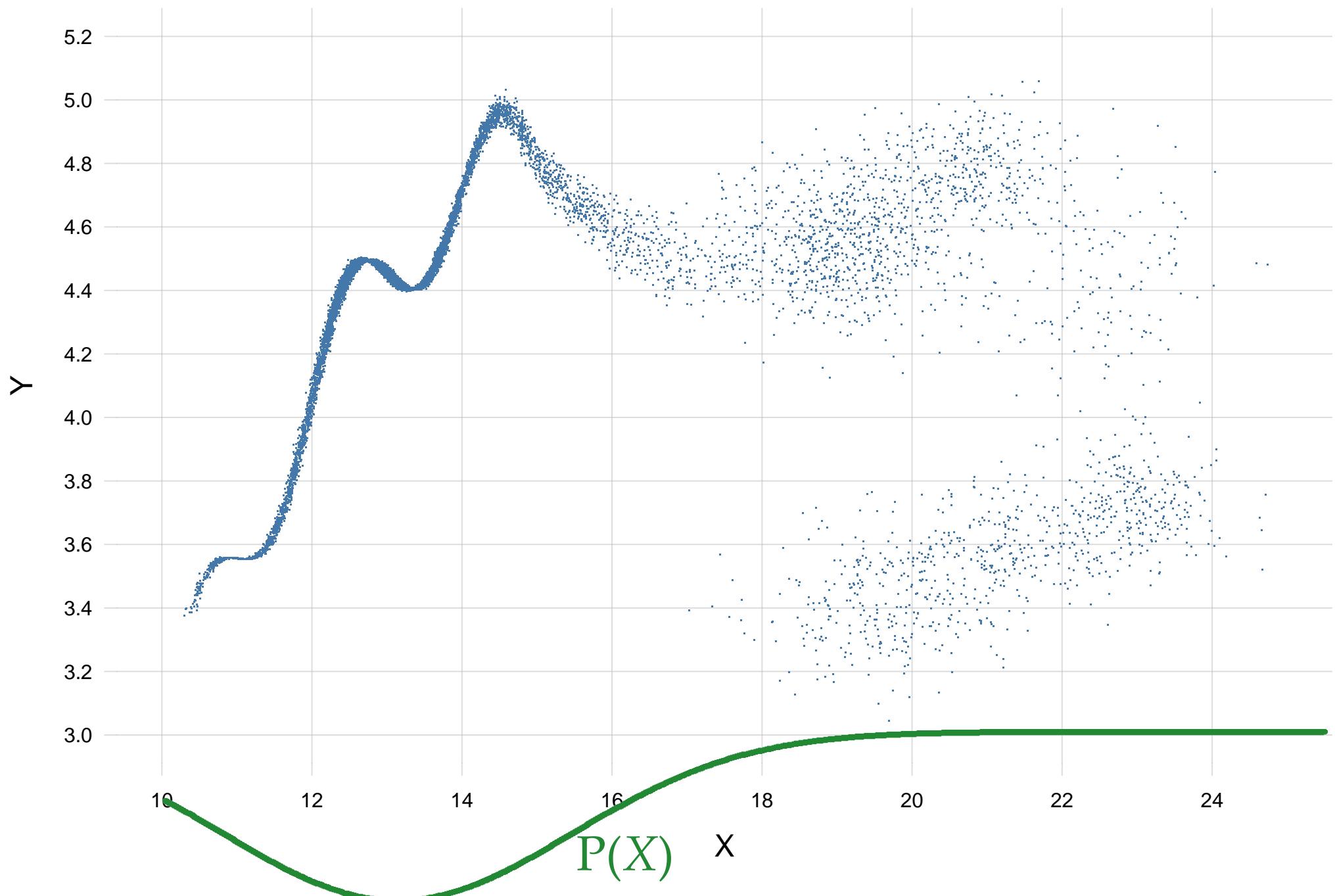


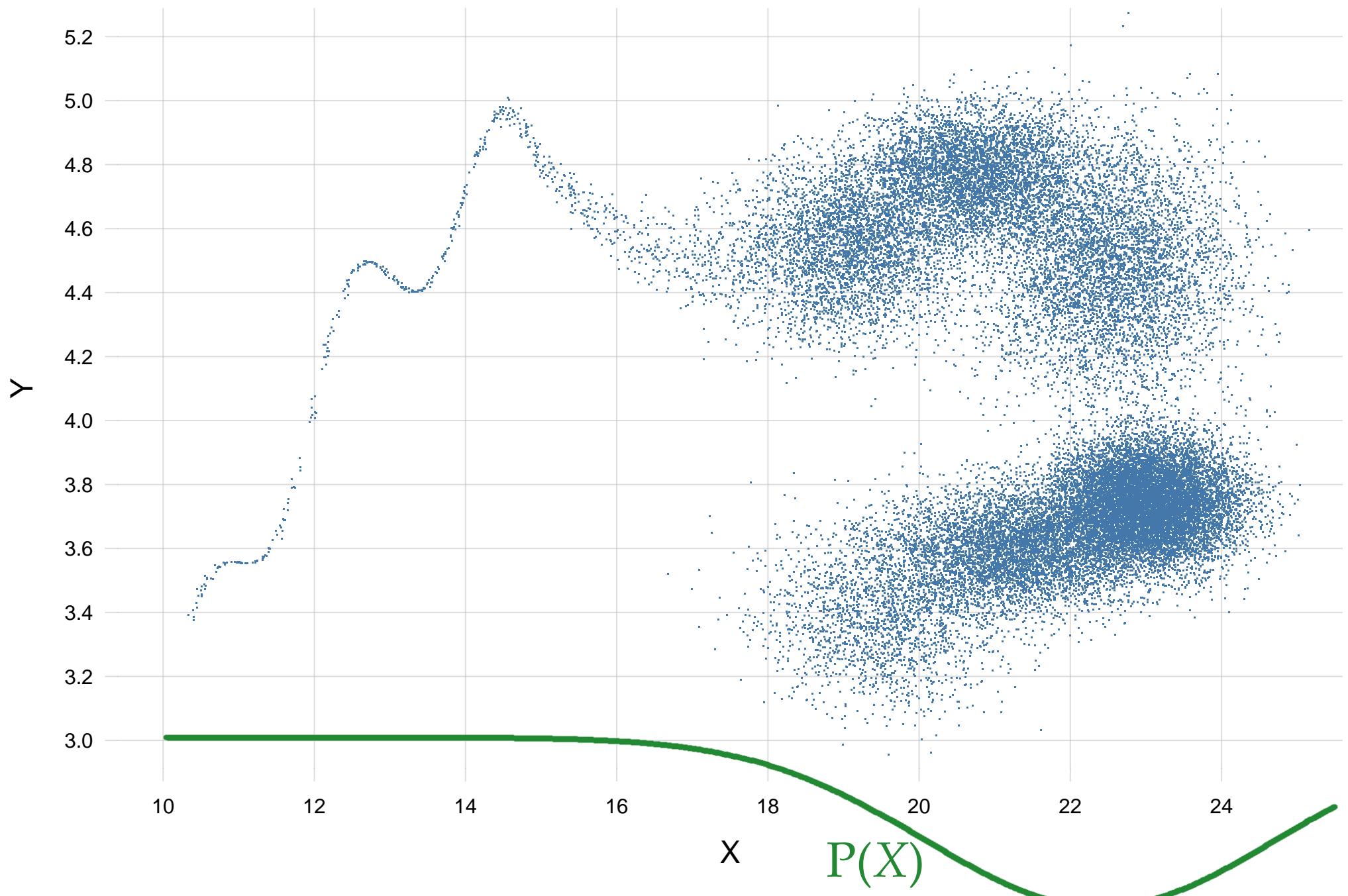
$x = 22 \Rightarrow y \approx 3.50\text{--}3.85$ or $4.25\text{--}4.90$



