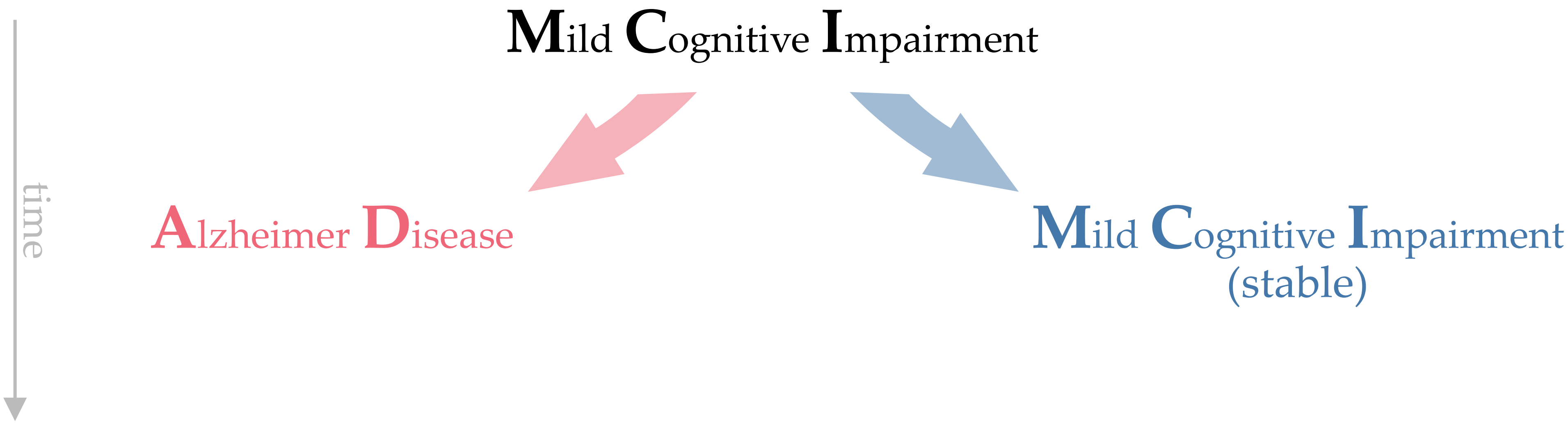
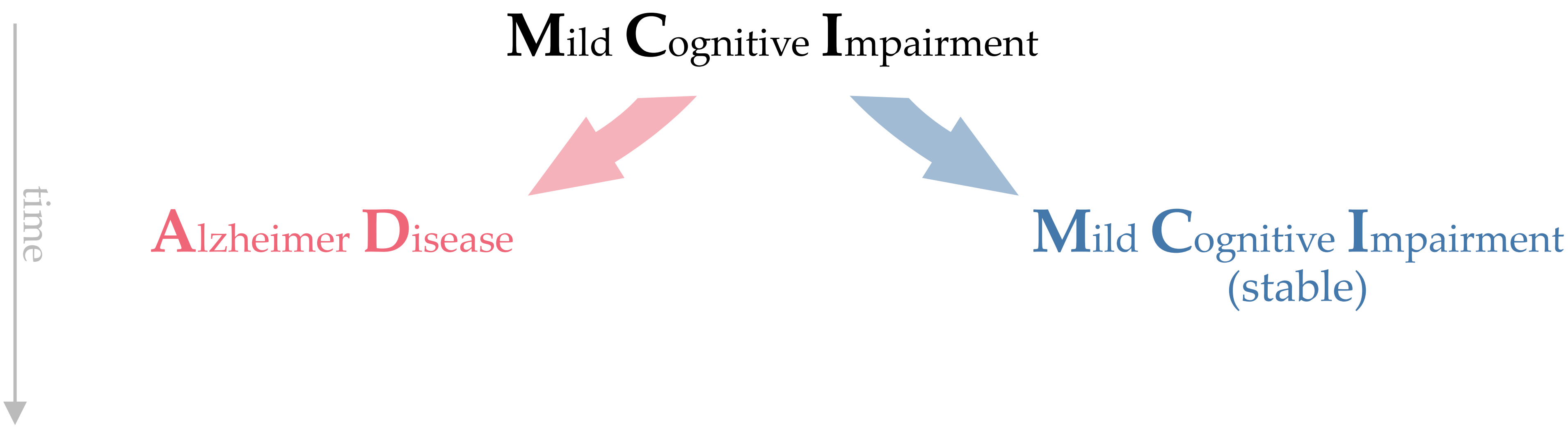
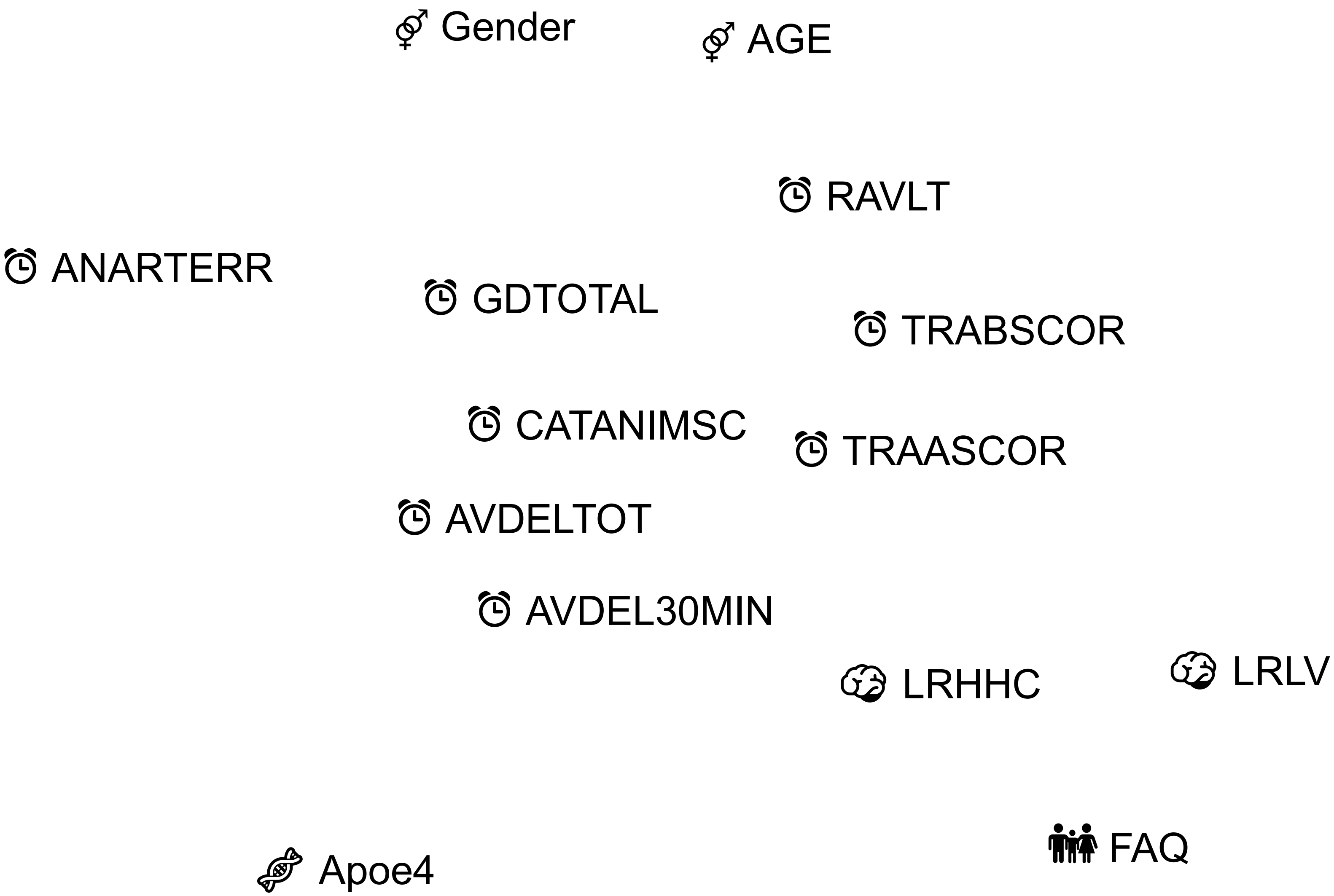
Mild Cognitive Impairment

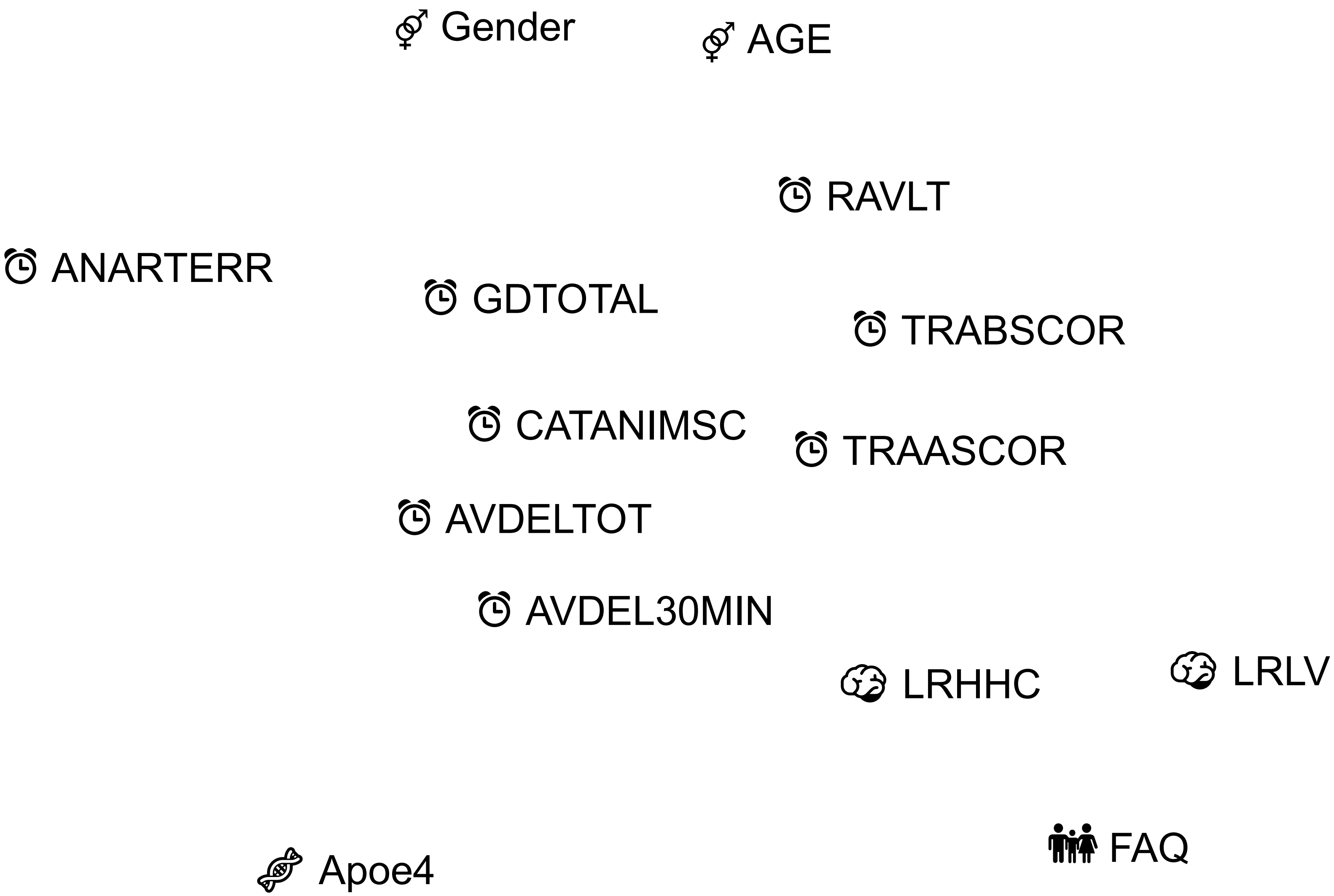

Mild Cognitive Impairment
time
Alzheimer Disease
Mild Cognitive Impairment
(stable)


Mild Cognitive Impairment
time
Alzheimer Disease
Mild Cognitive Impairment
(stable)

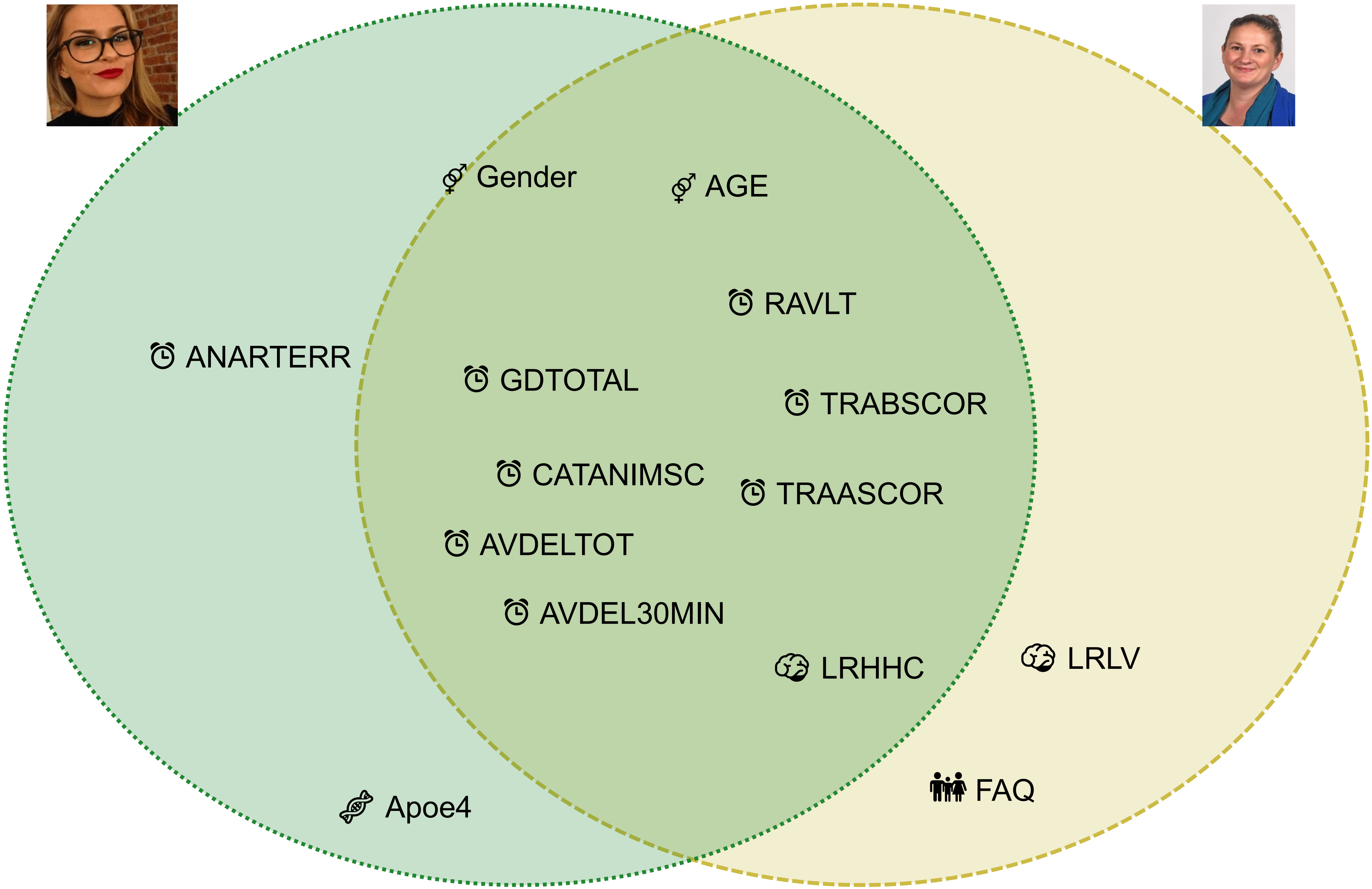




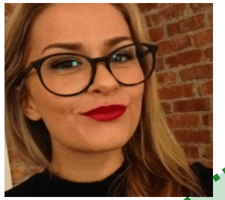


Gender
AGE
RAVLT
ANARTERR
GDTOTAL
TRABSCOR
CATANIMSC
TRAASCOR
AVDELTOT
AVDEL30MIN
LRHHC
LRLV
FAQ
Apoe4

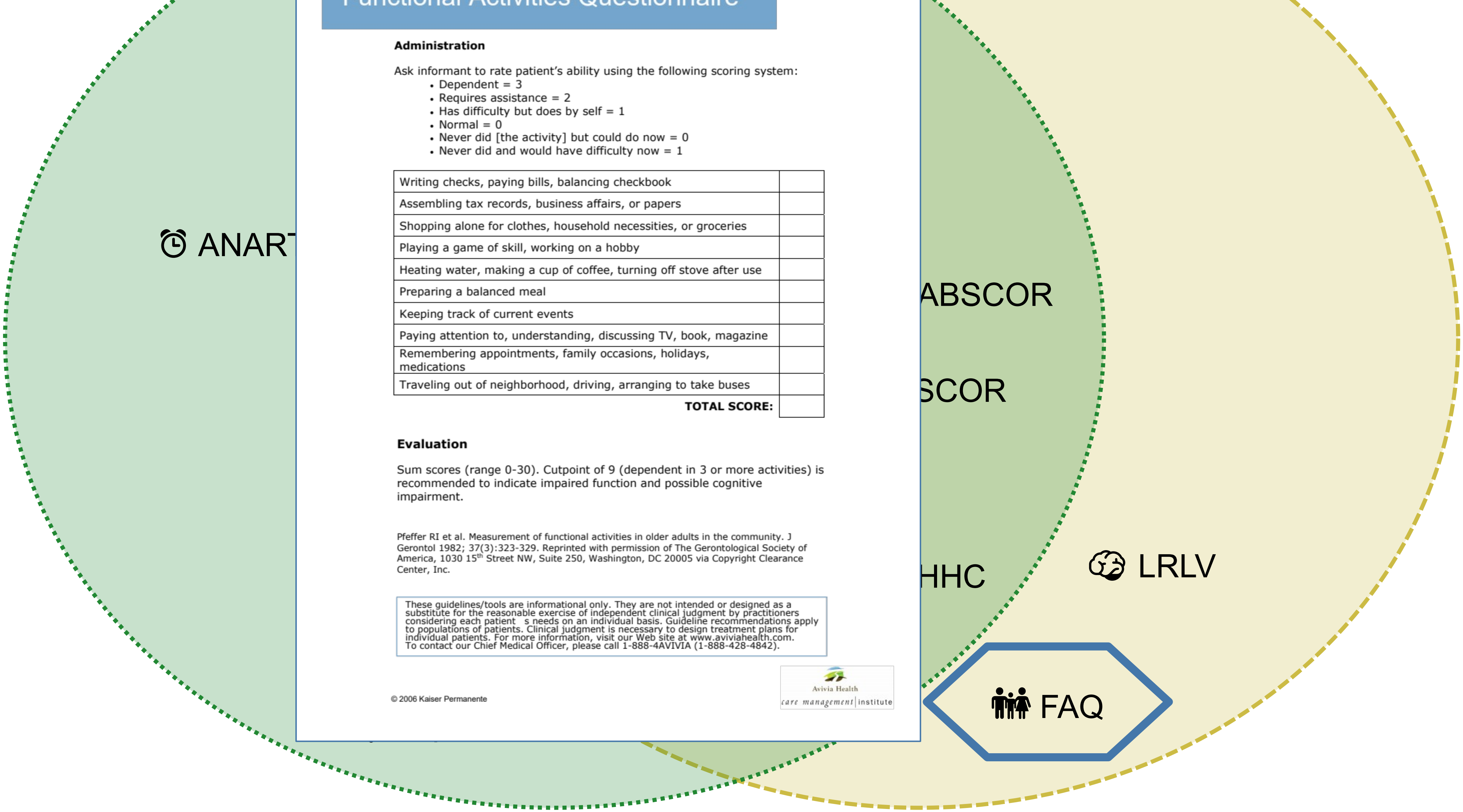


How ‘good’ are these features at prognosing the later onset of Alzheimer?



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	
TOTAL SCORE:	

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.

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

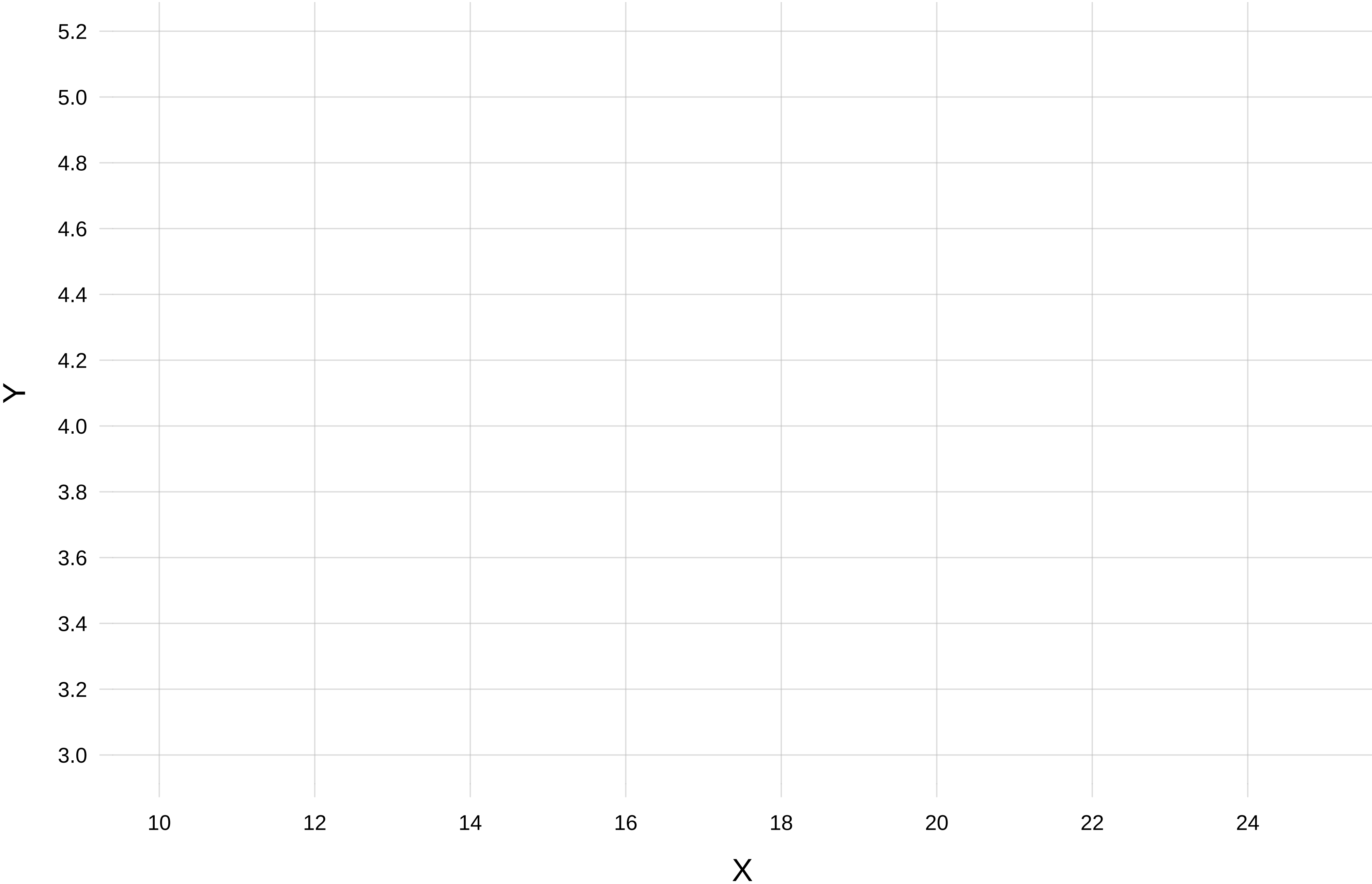
Data source: ADNI Alzheimer's Disease Neuroimaging Initiative

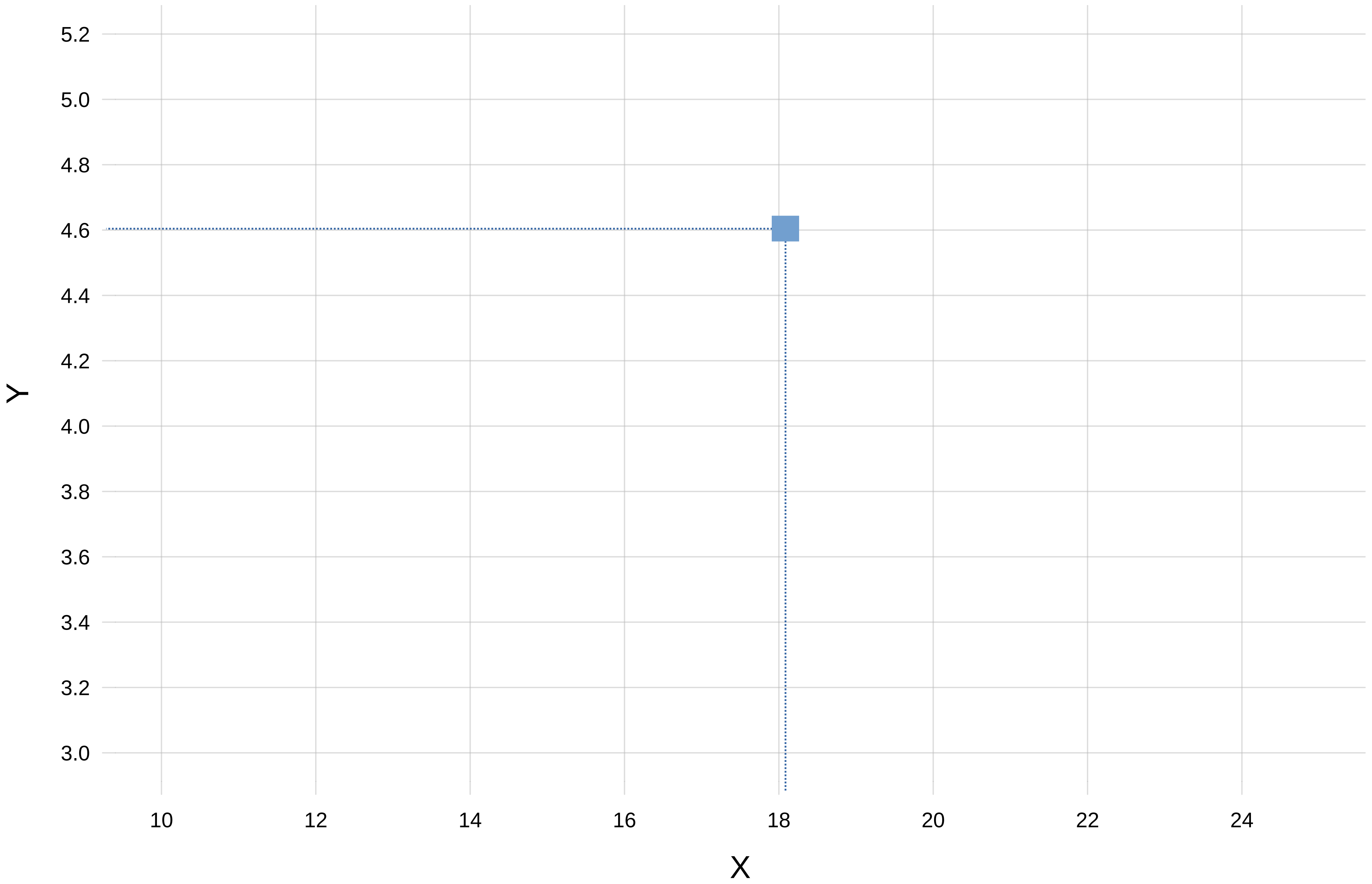
Ingrid's study: $12+1$ variates, 678 datapoints