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’! ⚠

Information Theory

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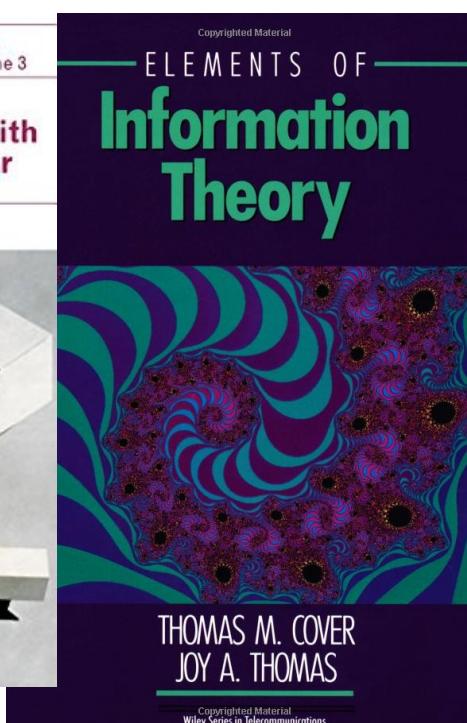
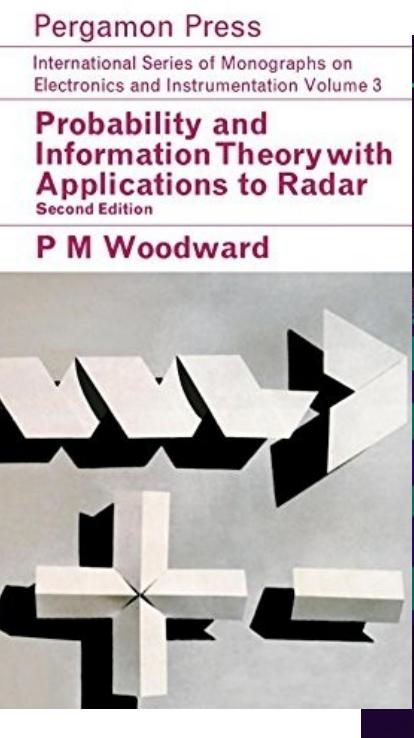
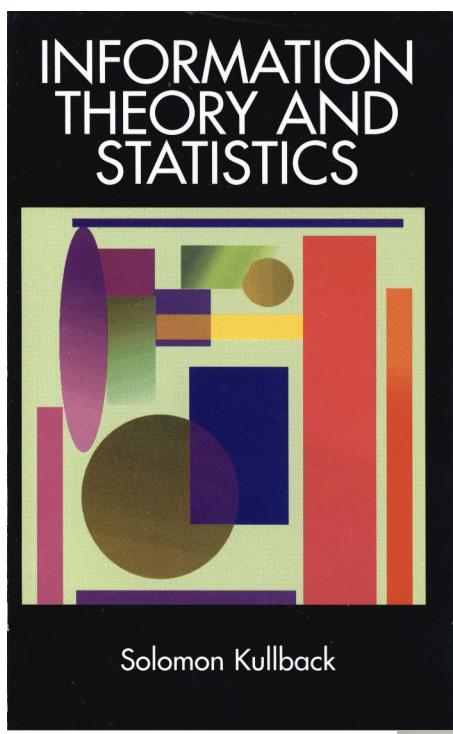
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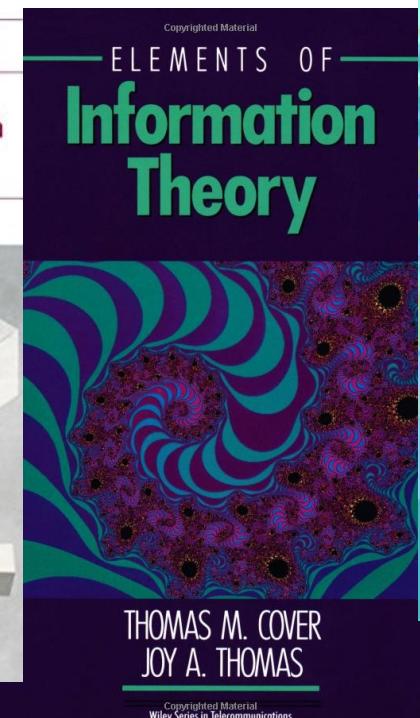
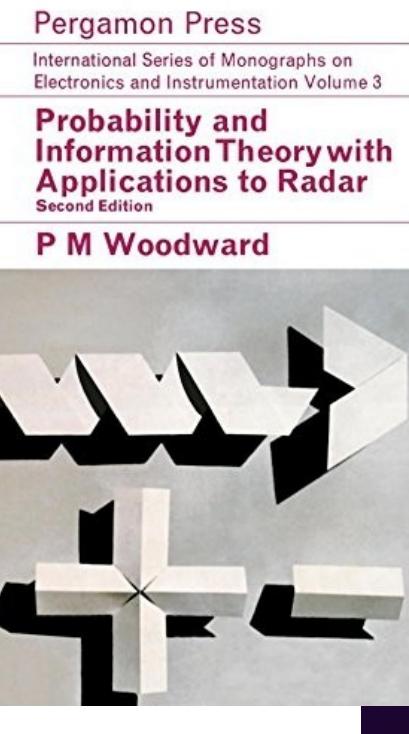
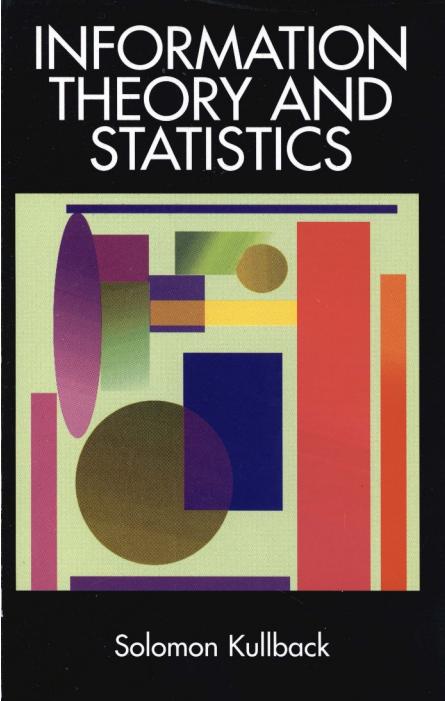
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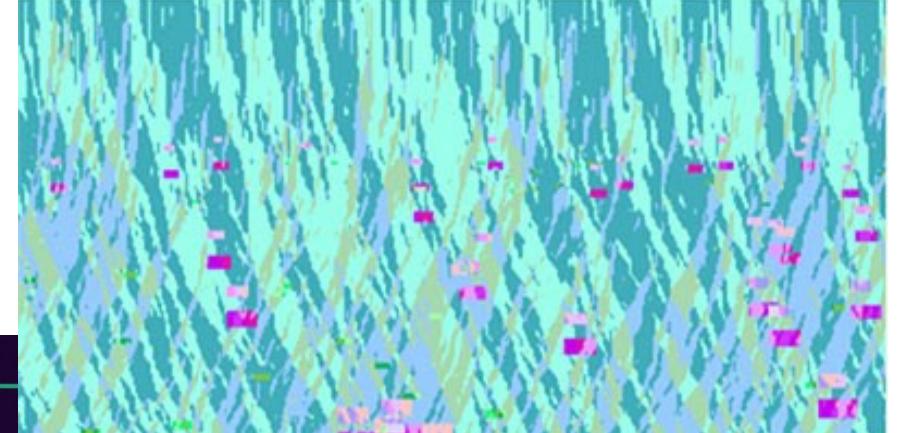


David J.C. MacKay

Information Theory, Inference, and Learning Algorithms

<https://www.inference.org.uk/itila/book.html>

<https://youtube.com/playlist?list=PLruBu5BI5n4aFpG32iMbdWoRVAA-Vcs06>



Cambridge University Press, 2003

'predictive power' of X for Y := **Mutual information** between Y and X
(mean transinformation content)

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

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

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

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

INTERNATIONAL STANDARD

NORME INTERNATIONALE

**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 quantité (f) d'information</i>	$I(x)$	$I(x) = \text{lb} \frac{1}{p(x)} \text{ Sh} = \lg \frac{1}{p(x)} \text{ Hart} =$ $\ln \frac{1}{p(x)} \text{ nat}$ <p>where $p(x)$ is the probability of event x</p>	See ISO/IEC 2382-16, item 16.03.02. See also IEC 60027-3.
13-25 (903)	entropy <i>fr entropie (f)</i>	H	$H(X) = \sum_{i=1}^n p(x_i)I(x_i)$ <p>for the set $X = \{x_1, \dots, x_n\}$ where $p(x_i)$ is the probability and $I(x_i)$ is the information content of event x_i</p>	See ISO/IEC 2382-16, item 16.03.03.
13-30 (908)	joint information content <i>fr quantité (f) d'information conjointe</i>	$I(x, y)$	$I(x, y) = \text{lb} \frac{1}{p(x, y)} \text{ Sh} = \lg \frac{1}{p(x, y)} \text{ Hart} =$ $\ln \frac{1}{p(x, y)} \text{ nat}$ <p>where $p(x, y)$ is the joint probability of events x and y</p>	
13-35 (912)	transinformation content <i>fr transinformation (f)</i>	$T(x, y)$	$T(x, y) = I(x) + I(y) - I(x, y)$ <p>where $I(x)$ and $I(y)$ are the information contents (13-24) of events x and y, respectively, and $I(x, y)$ 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 transinformation (f) moyenne</i>	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 $X = \{x_1, \dots, x_n\}$, $Y = \{y_1, \dots, y_m\}$, where $p(x_i, y_j)$ is the joint probability of events x_i and y_j, and $T(x_i, y_j)$ 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 ≈ 0,693 nat ≈ 0,301 Hart	
13-24.b	hartley	Hart	value of the quantity when the argument is equal to 10	1 Hart ≈ 3,322 Sh ≈ 2,303 nat	
13-24.c	natural unit of information	nat	value of the quantity when the argument is equal to e	1 nat ≈ 1,433 Sh ≈ 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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$$0 \text{ Sh} \leq I(Y;X) \leq 1 \text{ Sh}$$

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- we are **completely certain** about 22
- we are **completely uncertain** about $100 - 22 = 78$

→ approx $22 + 78/2 = 61$ correct prognoses (TP+TN)

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Upper bound \approx

$$\frac{1}{2} + \frac{1}{2} \sqrt{1 - (1 - 0.22)^{\frac{4}{3}}} \approx 77\% \pm 0.8\sqrt{N}\% \quad \text{correct prognoses}$$