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

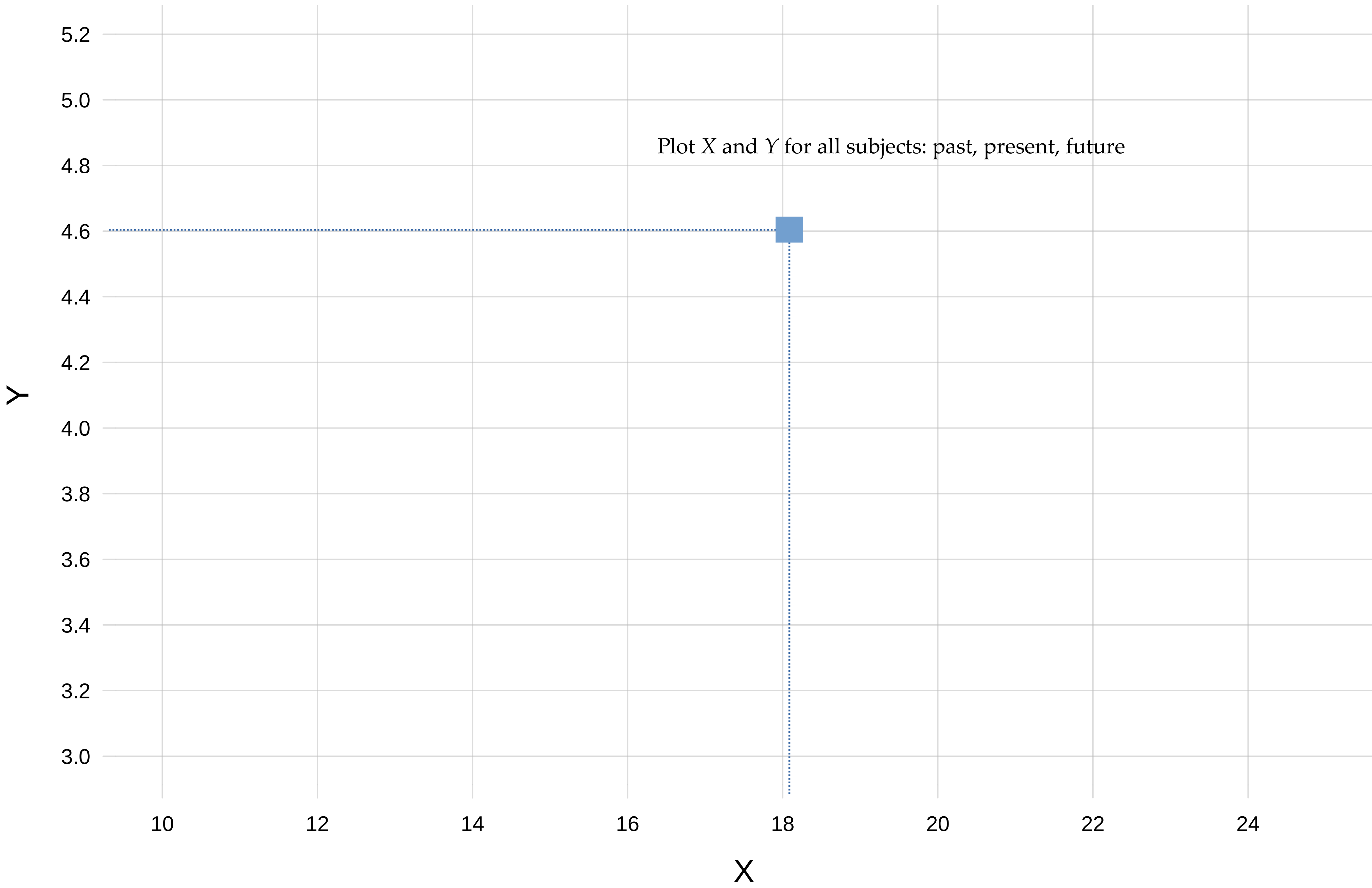
Computation time: ~65 h/study (3 parallel sessions to assess numeric convergence)

HPC UNINETT Sigma2

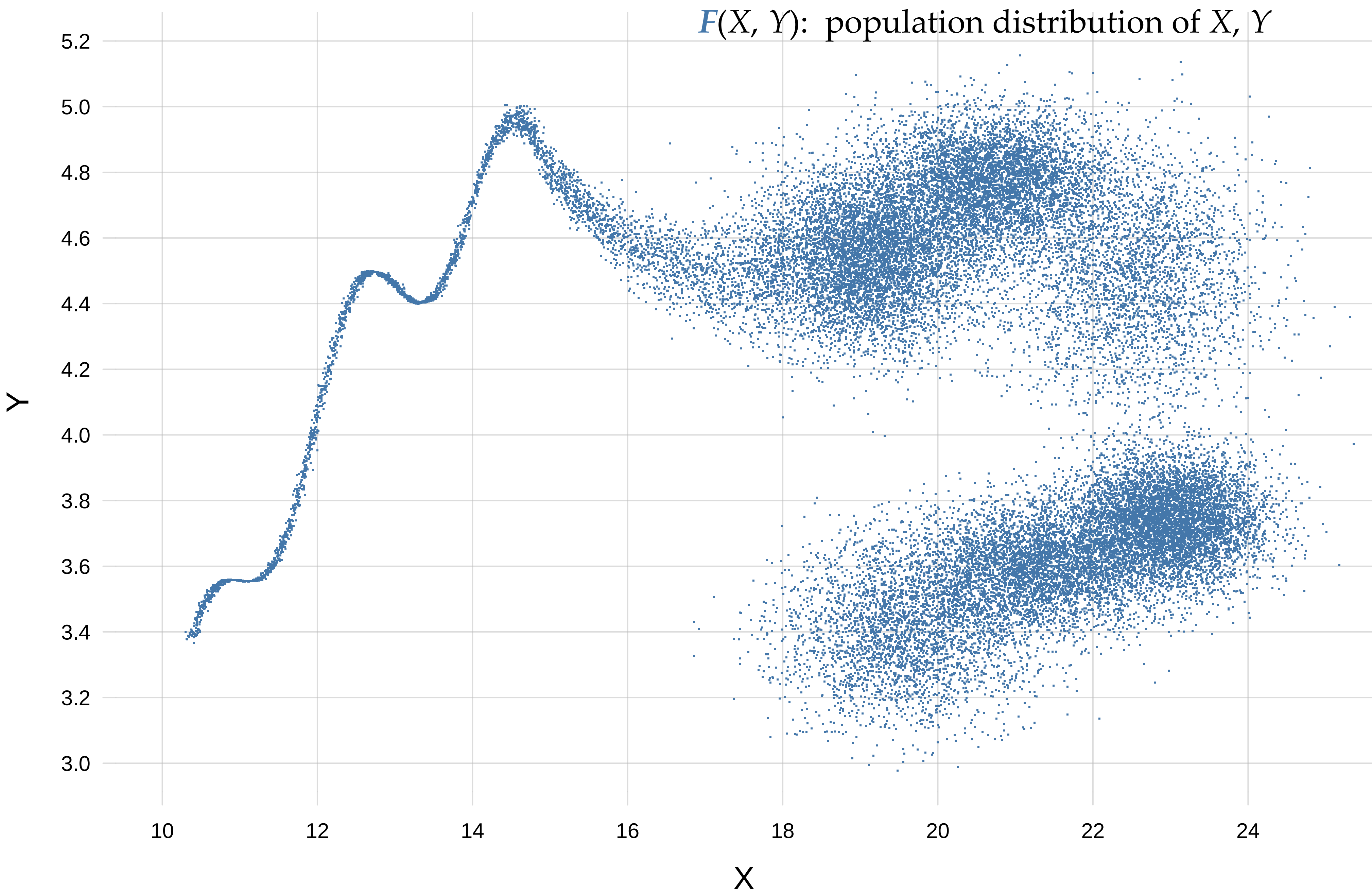

5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
Y
10
12
14
16
18
20
22
24
X



5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
Y
10
12
14
16
18
20
22
24
X

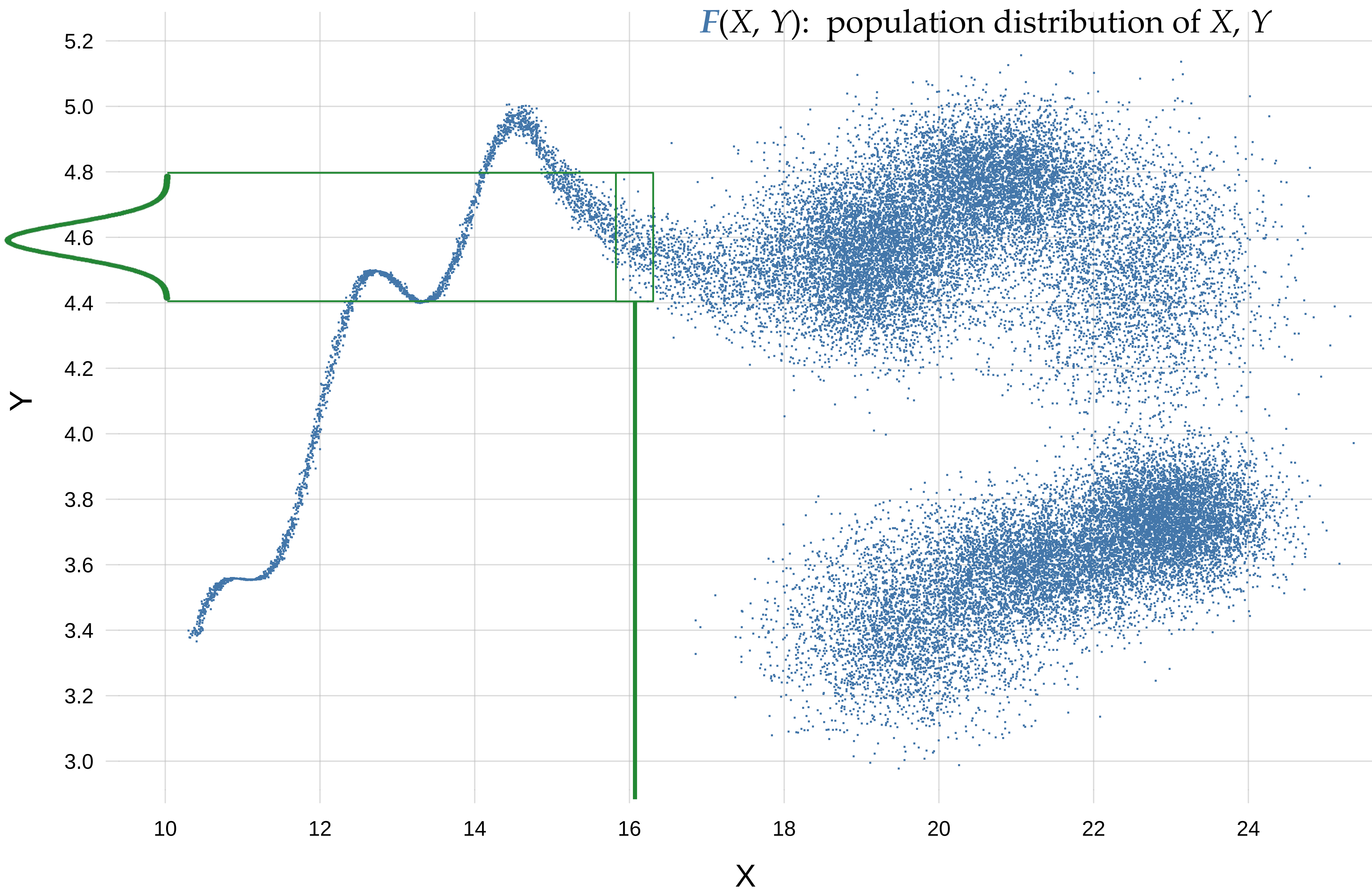


Plot X and Y for all subjects: past, present, future
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
Y
10
12
14
16
18
20
22
24
X

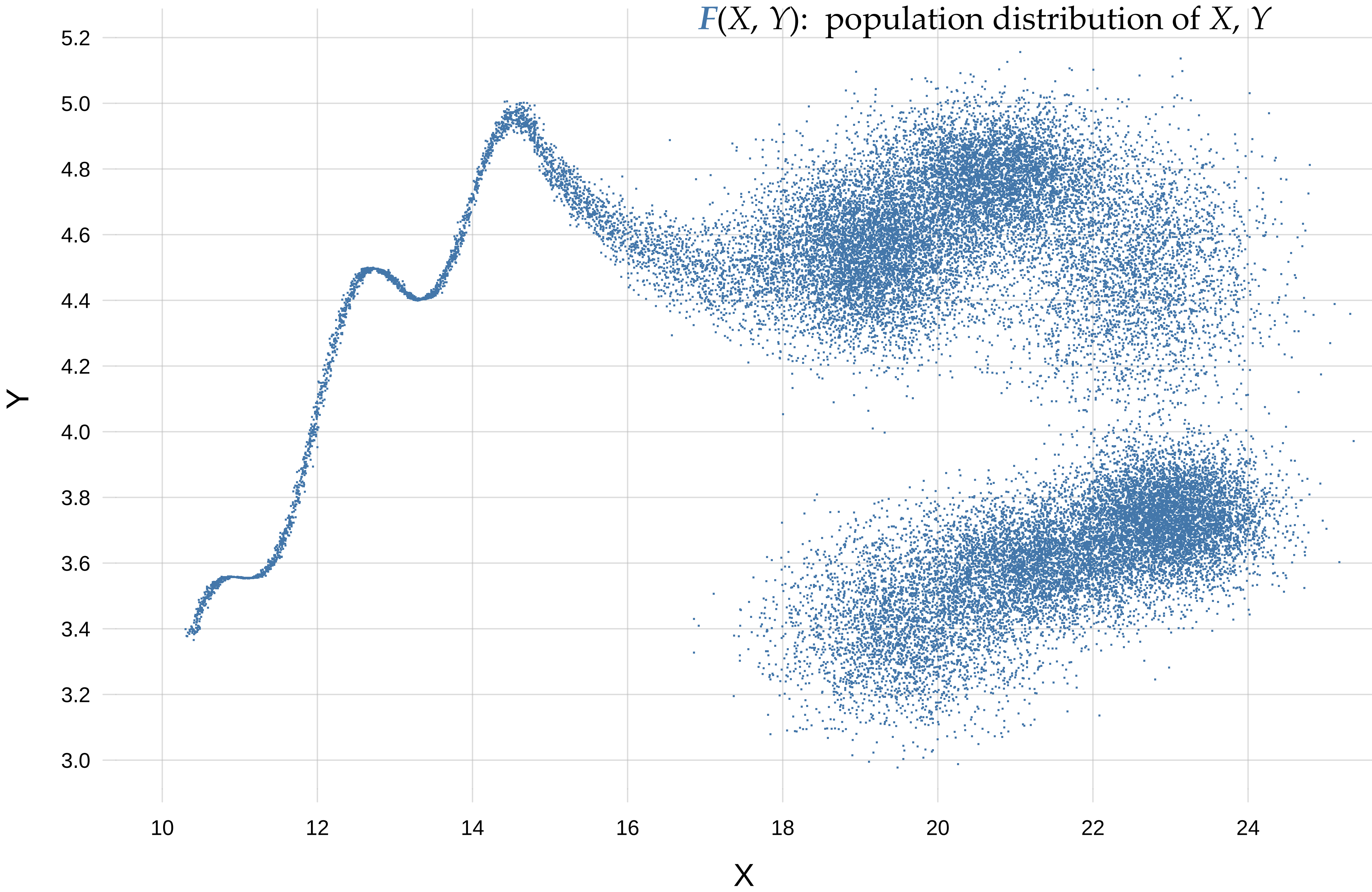

$F(X, Y)$: population distribution of X, Y
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
Y
10
12
14
16
18
20
22
24
X

New patient: $X = 16$

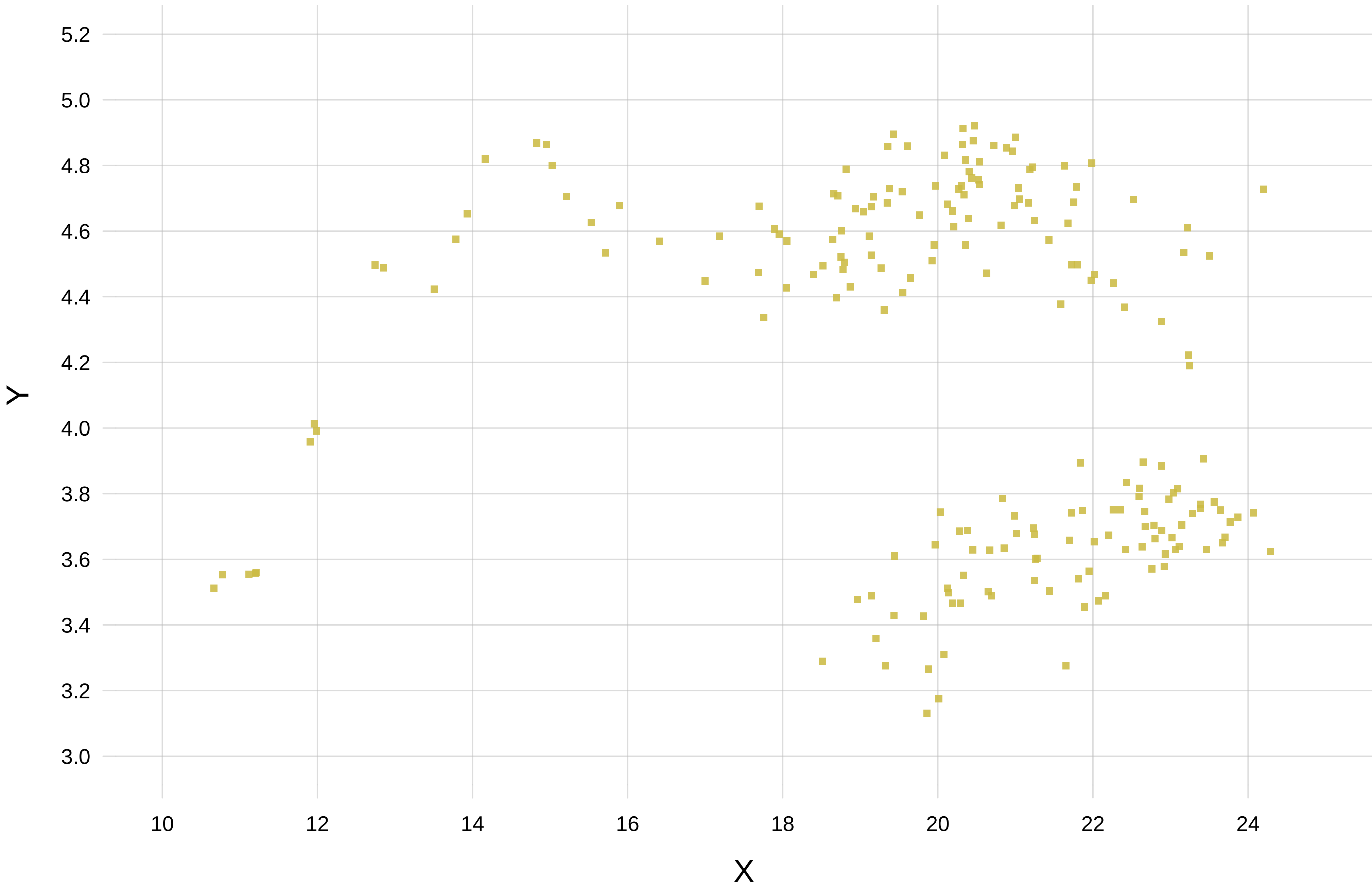
$\Rightarrow \quad Y \approx 4.5\text{–}4.7$



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



$F(X, Y)$: population distribution of X, Y
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
Y
10
12
14
16
18
20
22
24
X


Y
X
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
10
12
14
16
18
20
22
24

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

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

probability = average over all possible population distributions

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

probability = average over all possible population distributions

$$p(F \mid \text{data})$$

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

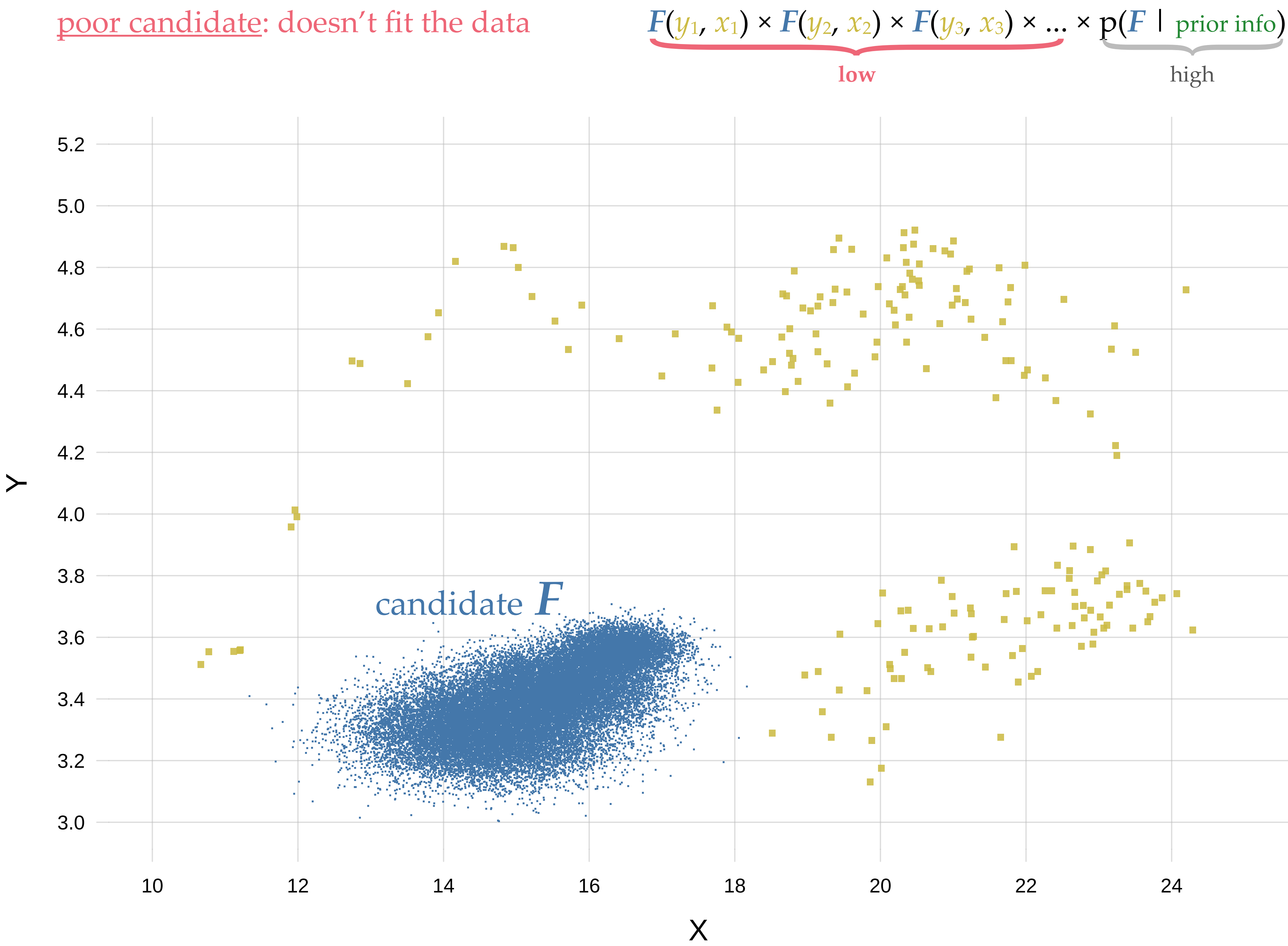
probability = average over all possible population distributions

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

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

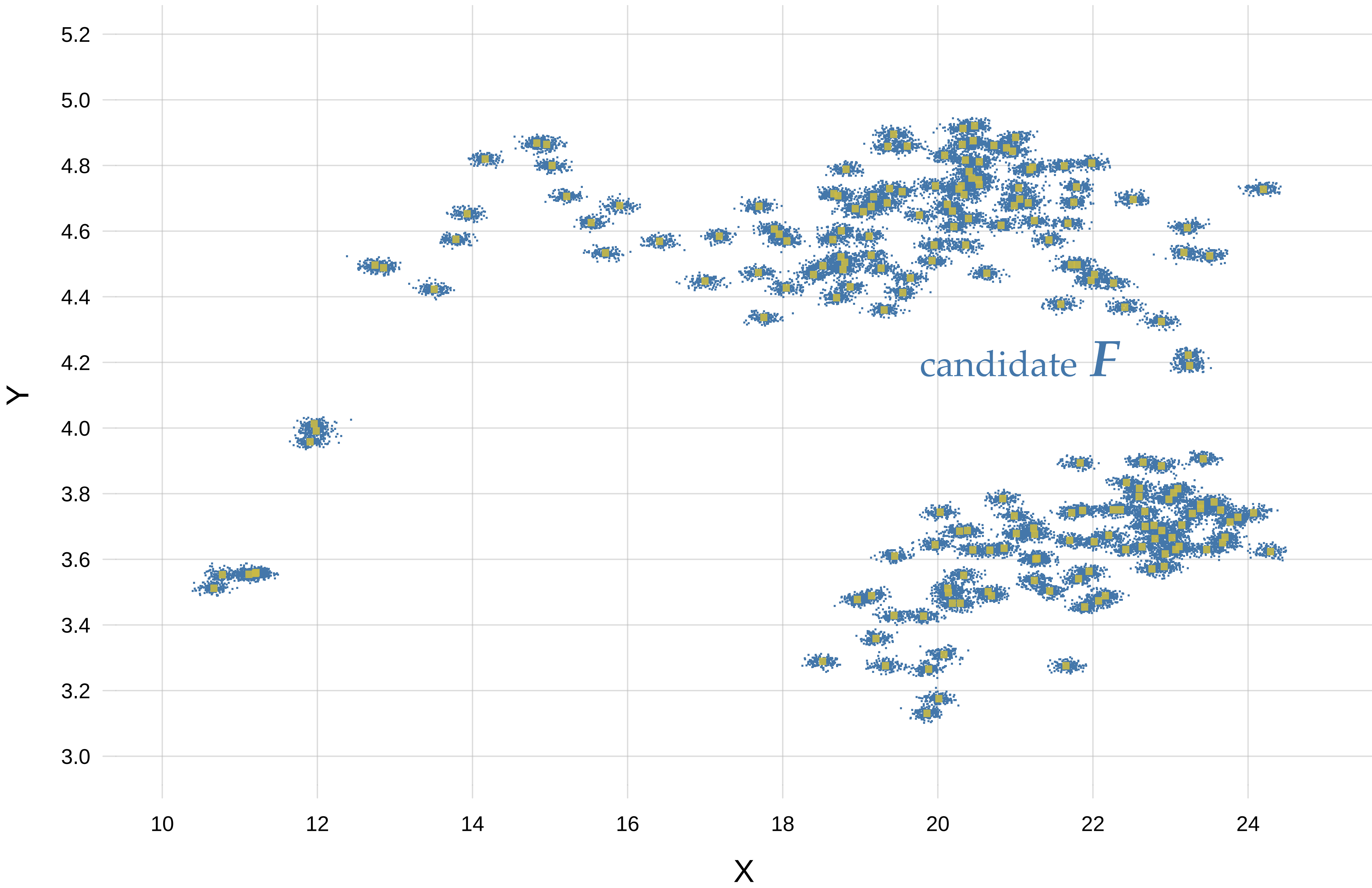
probability = average over all possible population distributions

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


poor candidate: doesn't fit the data
$F(y_1, x_1) \times F(y_2, x_2) \times F(y_3, x_3) \times \ldots \times p(F \mid \text{prior info})$
low
high
candidate F
Y
X
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
10
12
14
16
18
20
22
24