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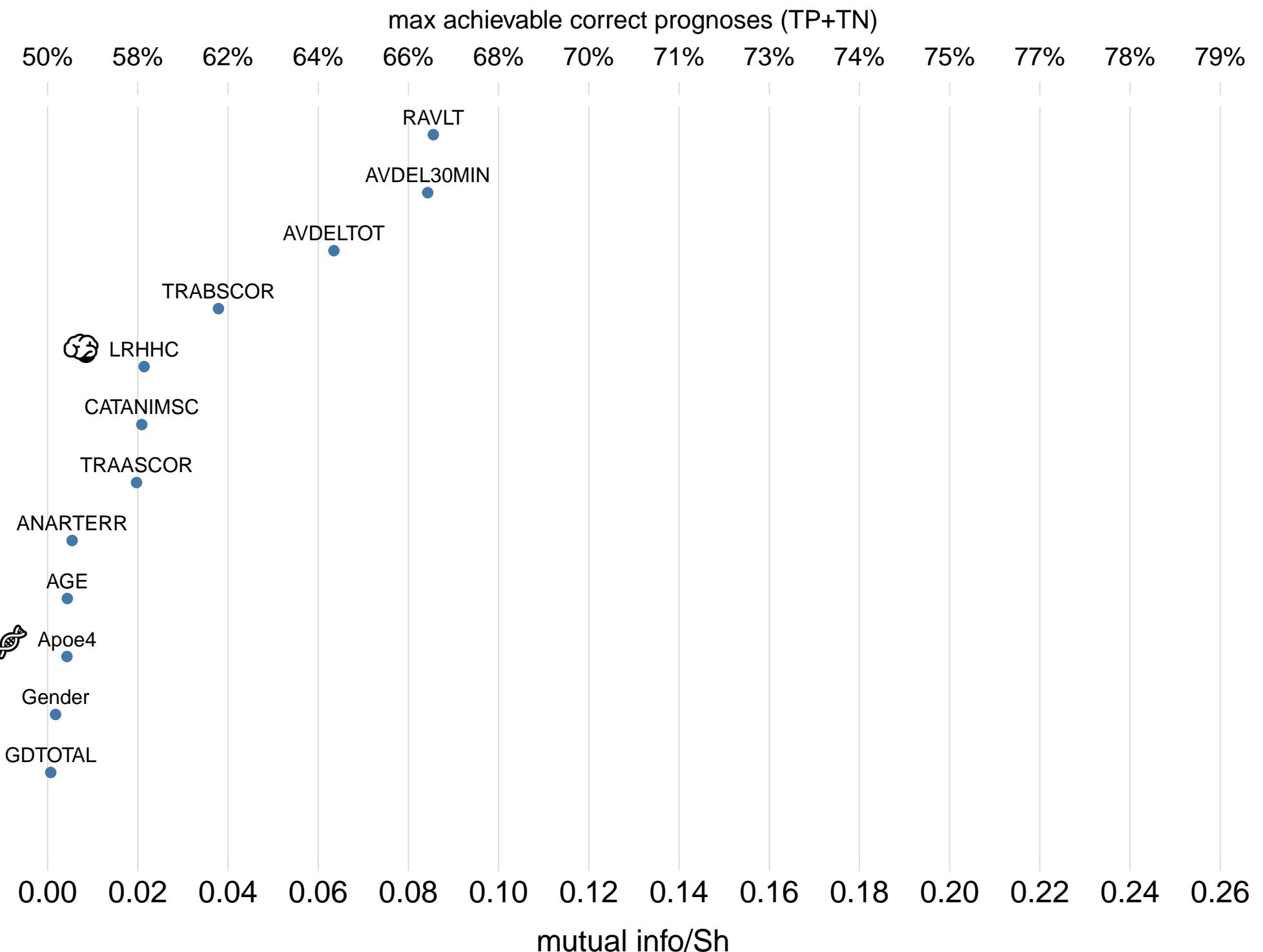
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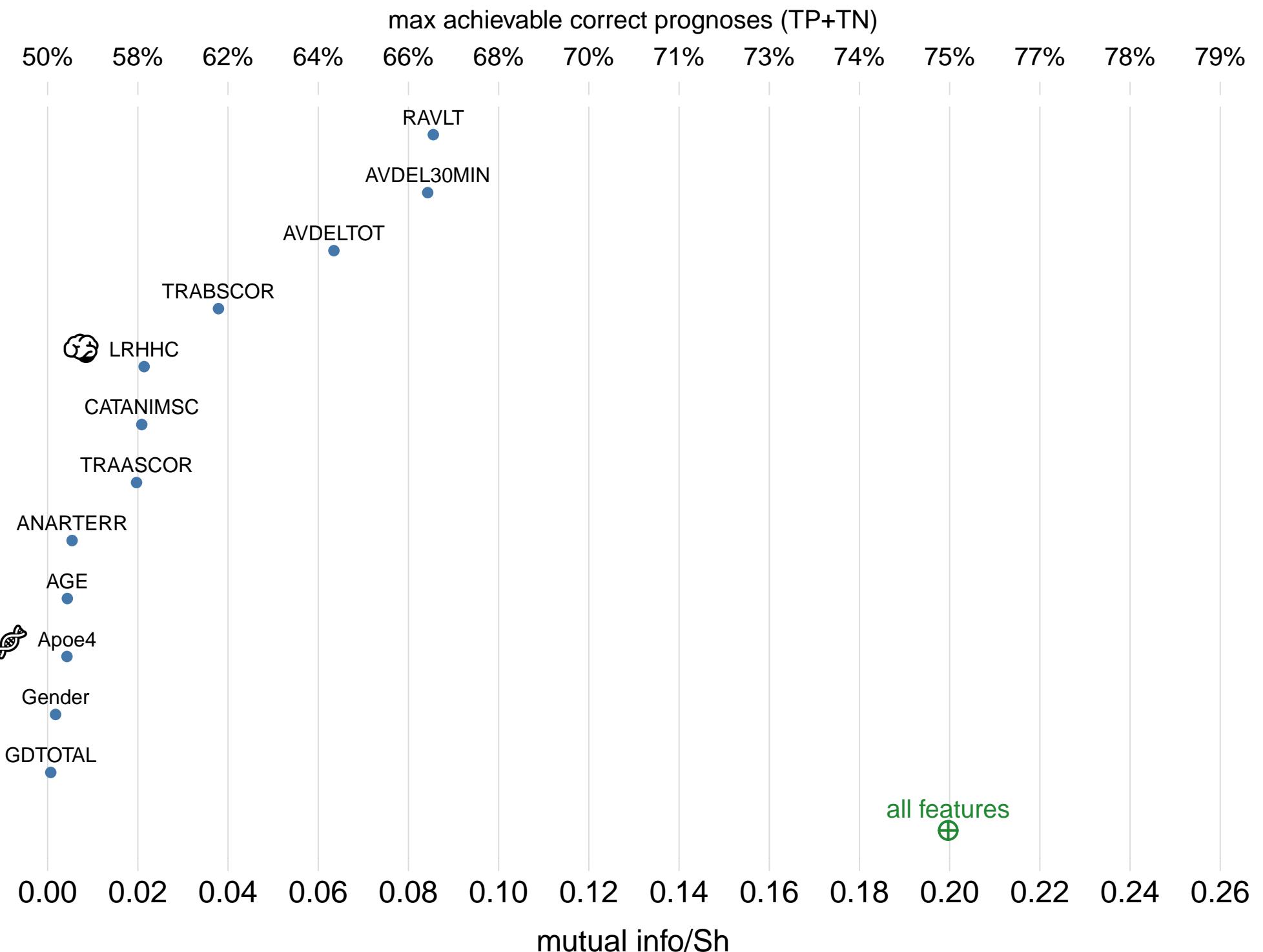
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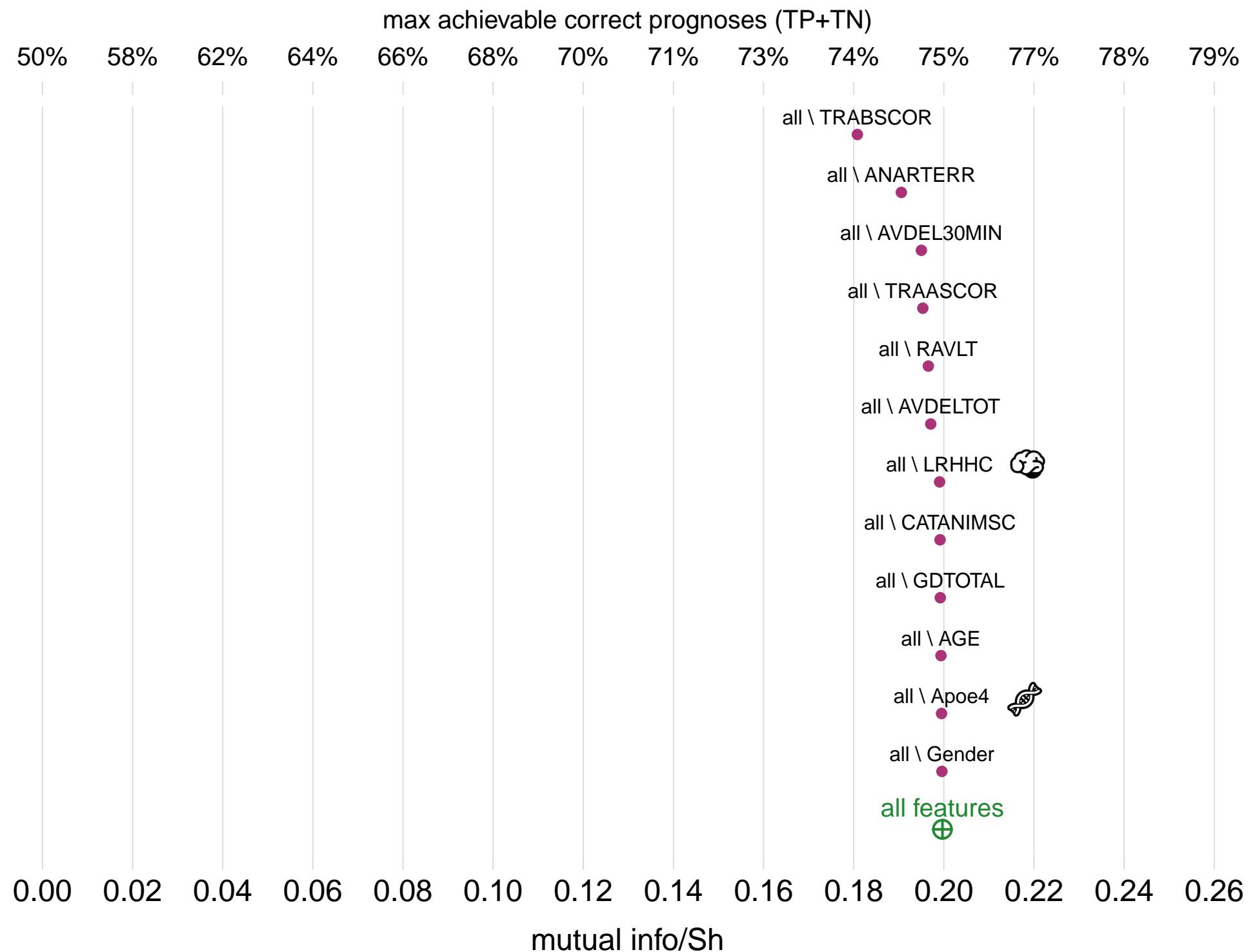
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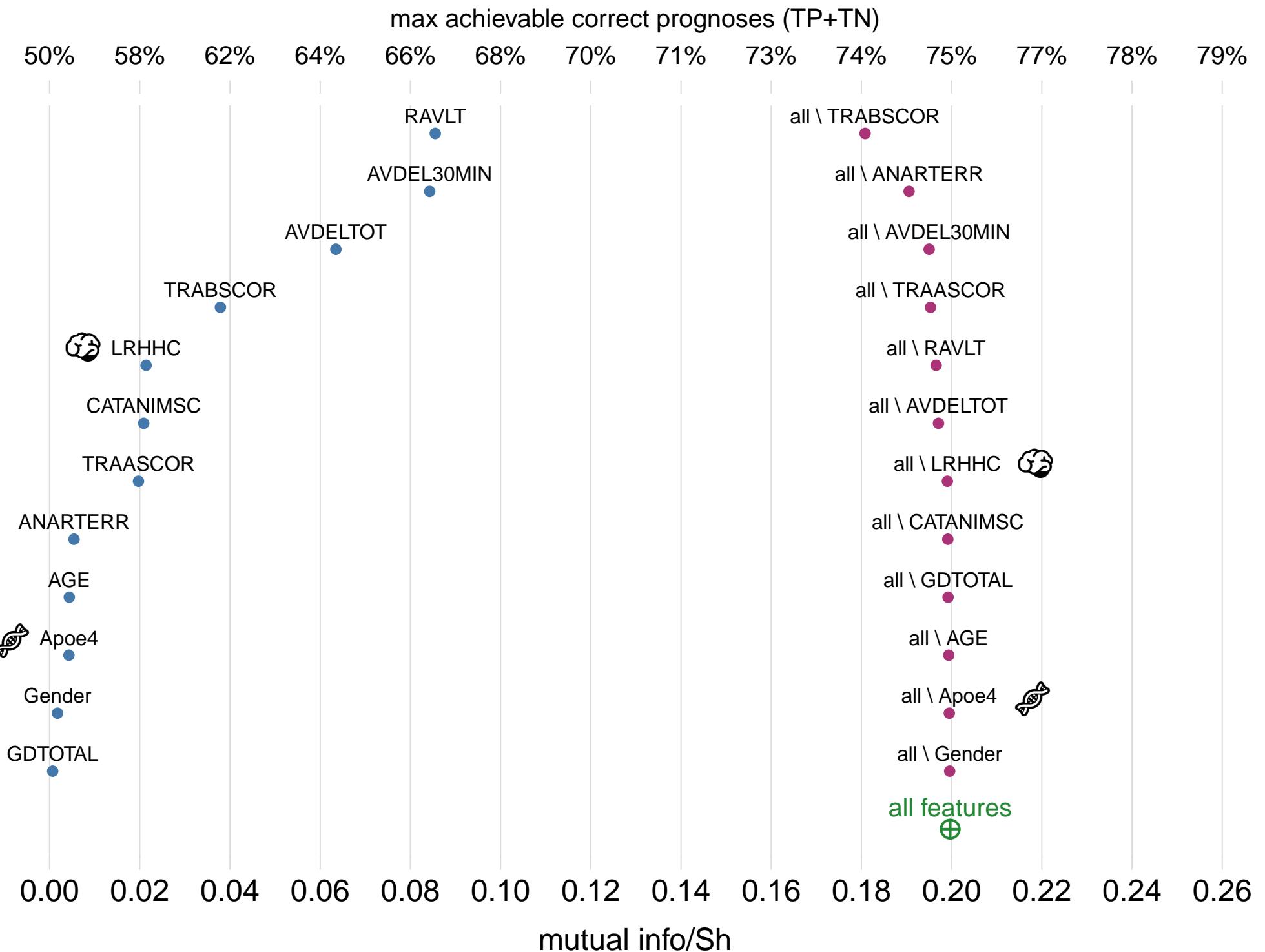
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Maximum accuracy attainable
by *any* algorithm which uses only feature set X