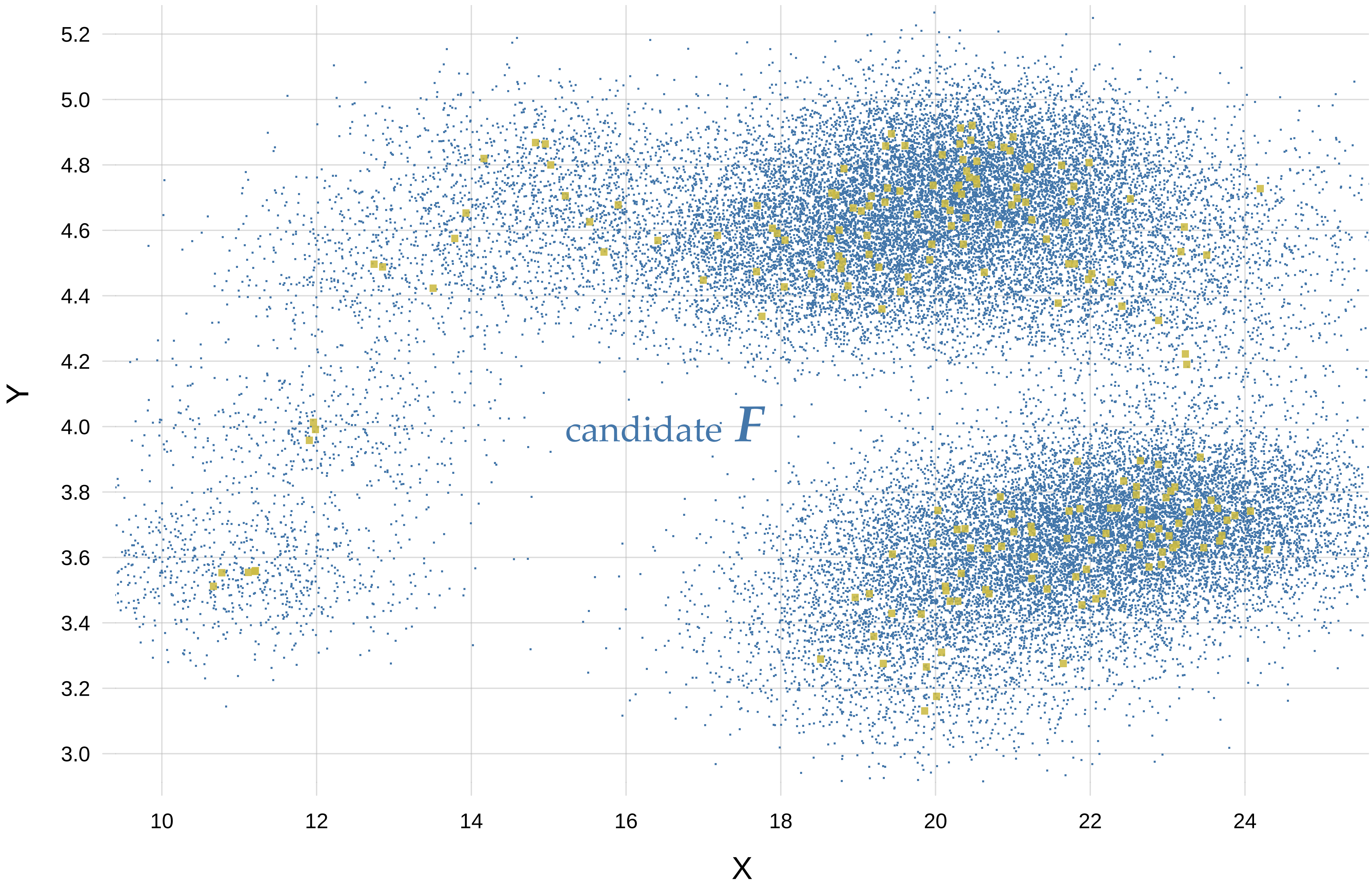
poor candidate: biologically implausible

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



reasonable candidate

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

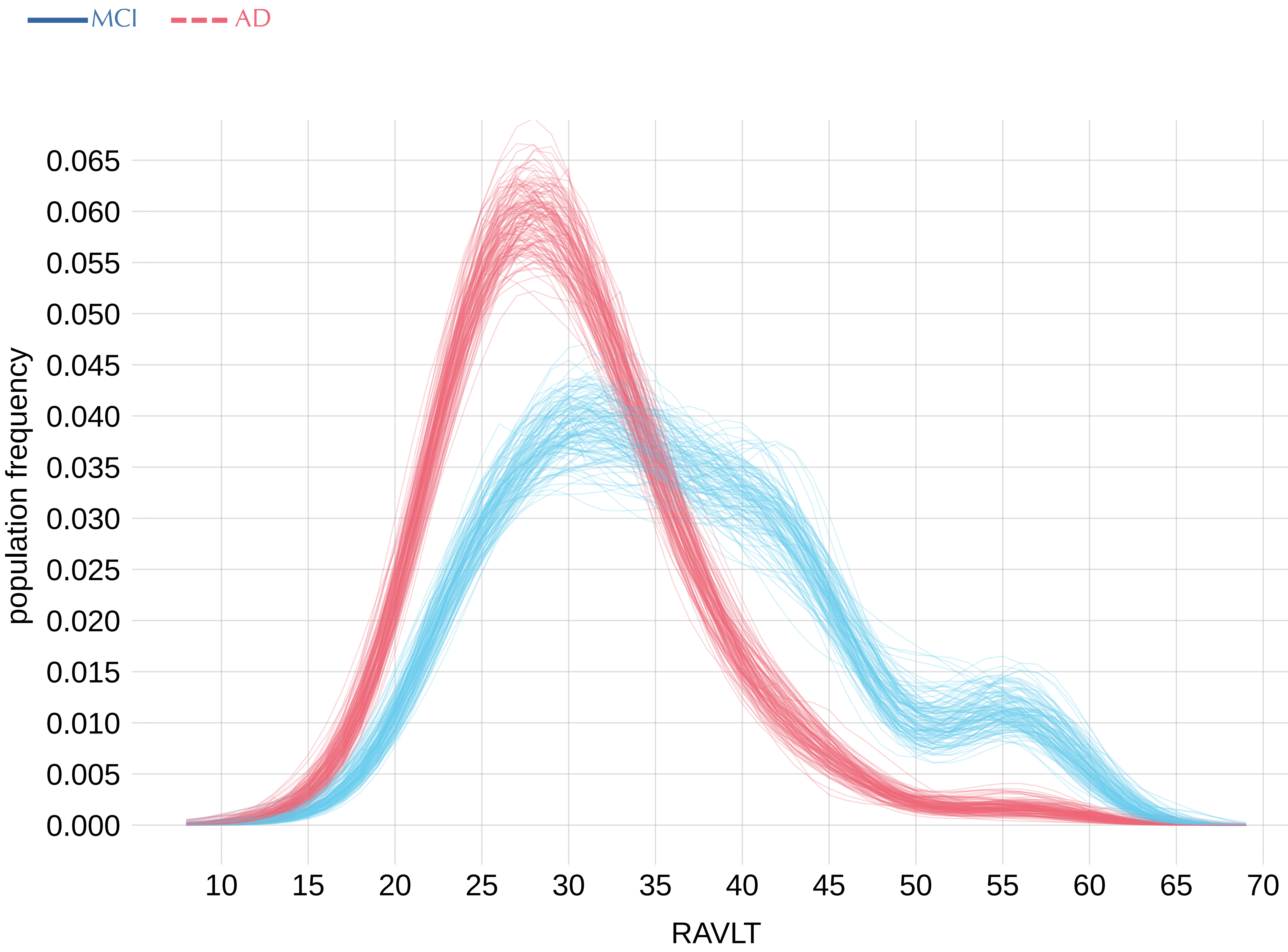


intuition $\longrightarrow$ *mathematics*

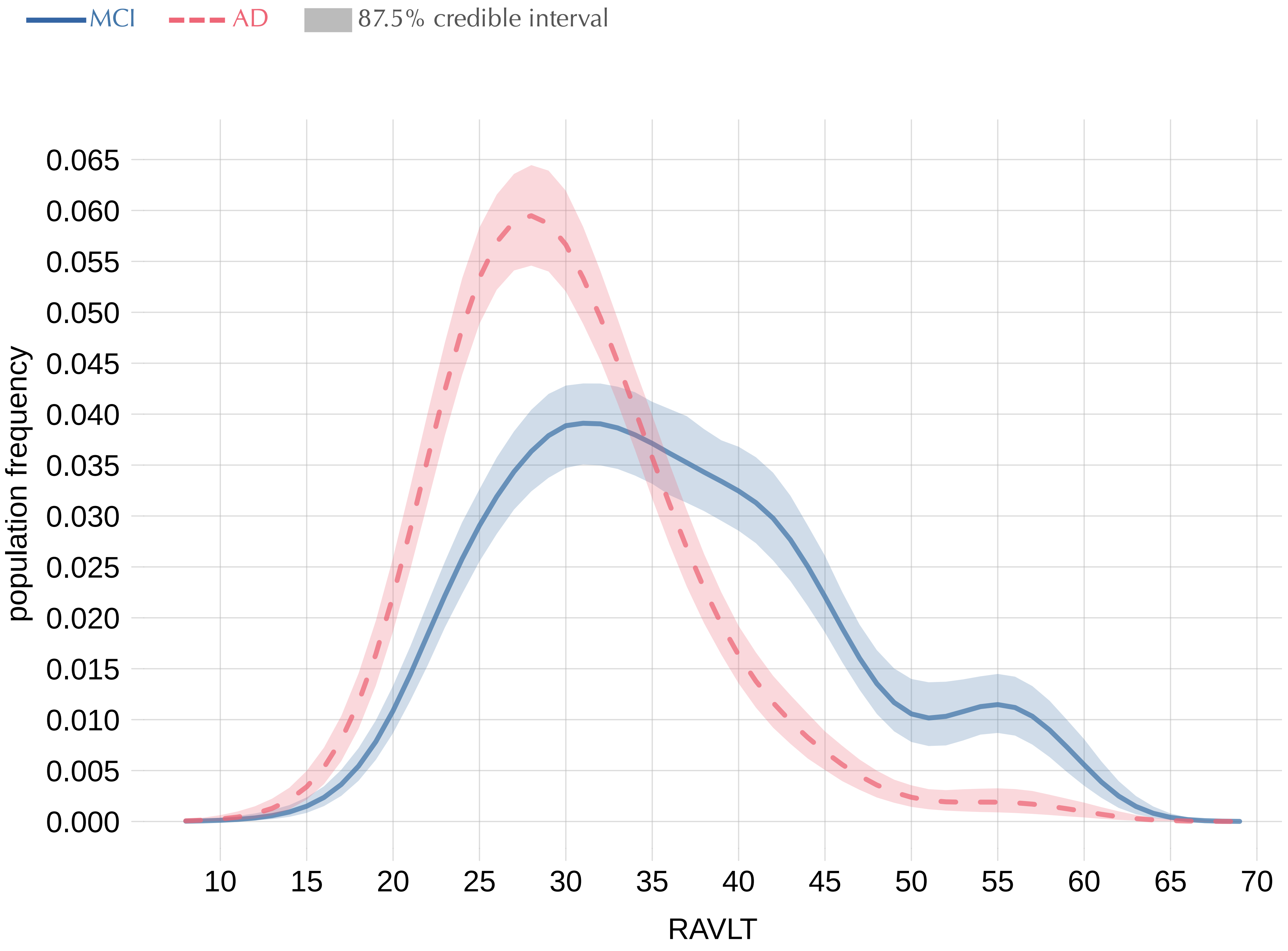
~~*intuition* $\longrightarrow$ *mathematics*~~

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

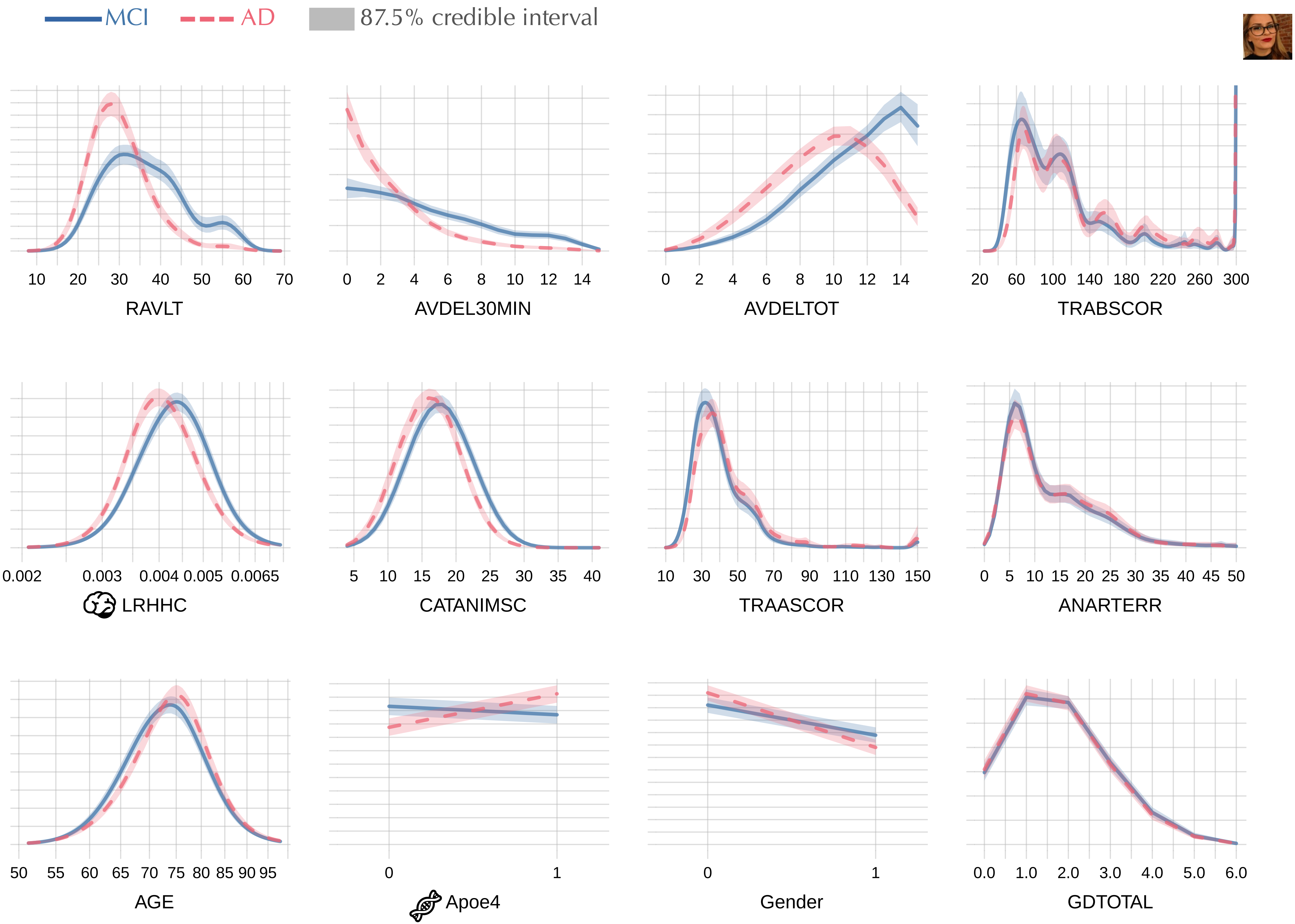
('Bayesian')