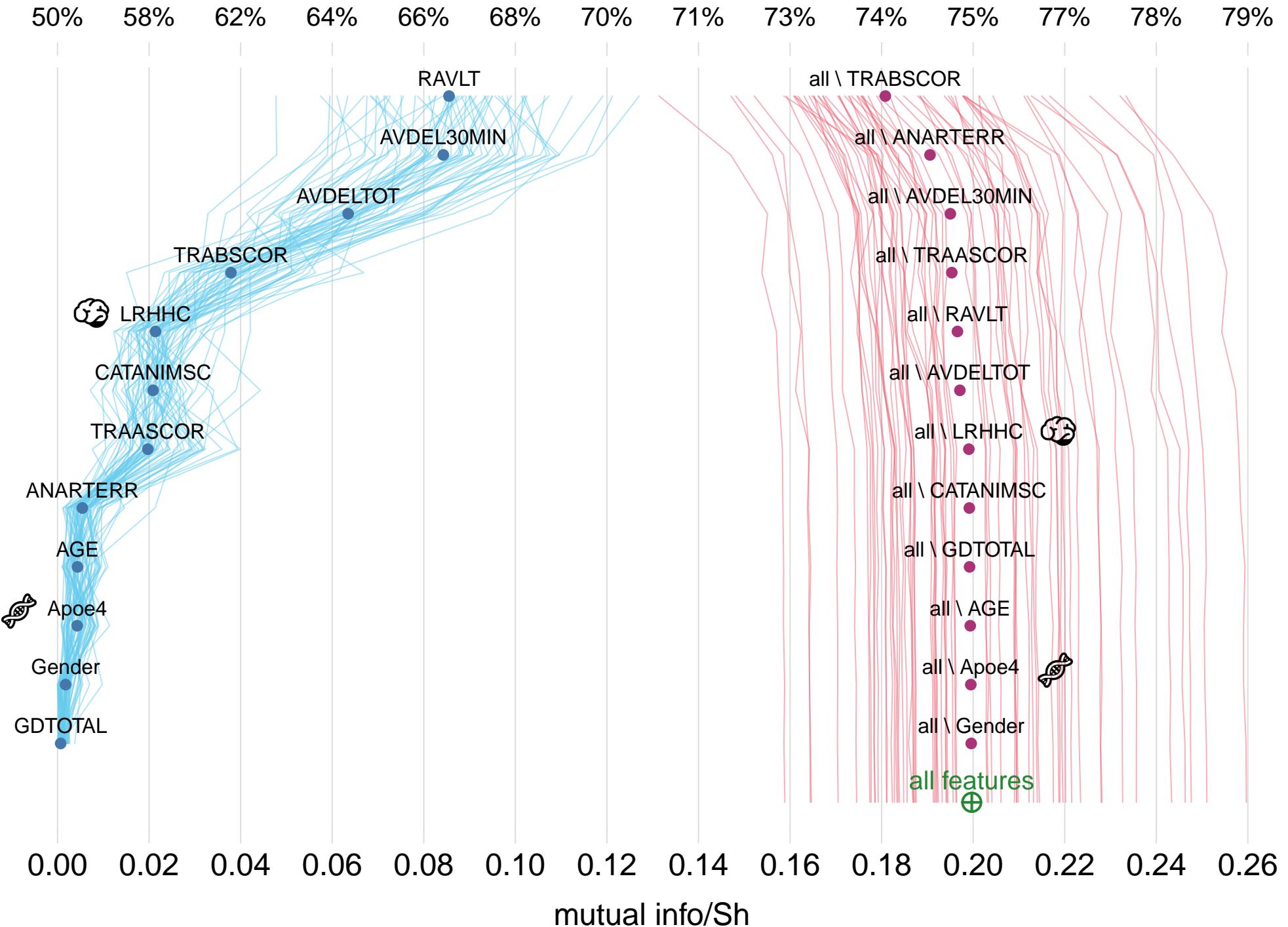


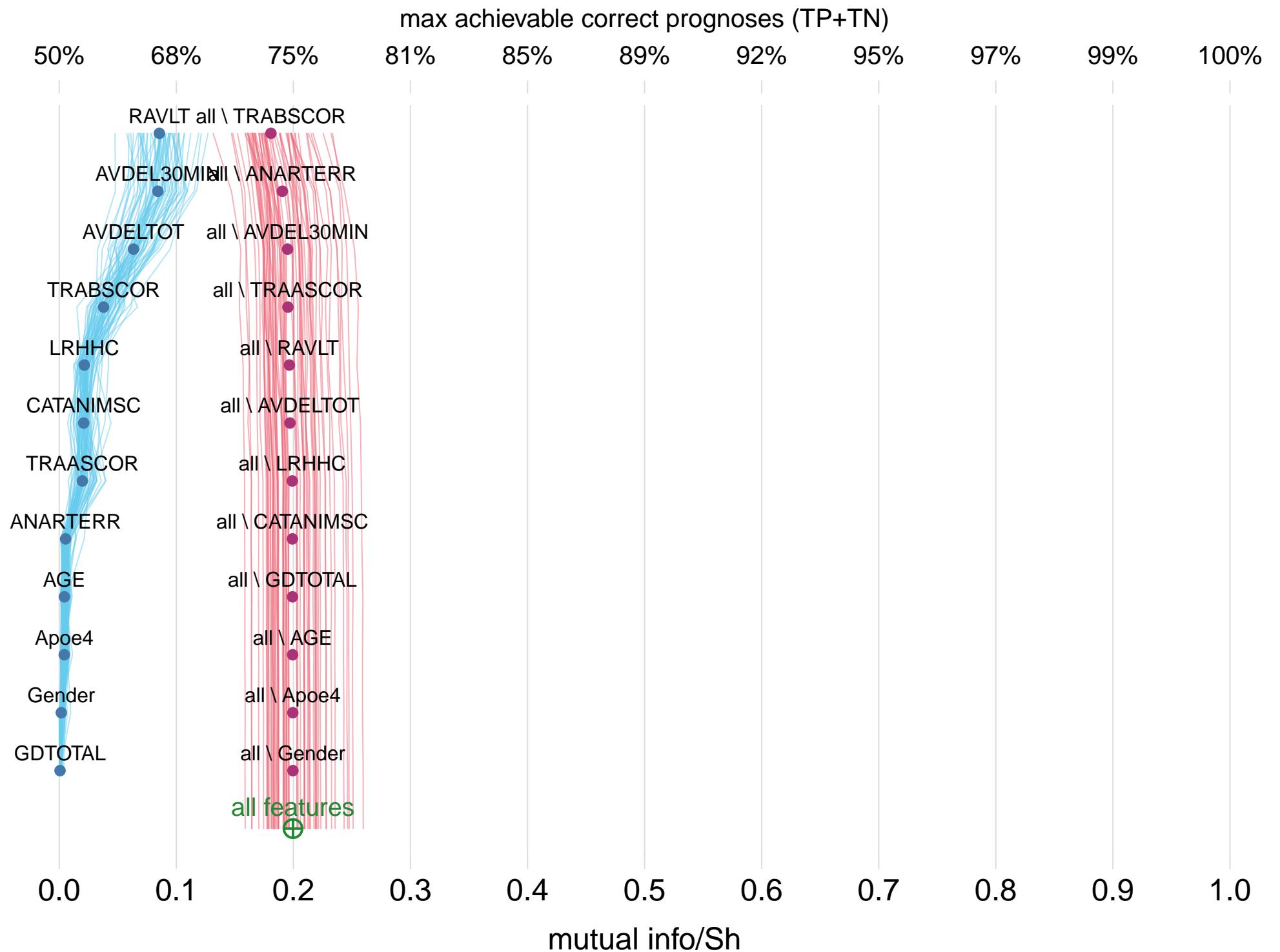


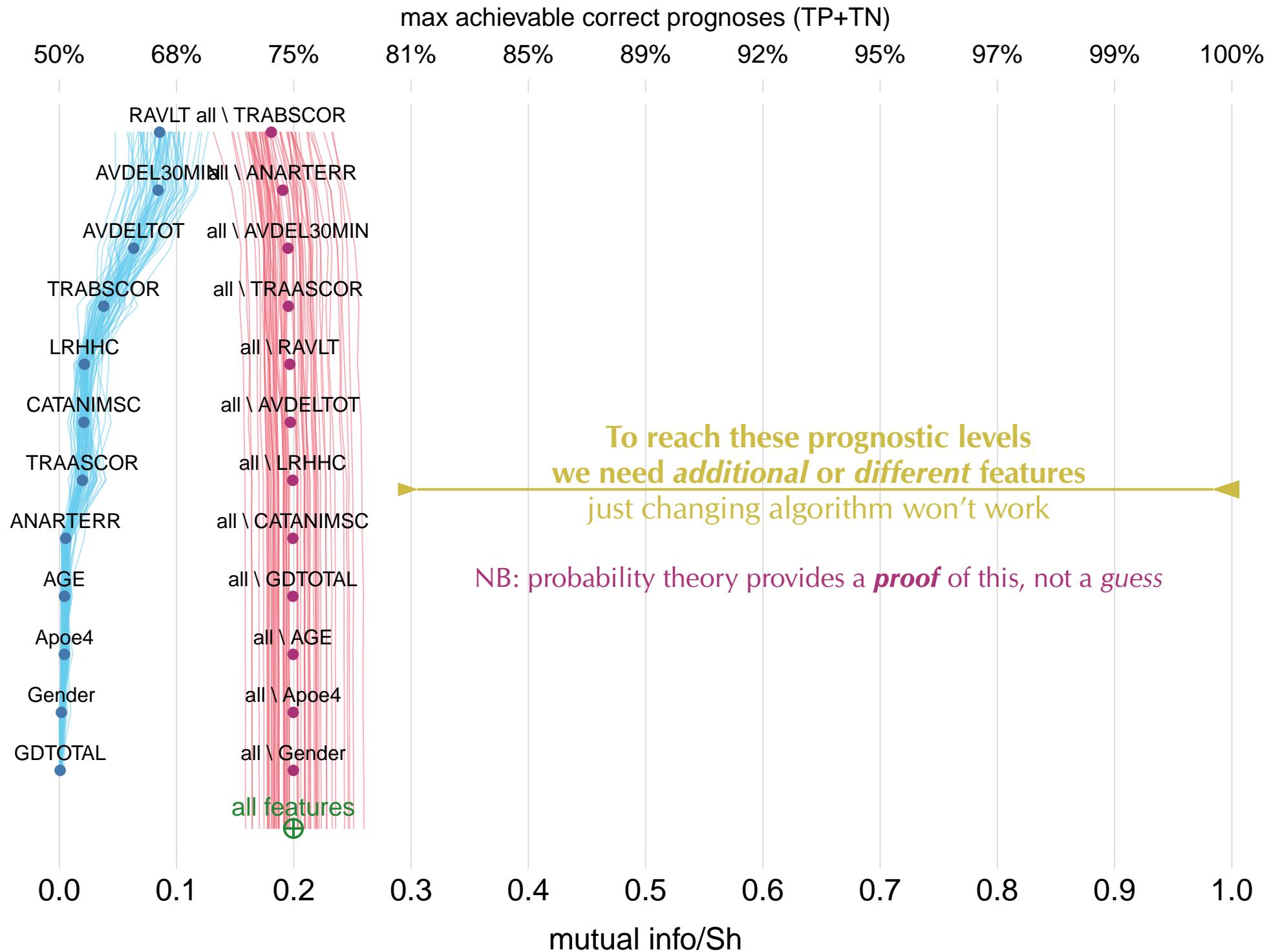




max achievable correct prognoses (TP+TN)