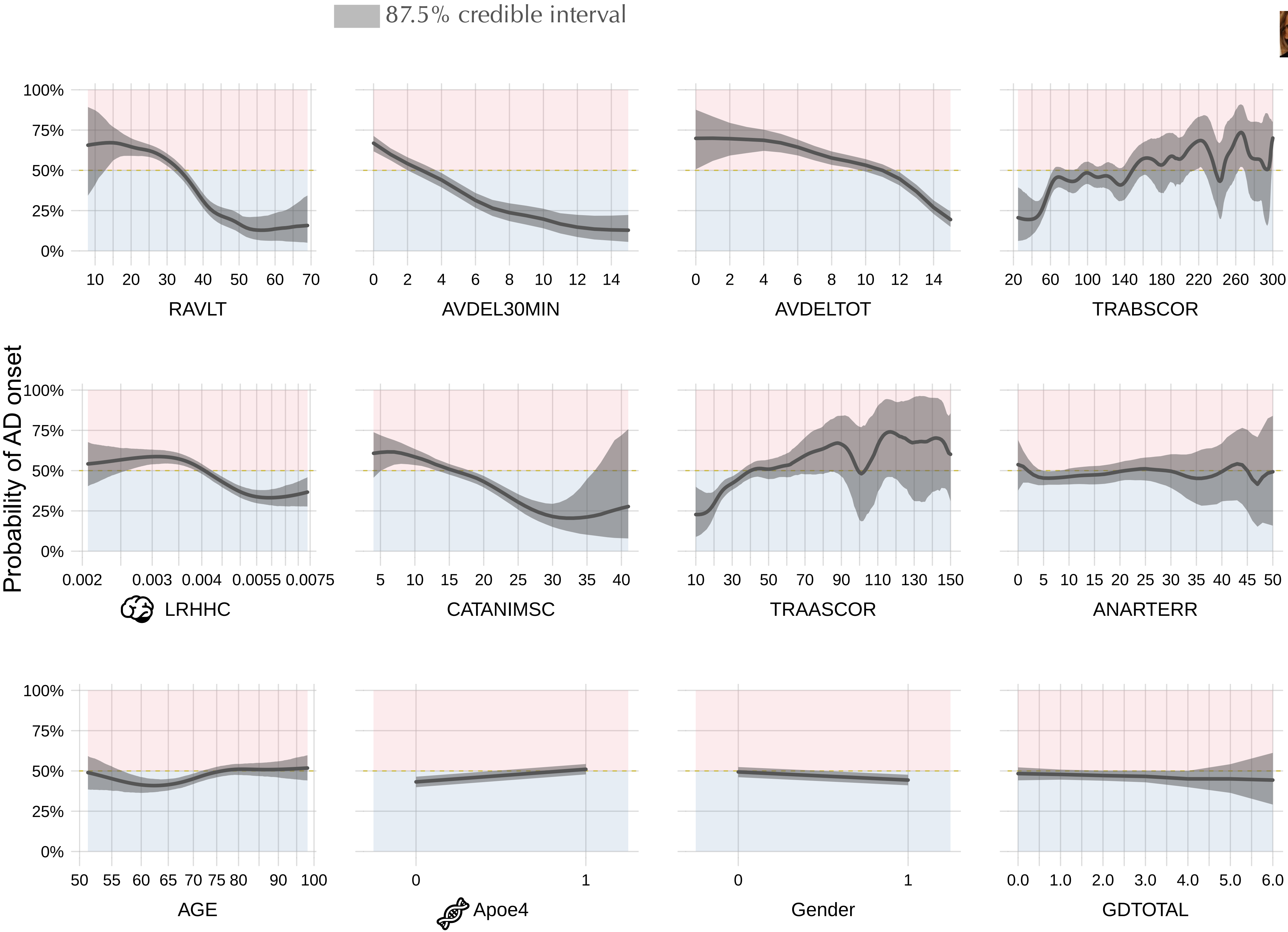


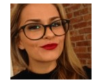
MCI
AD
population frequency
0.065
0.060
0.055
0.050
0.045
0.040
0.035
0.030
0.025
0.020
0.015
0.010
0.005
0.000
10
15
20
25
30
35
40
45
50
55
60
65
70
RAVLT

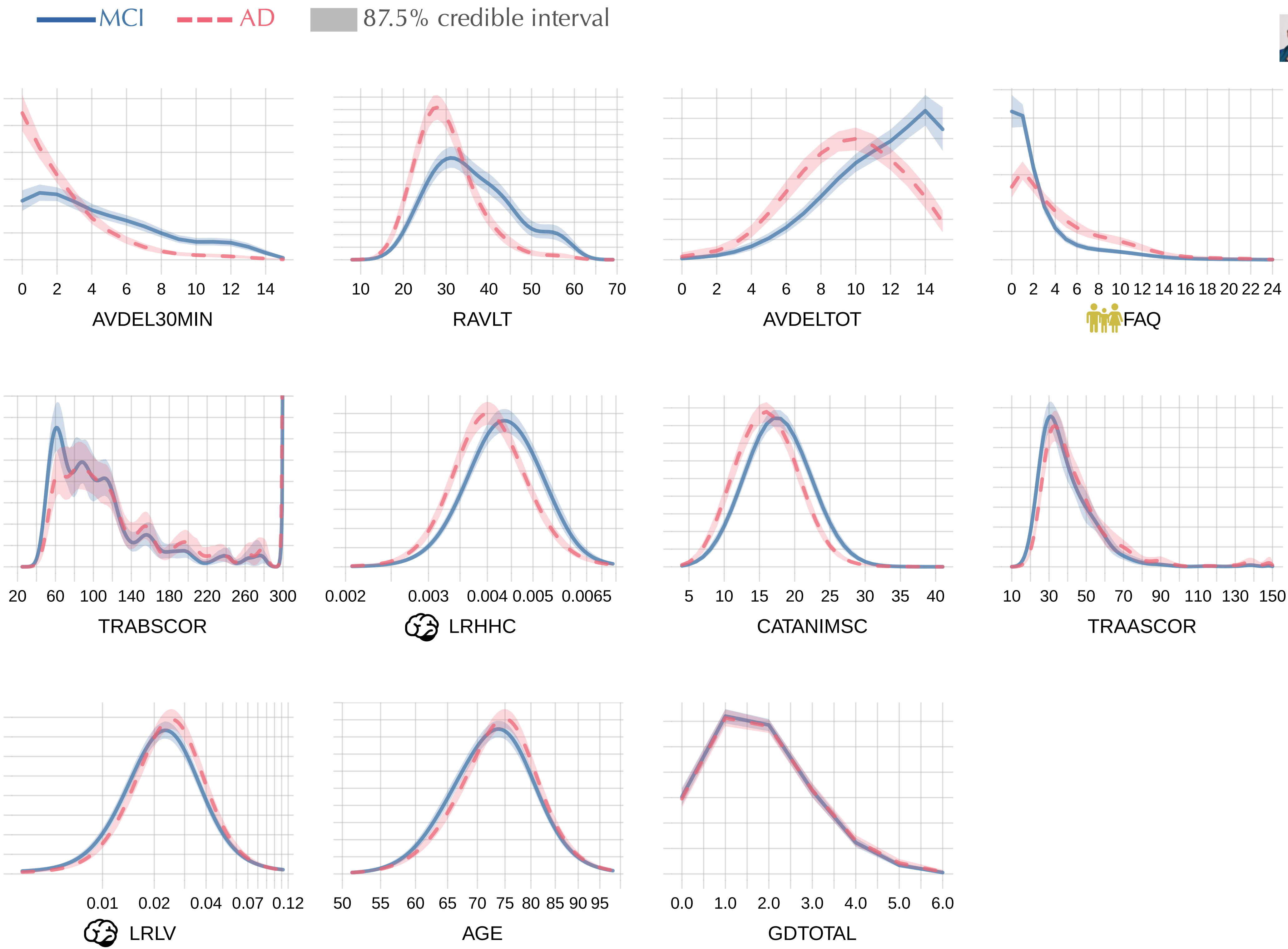


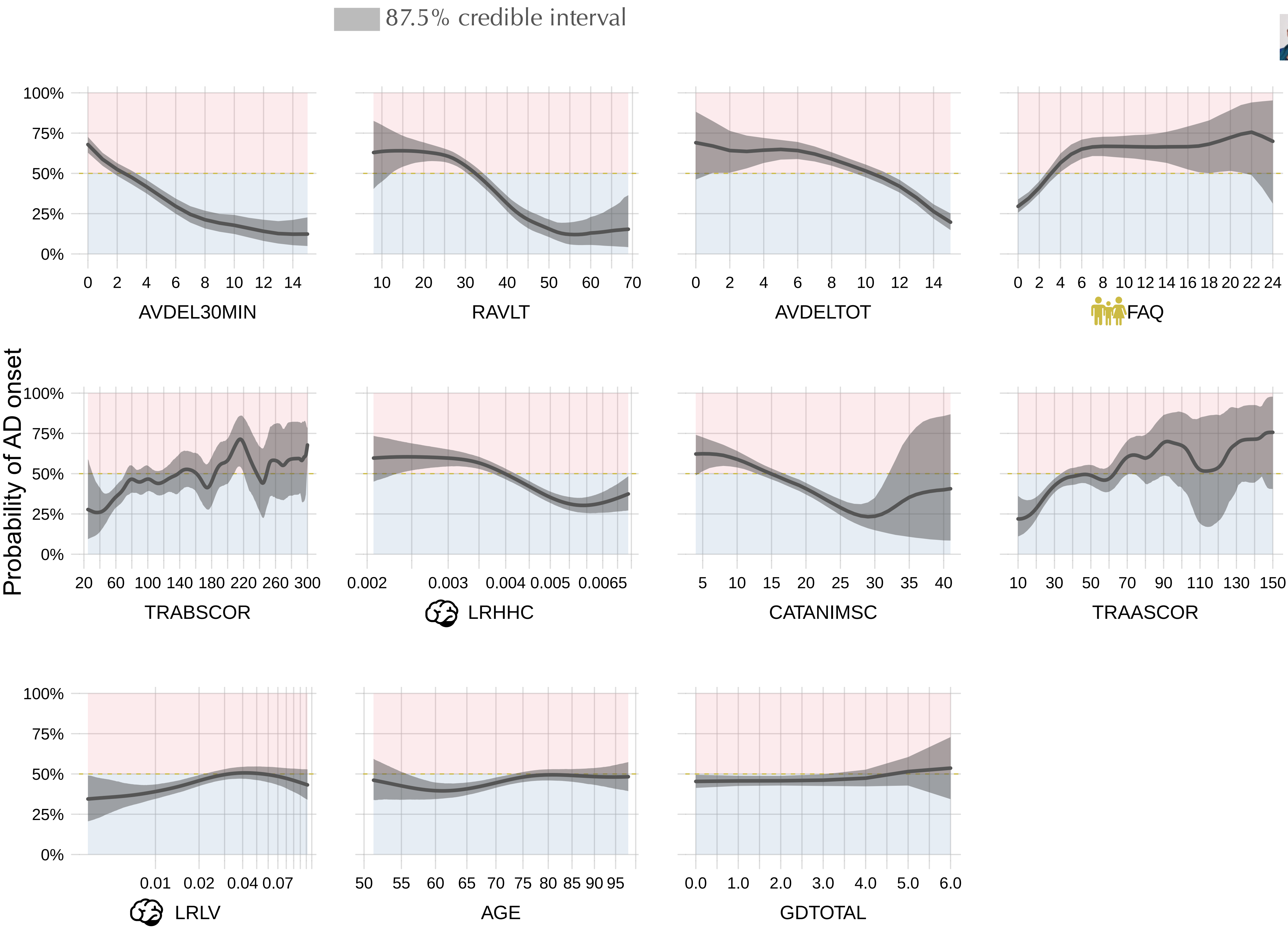
MCI
AD
87.5% credible interval
population frequency
RAVLT
0.065
0.060
0.055
0.050
0.045
0.040
0.035
0.030
0.025
0.020
0.015
0.010
0.005
0.000
10
15
20
25
30
35
40
45
50
55
60
65
70


MCI
AD
87.5% credible interval
10 20 30 40 50 60 70
RAVLT
0 2 4 6 8 10 12 14
AVDEL30MIN
0 2 4 6 8 10 12 14
AVDELTOT
20 60 100 140 180 220 260 300
TRABSCOR
0.002 0.003 0.004 0.005 0.0065
LRHHC
5 10 15 20 25 30 35 40
CATANIMSC
10 30 50 70 90 110 130 150
TRAASCOR
0 5 10 15 20 25 30 35 40 45 50
ANARTERR
50 55 60 65 70 75 80 85 90 95
AGE
0 1
Apoe4
0 1
Gender
0.0 1.0 2.0 3.0 4.0 5.0 6.0
GDTOTAL


87.5% credible interval
Probability of AD onset
RAVLT
AVDEL30MIN
AVDELTOT
TRABSCOR
LRHHC
CATANIMSC
TRAASCOR
ANARTERR
AGE
Apoe4
Gender
GDTOTAL




MCI
AD
87.5% credible interval
0 2 4 6 8 10 12 14
AVDEL30MIN
10 20 30 40 50 60 70
RAVLT
0 2 4 6 8 10 12 14
AVDELTOT
0 2 4 6 8 10 12 14 16 18 20 22 24
FAQ
20 60 100 140 180 220 260 300
TRABSCOR
0.002 0.003 0.004 0.005 0.0065
LRHHC
5 10 15 20 25 30 35 40
CATANIMSC
10 30 50 70 90 110 130 150
TRAASCOR
0.01 0.02 0.04 0.07 0.12
LRLV
50 55 60 65 70 75 80 85 90 95
AGE
0.0 1.0 2.0 3.0 4.0 5.0 6.0
GDTOTAL


87.5% credible interval
Probability of AD onset
100%
75%
50%
25%
0%
0 2 4 6 8 10 12 14
AVDEL30MIN
10 20 30 40 50 60 70
RAVLT
0 2 4 6 8 10 12 14
AVDELTOT
0 2 4 6 8 10 12 14 16 18 20 22 24
FAQ
20 60 100 140 180 220 260 300
TRABSCOR
0.002 0.003 0.004 0.005 0.0065
LRHHC
5 10 15 20 25 30 35 40
CATANIMSC
10 30 50 70 90 110 130 150
TRAASCOR
0.01 0.02 0.04 0.07
LRLV
50 55 60 65 70 75 80 85 90 95
AGE
0.0 1.0 2.0 3.0 4.0 5.0 6.0
GDTOTAL


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

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**: ???✔✔✔

increasing importance

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**'

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

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

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

Clue **A**: ✓✓✓✓??

Clue **B**: ✓✓✓?✓?