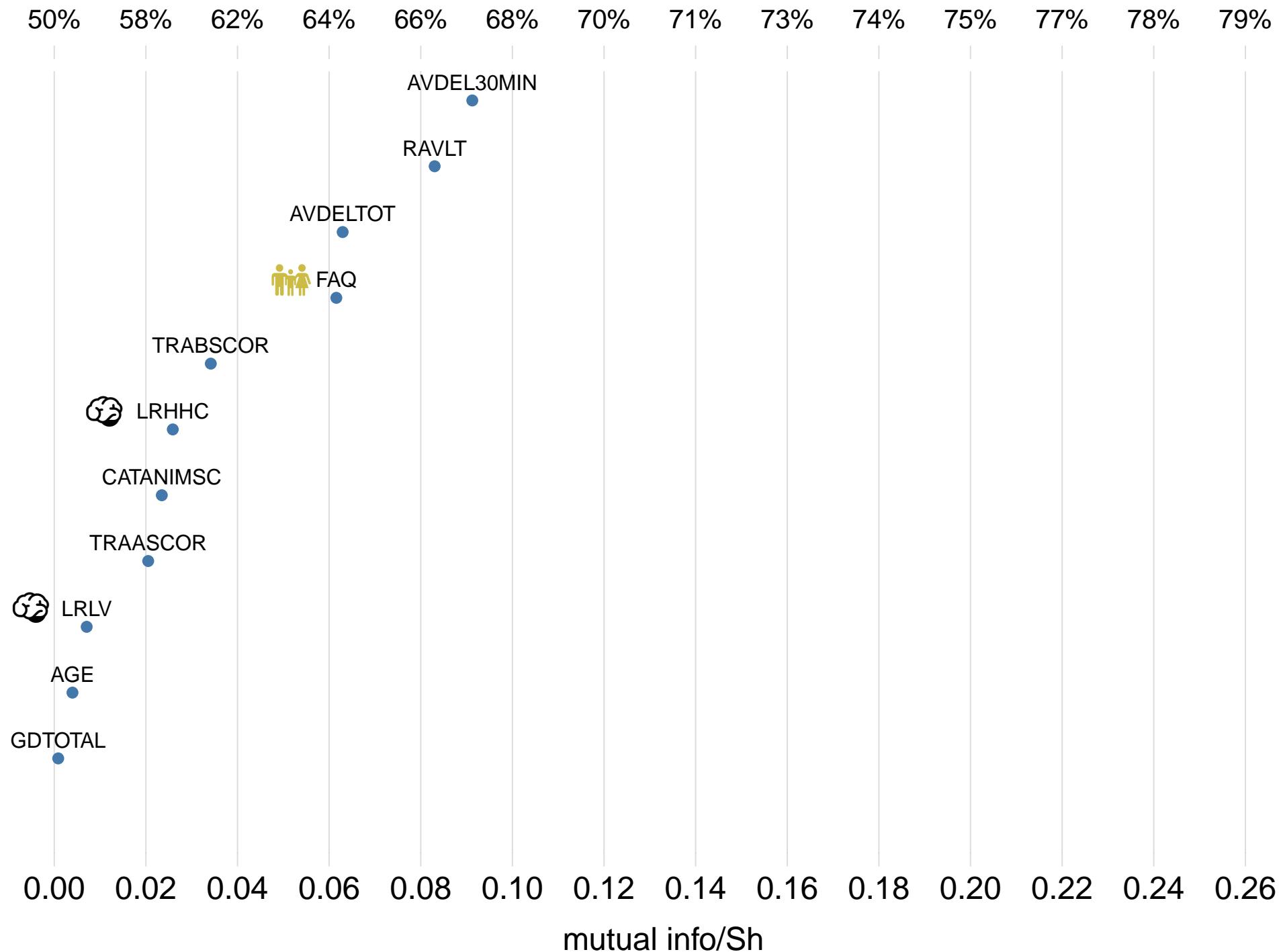






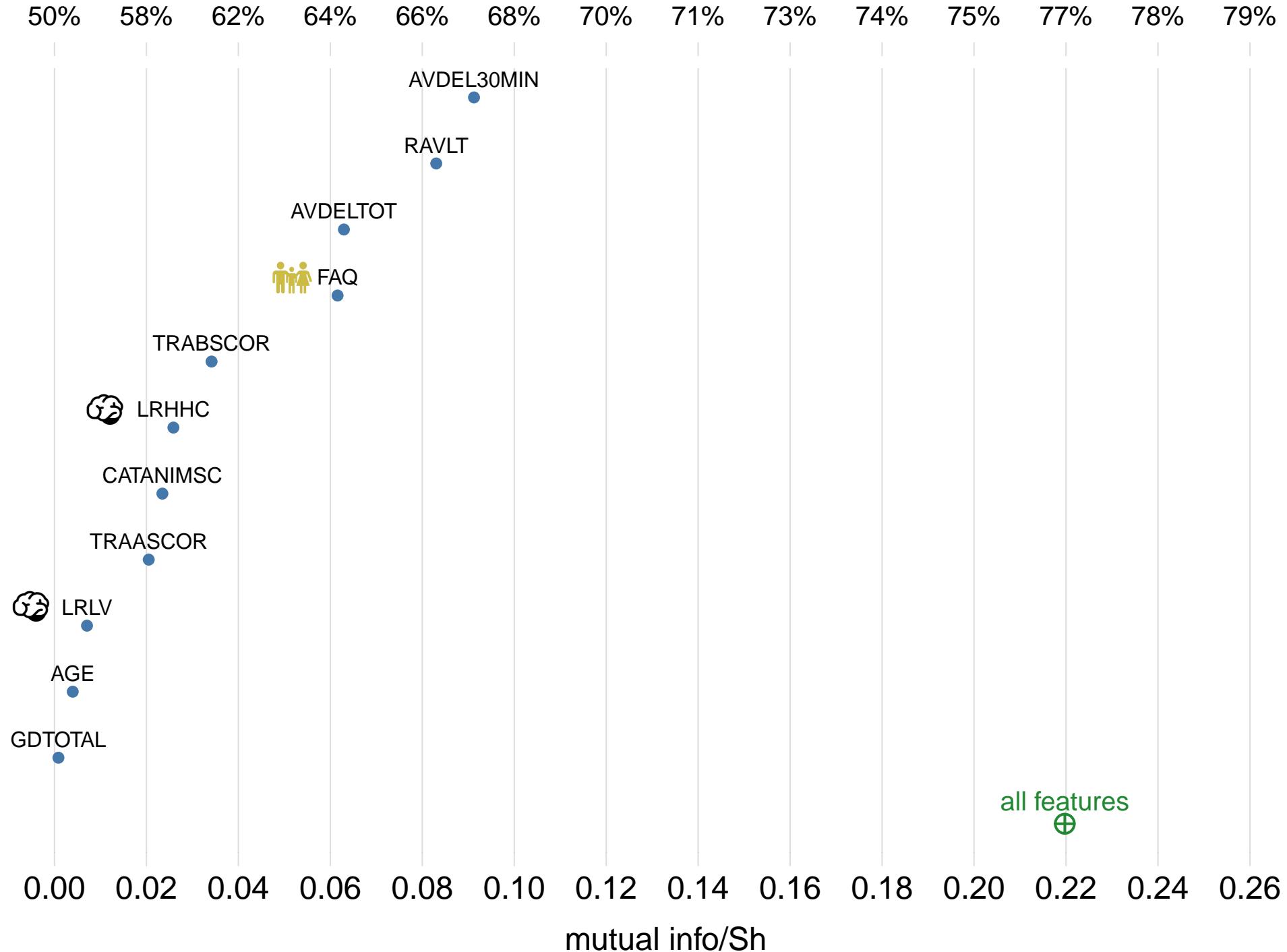


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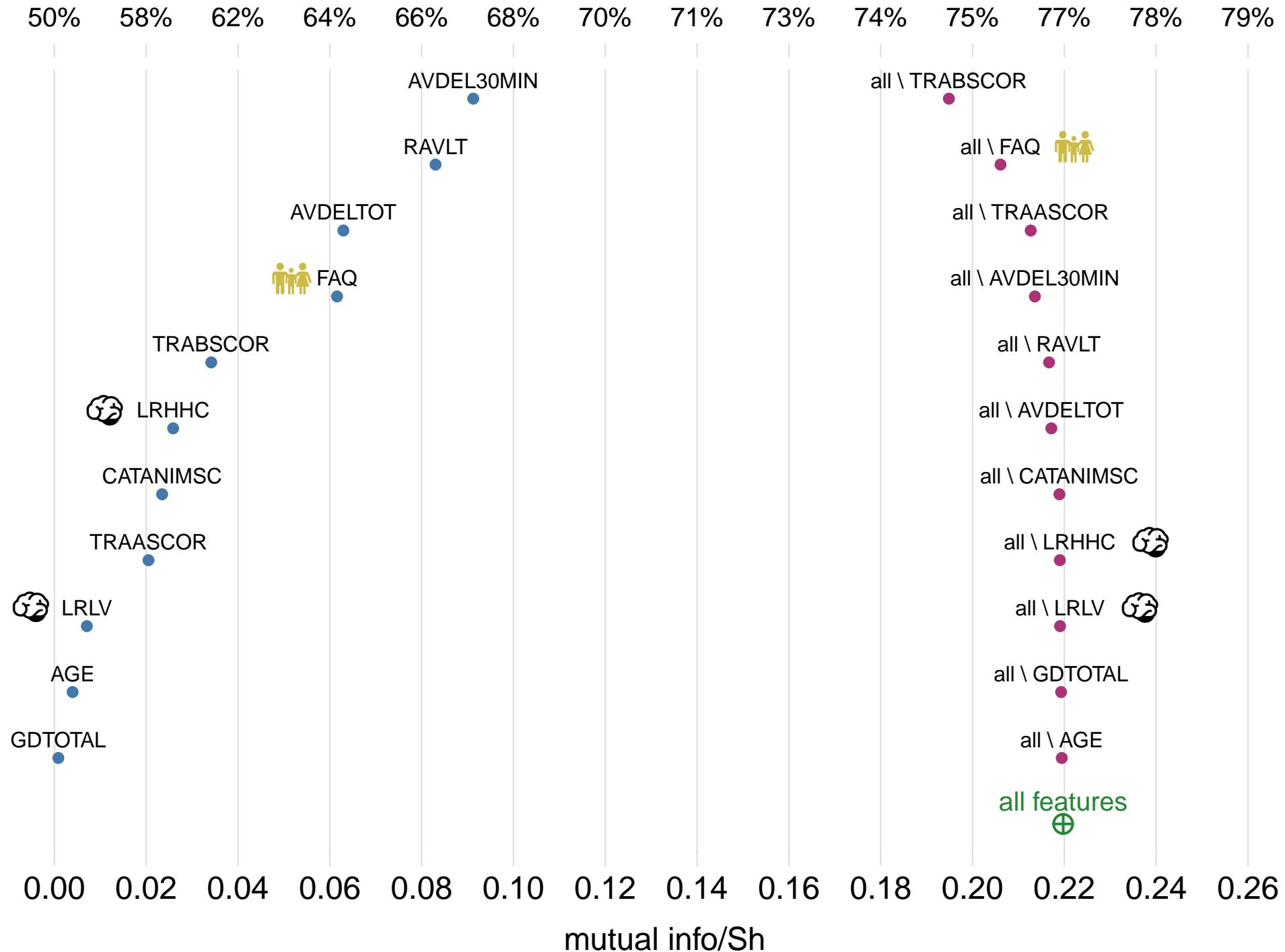