Clue **C**: ???✓✓✓

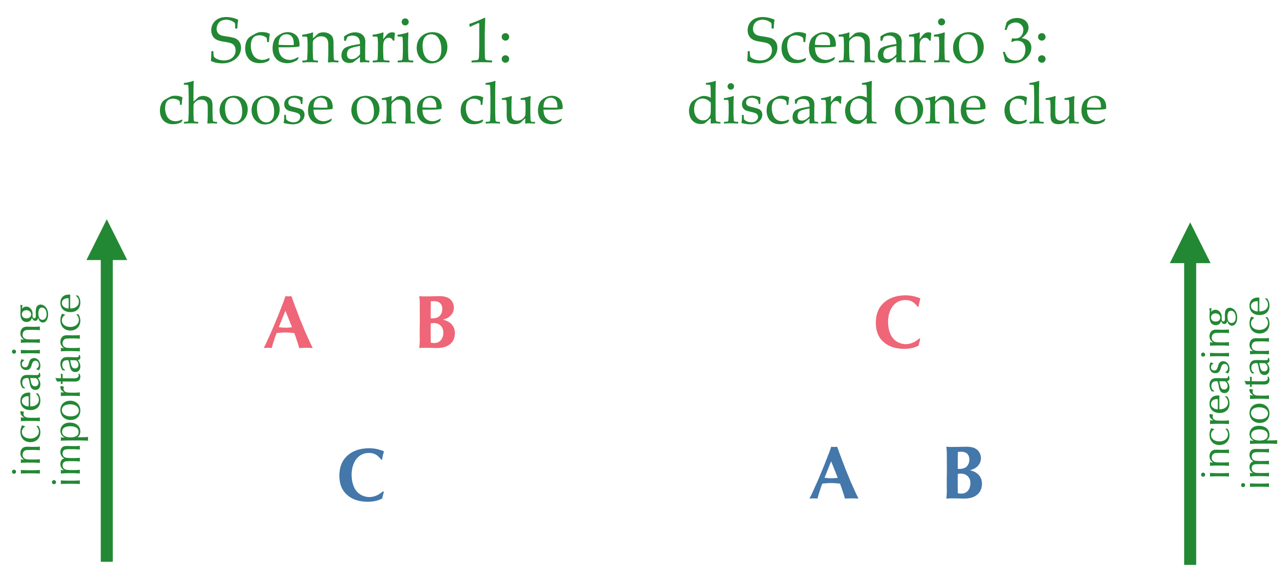
increasing importance

discard **A**: still 100% win

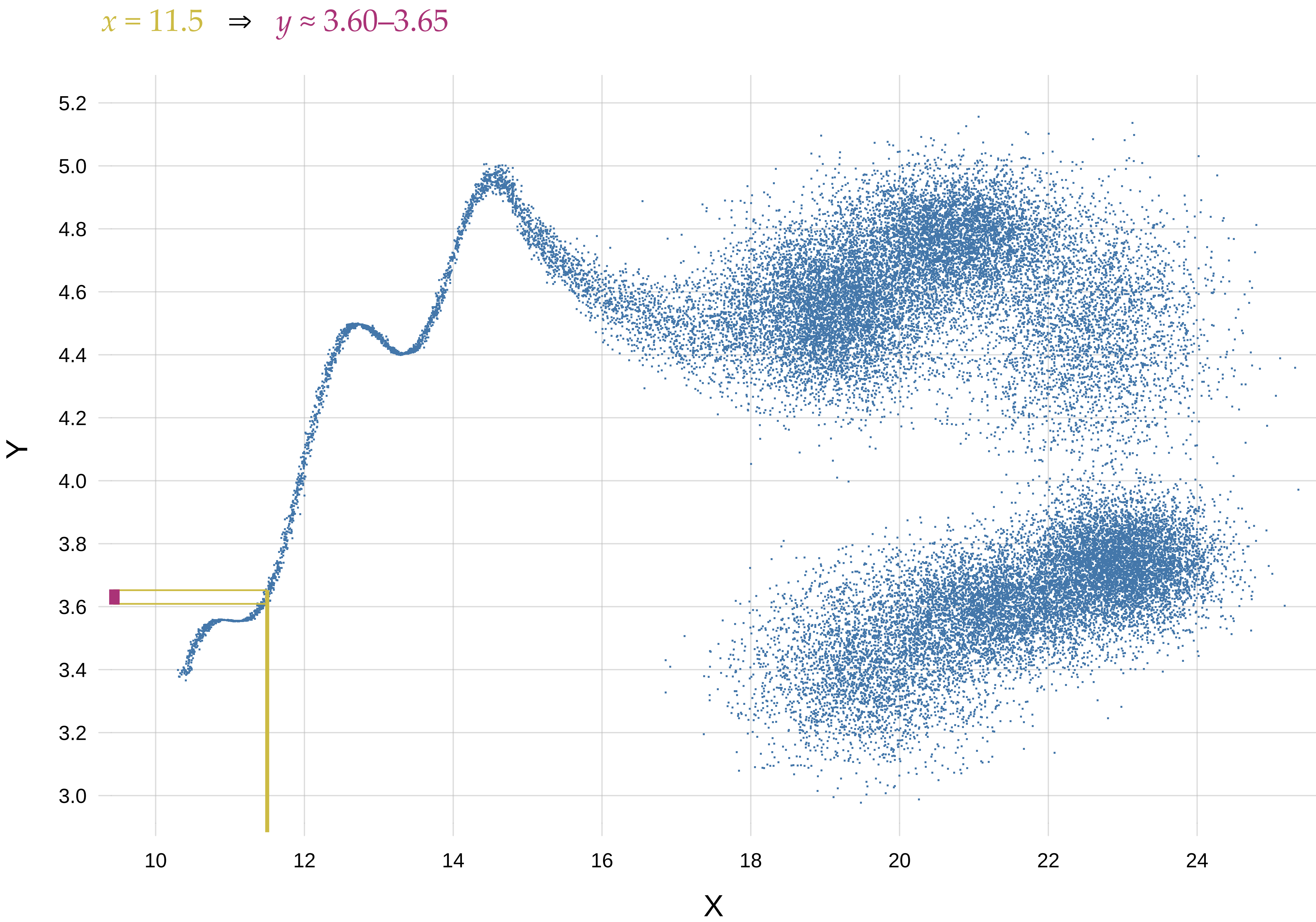
discard **B**: still 100% win

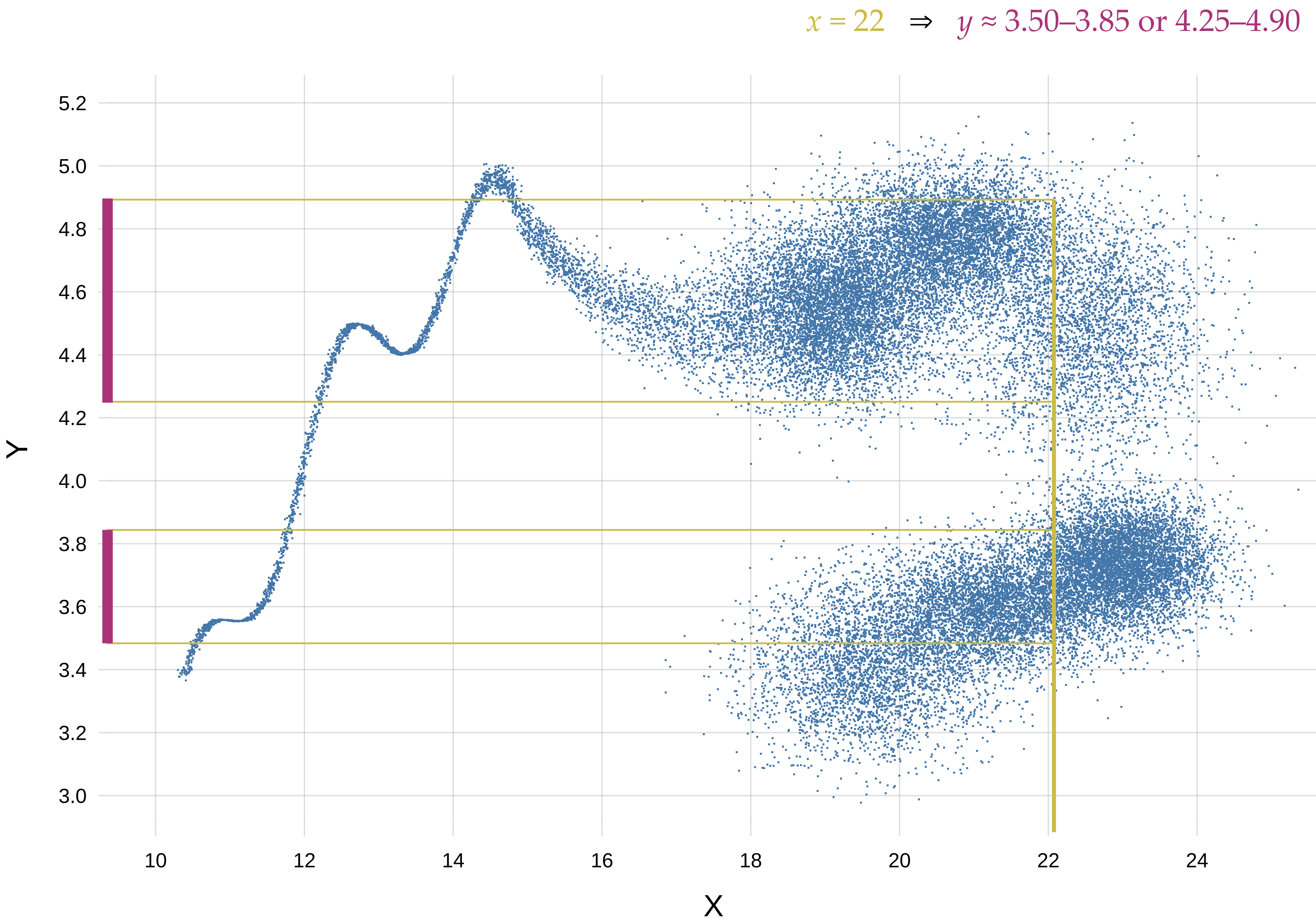
discard **C**: 1/9 winning chance

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


Scenario 1:
choose one clue
Scenario 3:
discard one clue
increasing importance
A
B
C
C
A
B
increasing importance

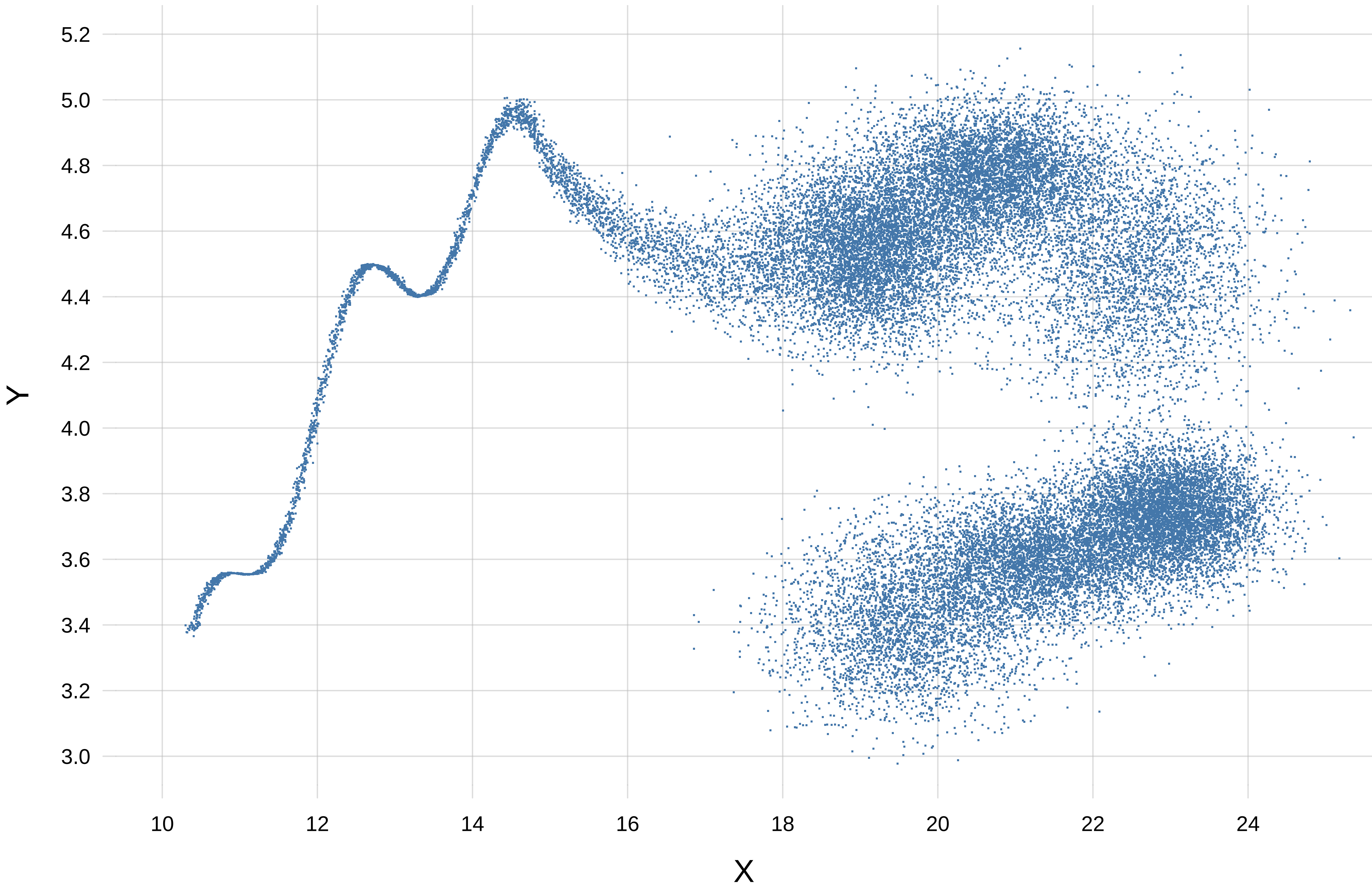
‘Importance’ or ‘predictive power’ is *context-dependent*