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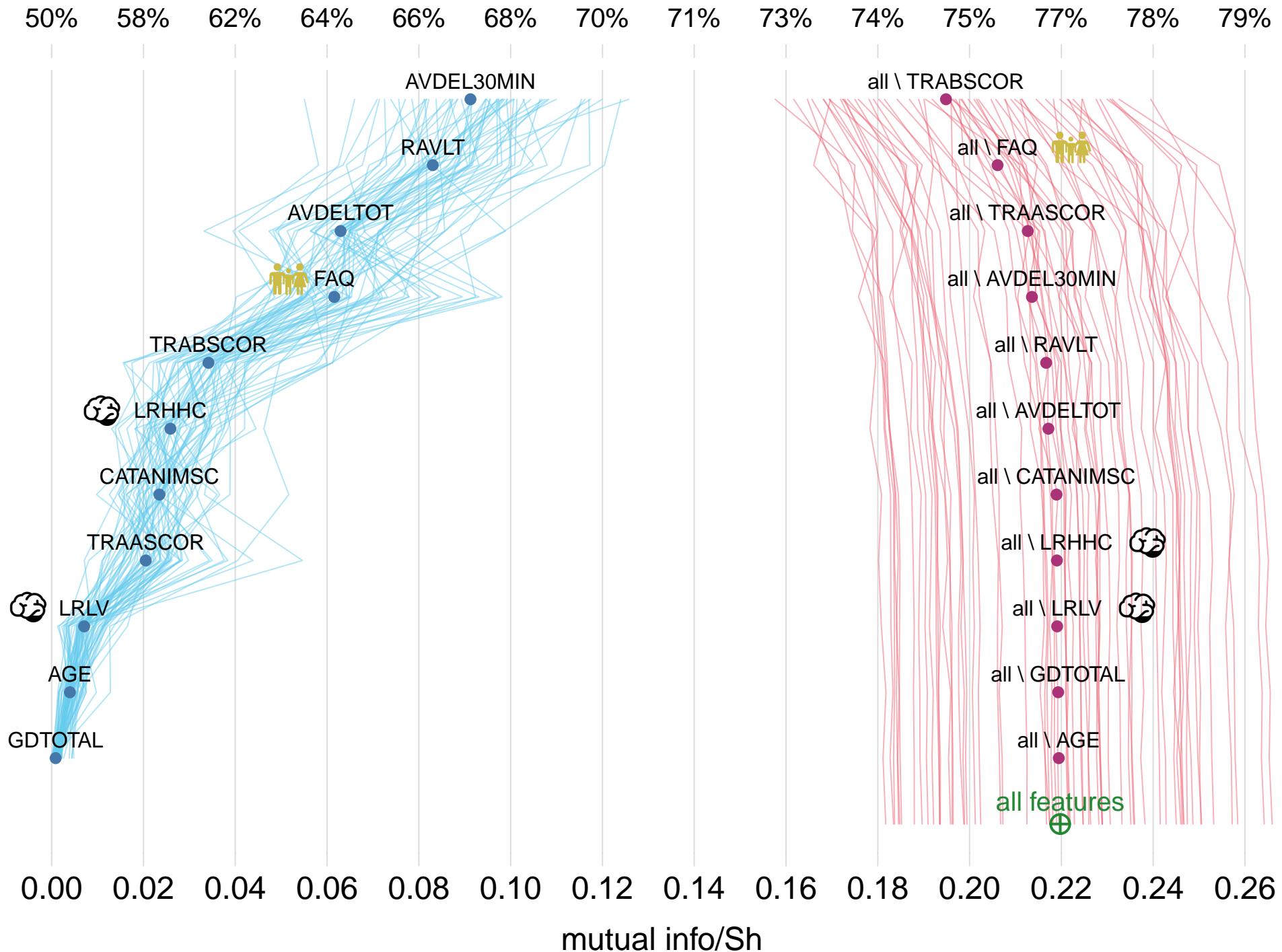


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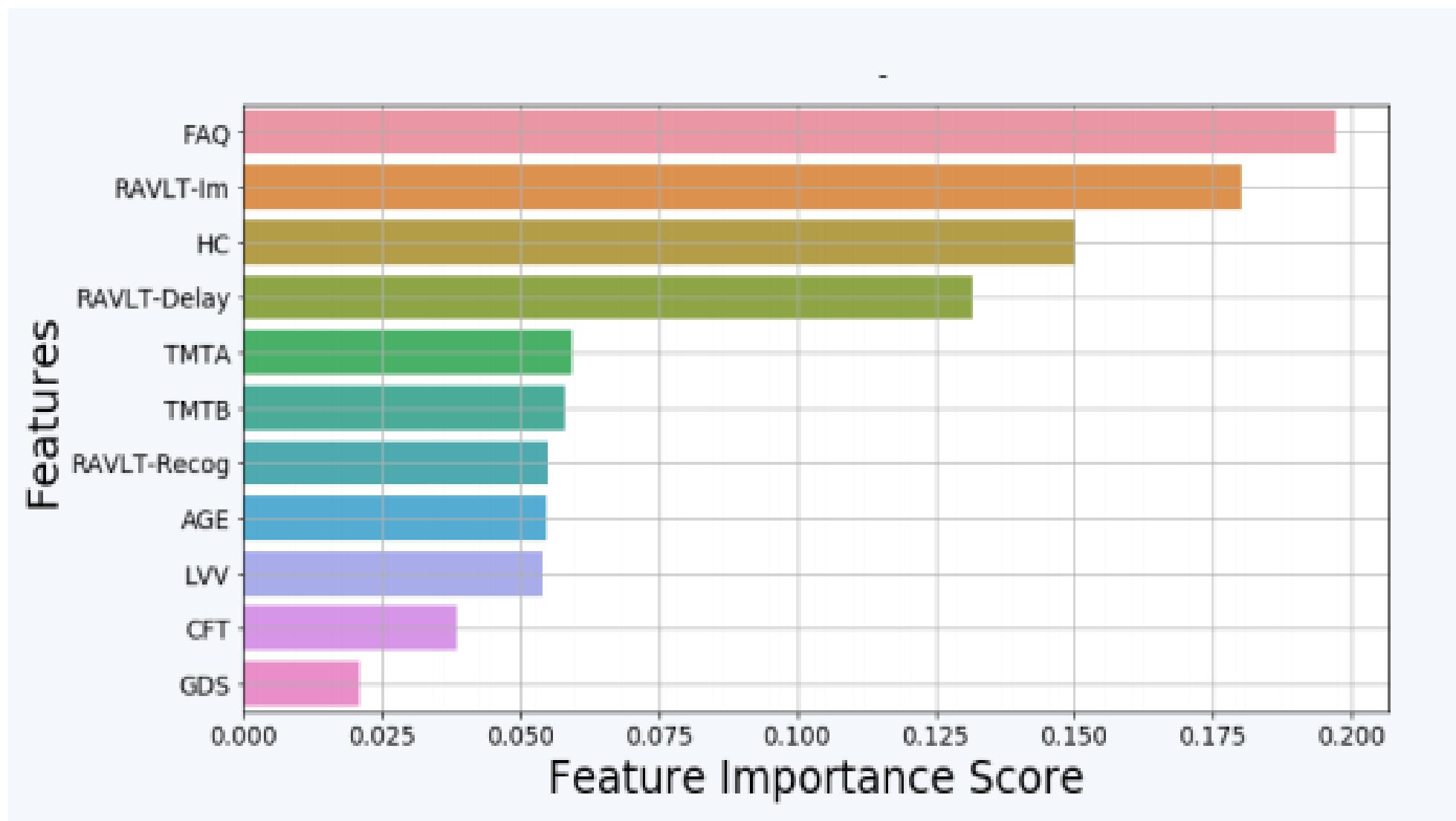


max achievable correct prognoses (TP+TN)



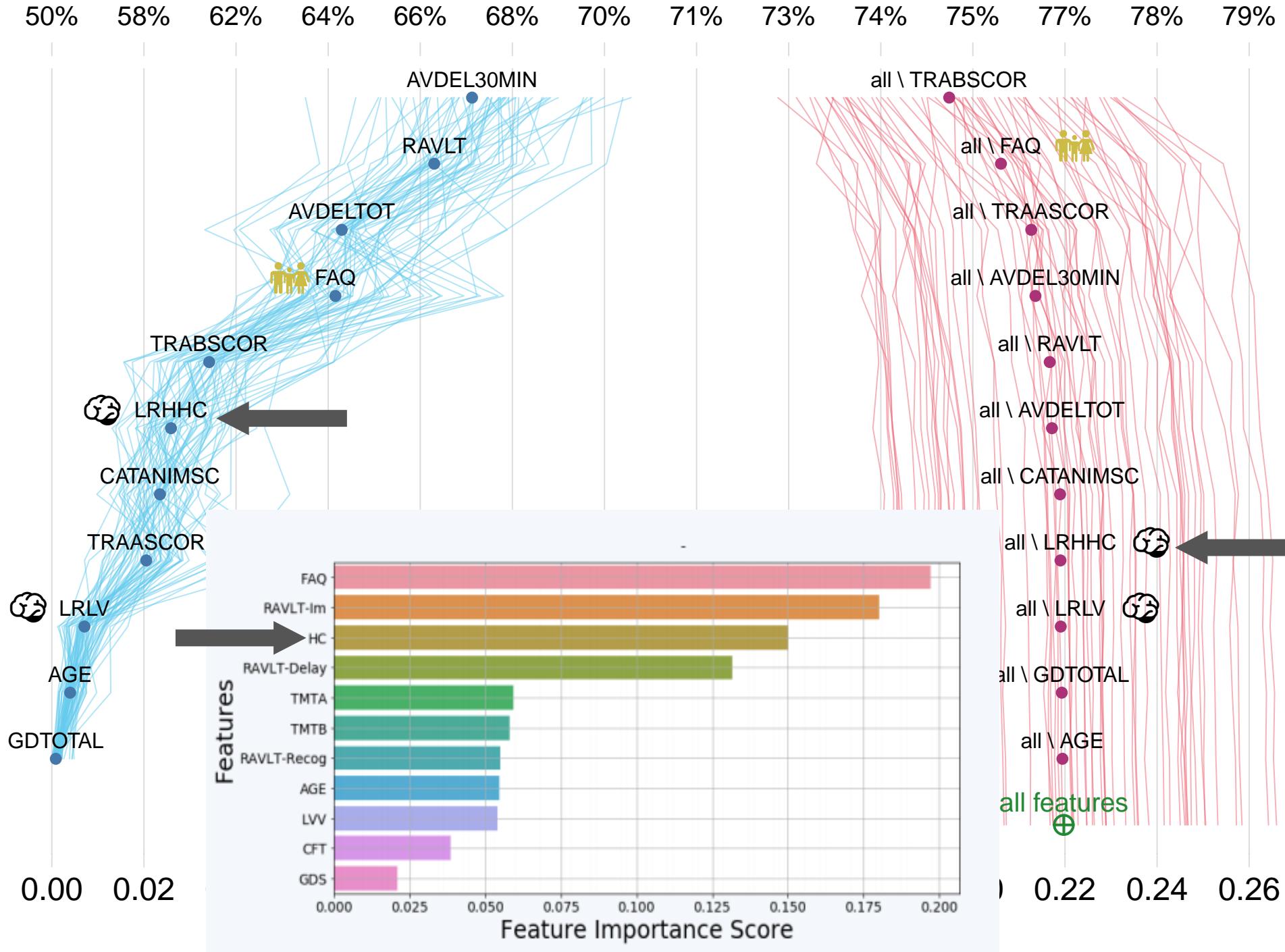


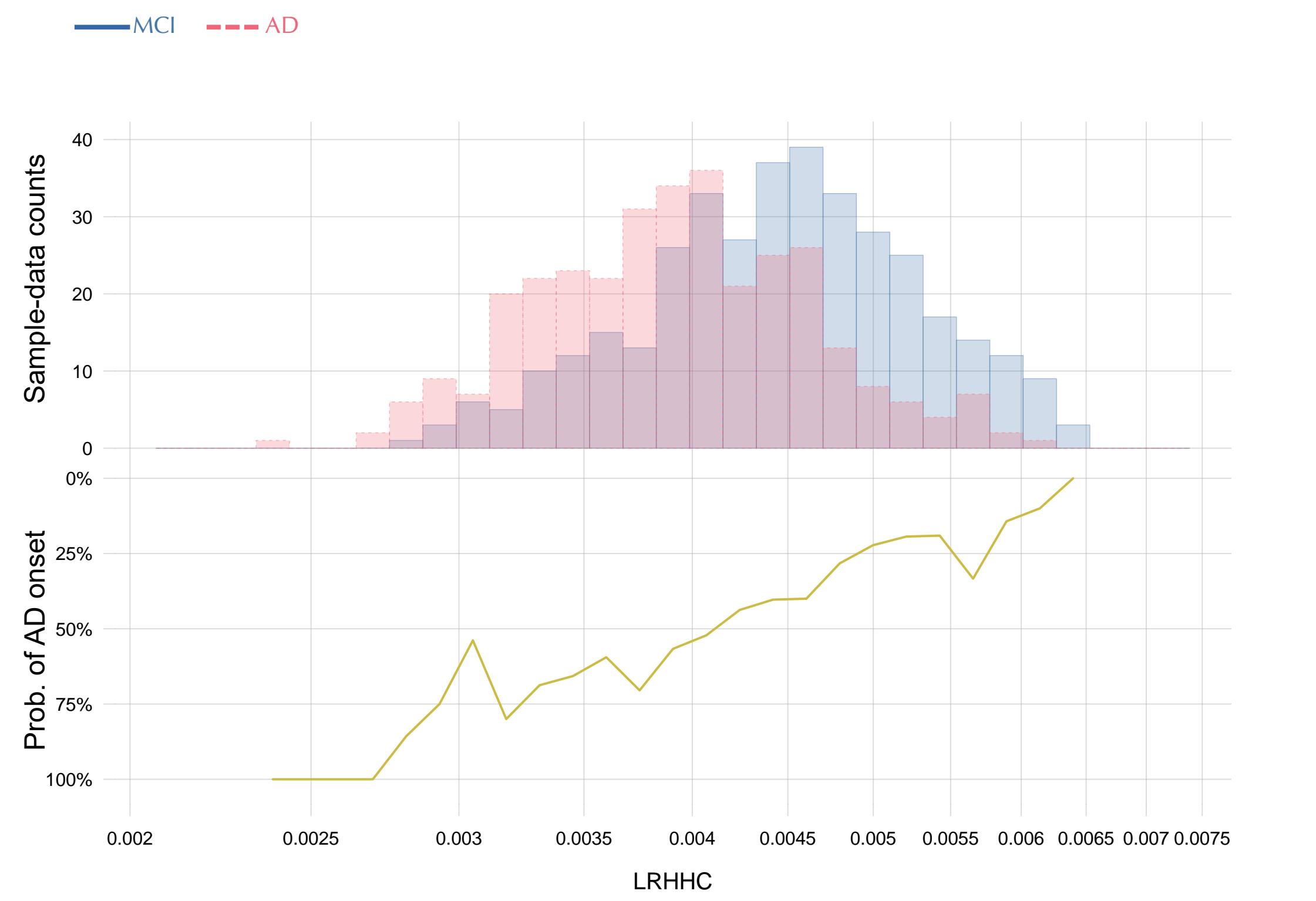
Alexandra's results



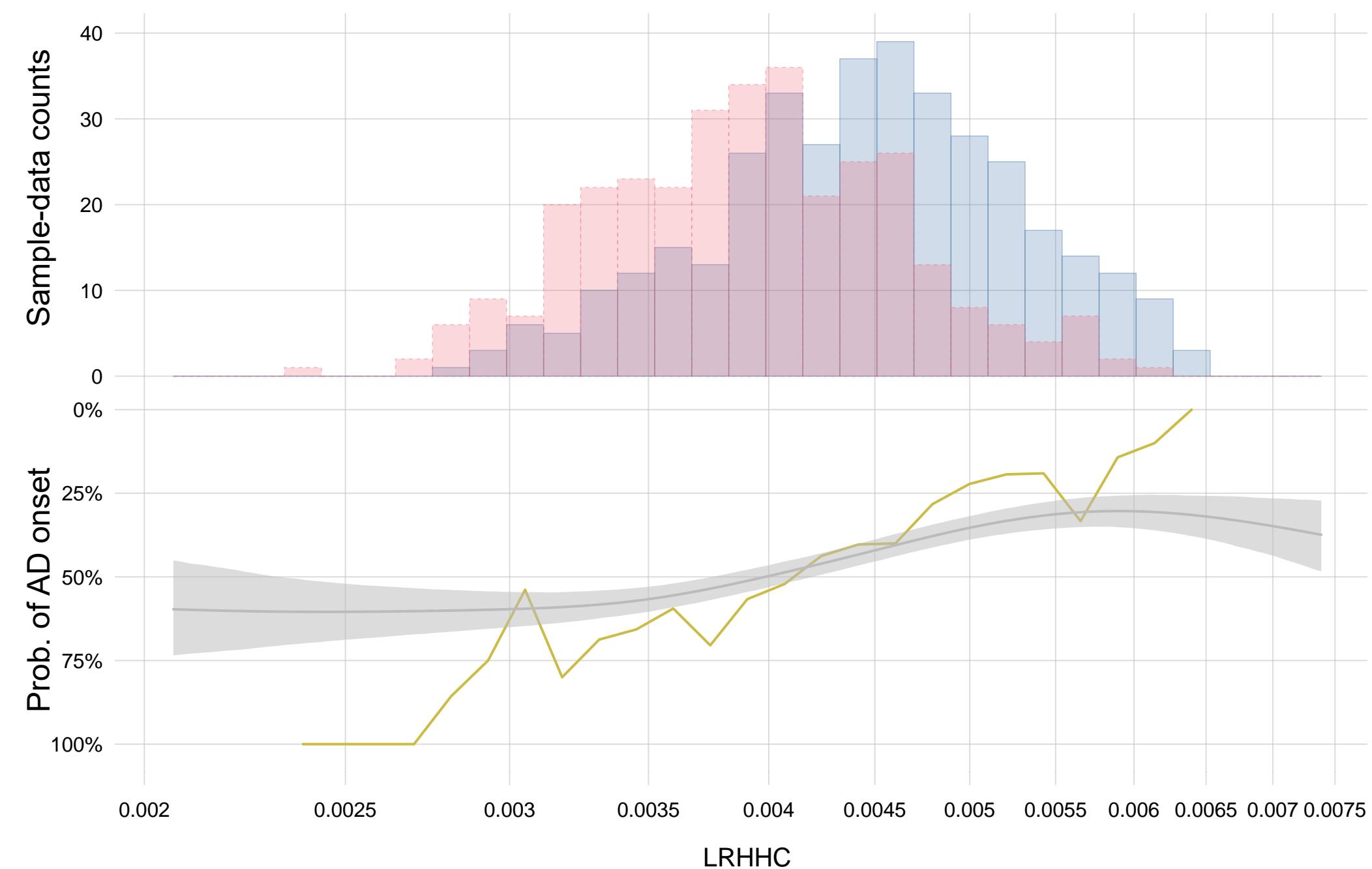


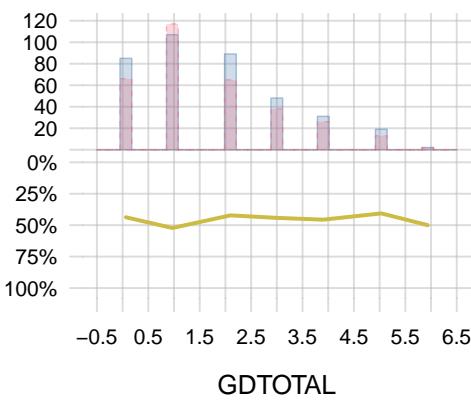
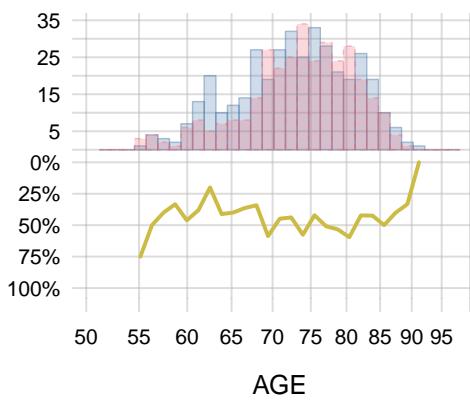
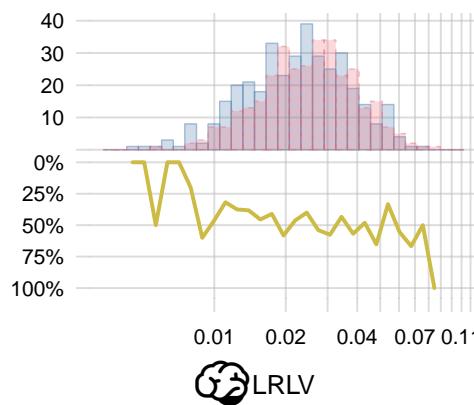
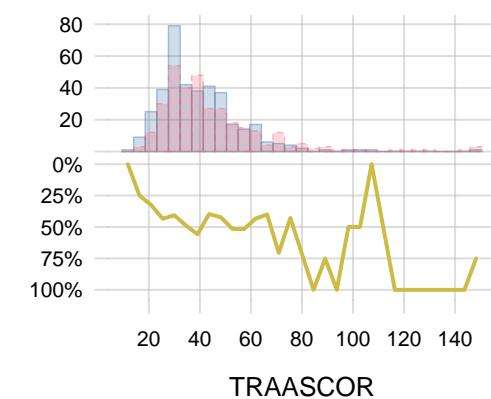
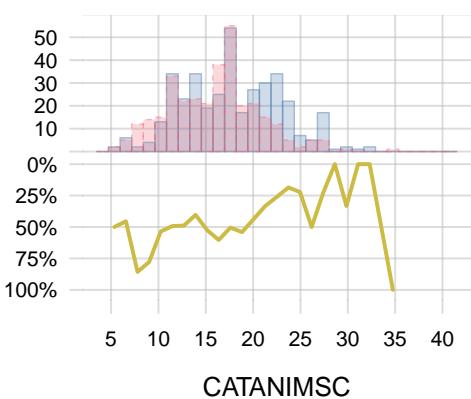
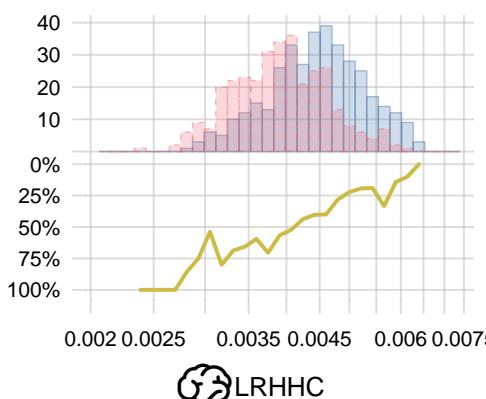
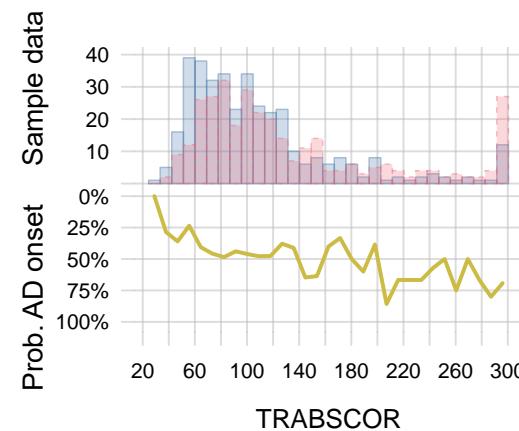
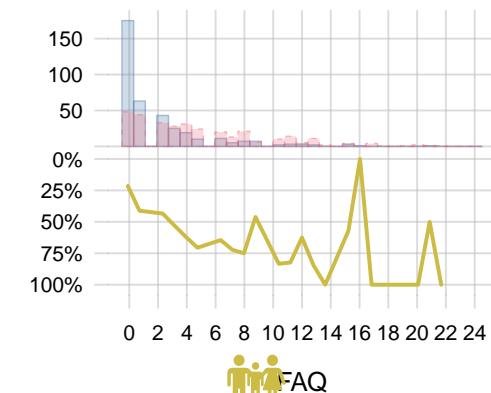
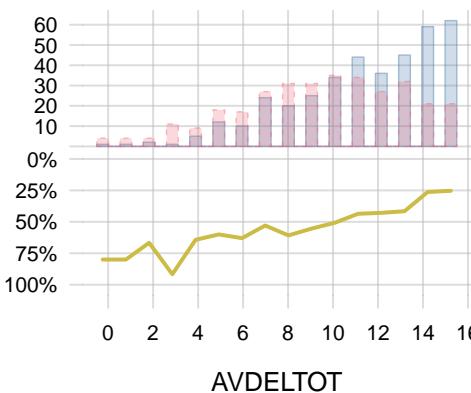
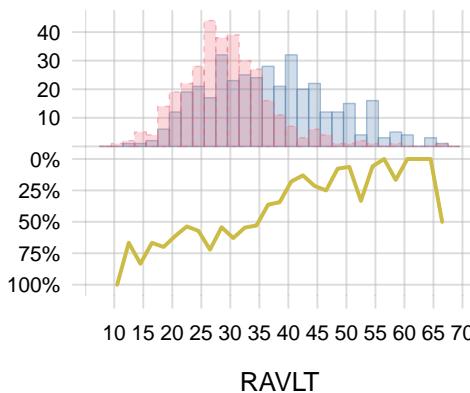
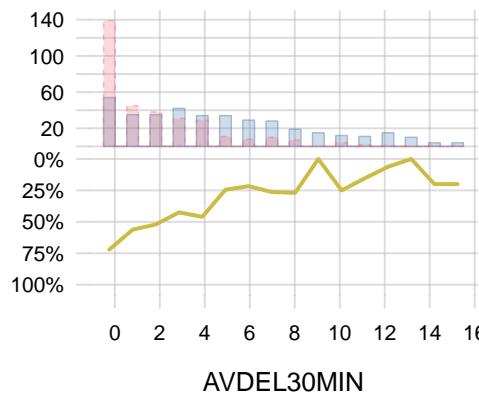
max achievable correct prognoses (TP+TN)





MCI AD 87.5% credible interval

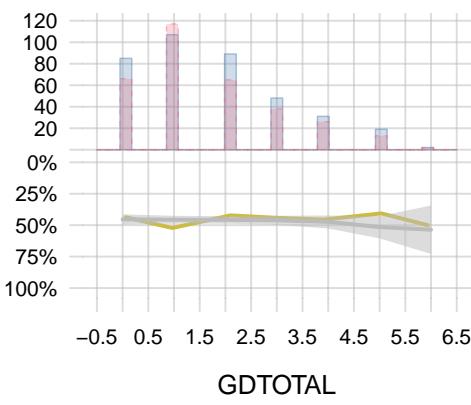
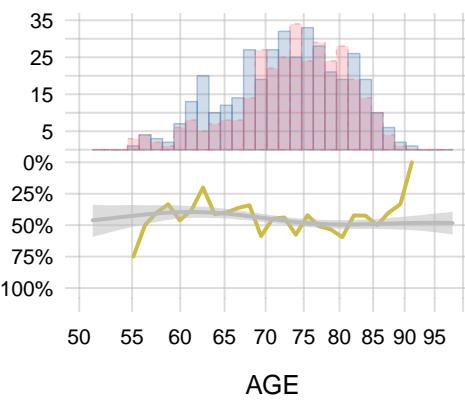
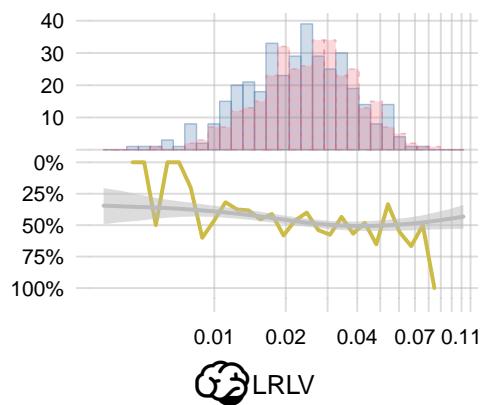
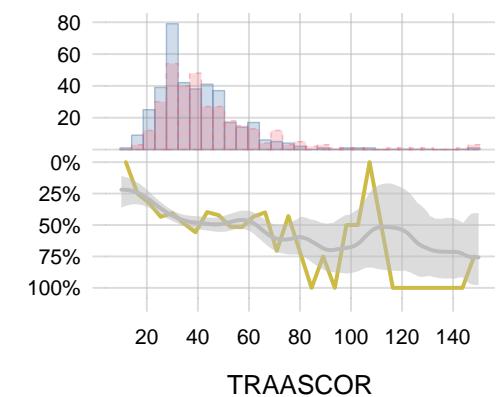
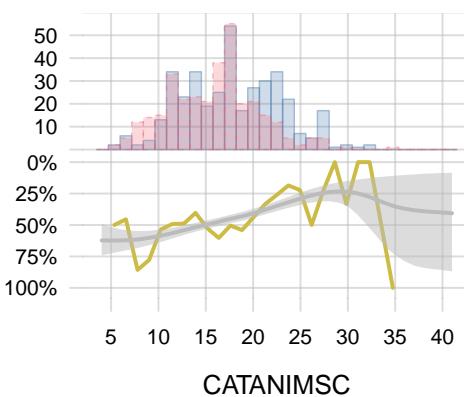
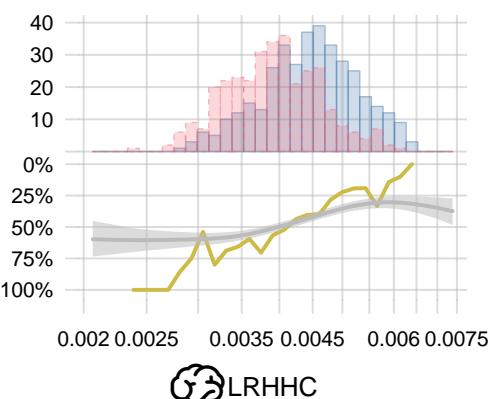
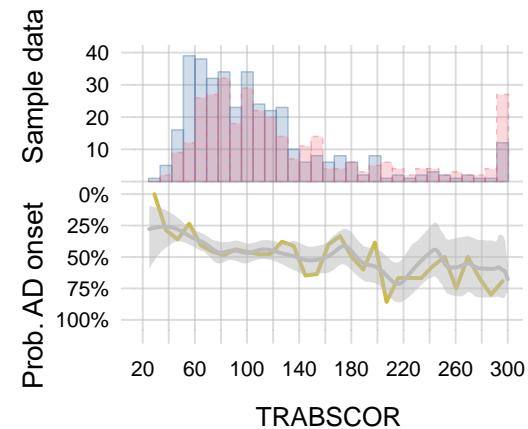
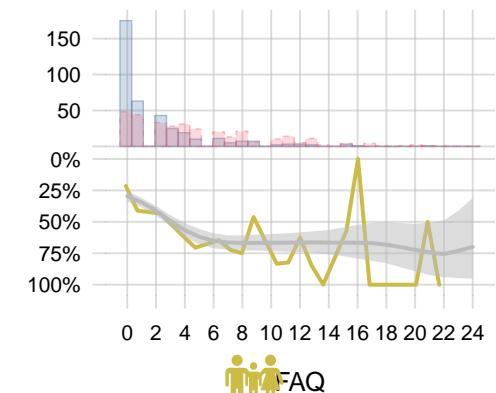
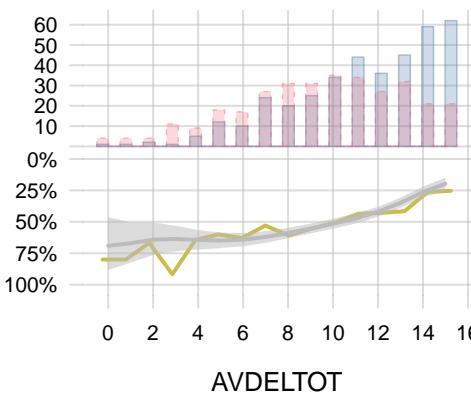
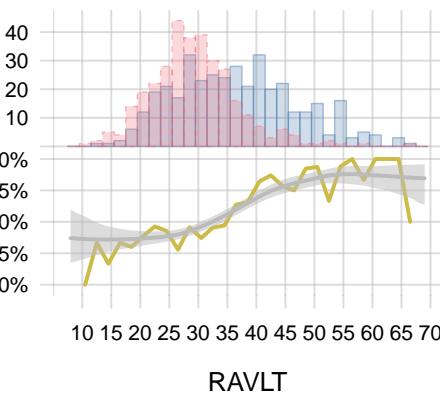
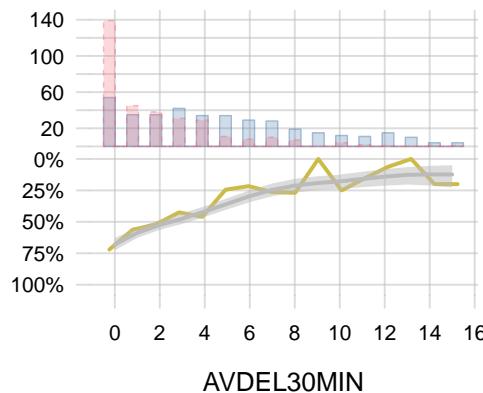




MCI

AD

87.5% credible interval



Thank you!