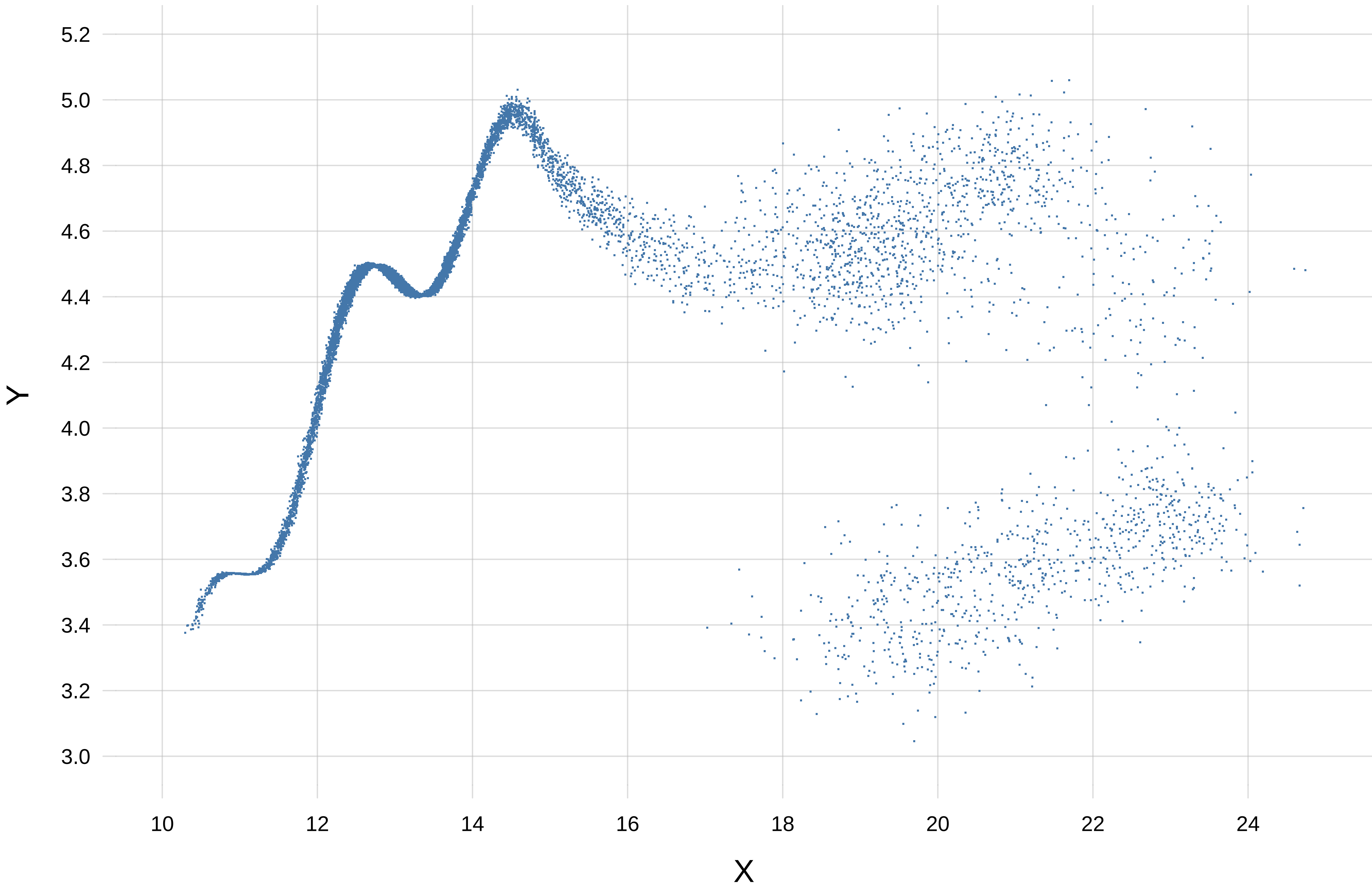

$x = 11.5 \Rightarrow y \approx 3.60–3.65$
Y
X
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
10
12
14
16
18
20
22
24



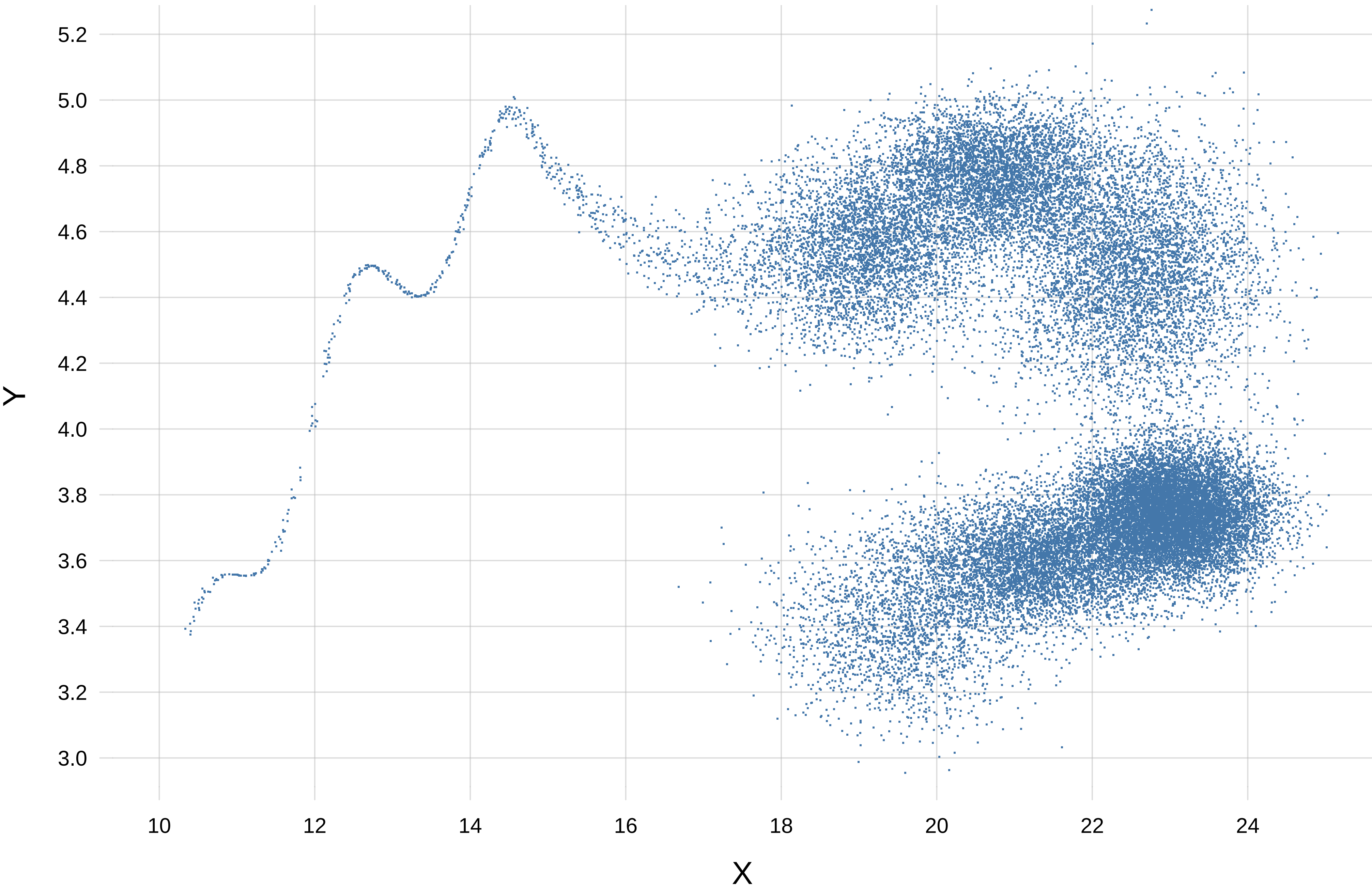
x = 22 ⇒ y ≈ 3.50–3.85 or 4.25–4.90
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
Y
10
12
14
16
18
20
22
24
X

What is the 'overall predictive power' of X?





5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
Y
10
12
14
16
18
20
22
24
X



5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
Y
10
12
14
16
18
20
22
24
X

The ‘predictive power’ of X depends on $\mathrm{P}(X)$

⚠ Careful with ‘balancing’! ⚠

Information Theory

The Bell System Technical Journal

Vol. XXVII *July, 1948* *No. 3*

A Mathematical Theory of Communication

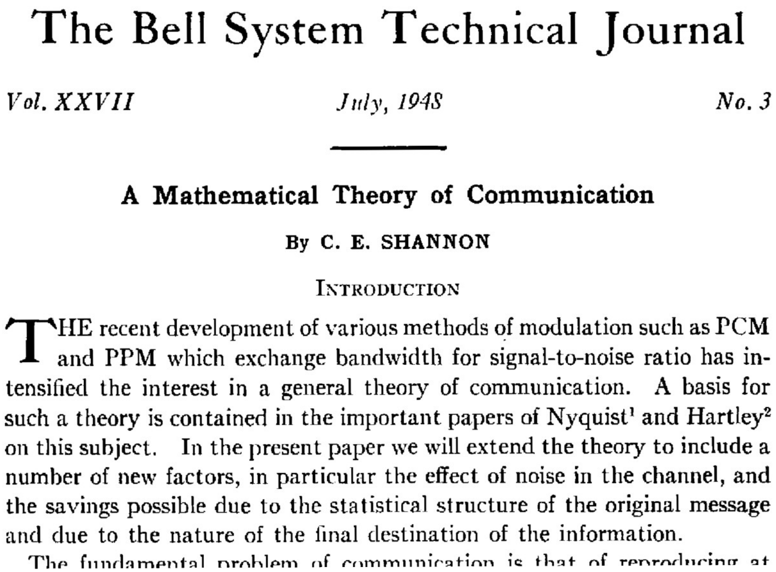
By C. E. SHANNON

Introduction

THE recent development of various methods of modulation such as PCM and PPM which exchange bandwidth for signal-to-noise ratio has intensified the interest in a general theory of communication. A basis for such a theory is contained in the important papers of Nyquist[1] and Hartley[2] on this subject. In the present paper we will extend the theory to include a number of new factors, in particular the effect of noise in the channel, and the savings possible due to the statistical structure of the original message and due to the nature of the final destination of the information.

The fundamental problem of communication is that of reproducing at

Information Theory



The Bell System Technical Journal

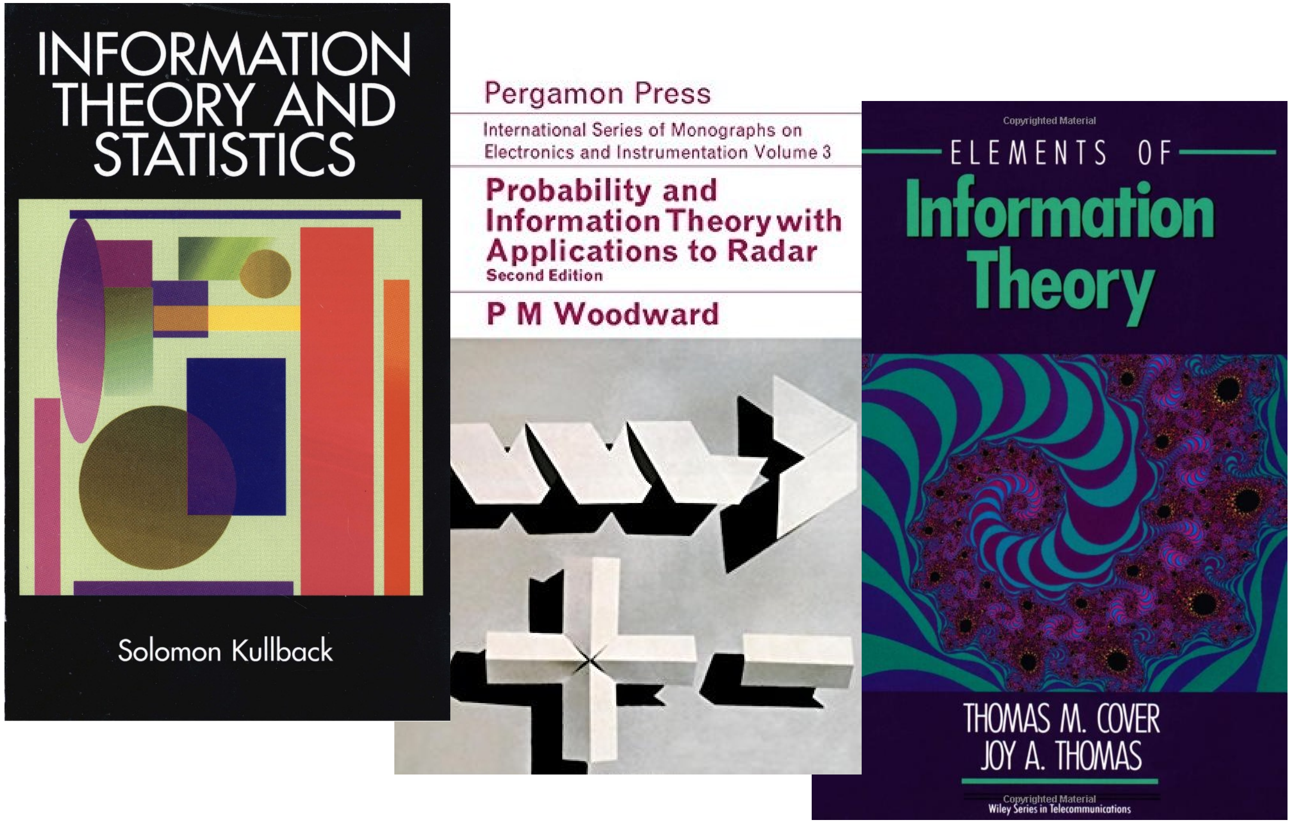
Vol. XXVII July, 1948 No. 3

A Mathematical Theory of Communication

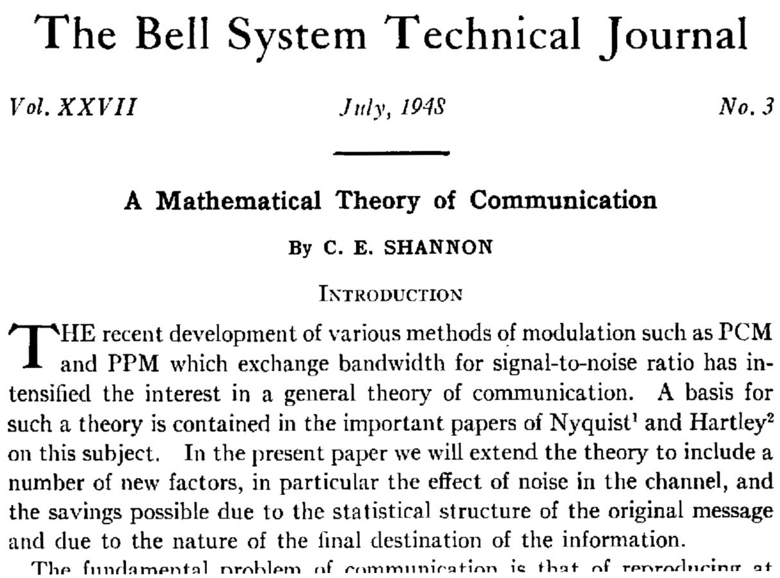
By C. E. SHANNON

INTRODUCTION

THE recent development of various methods of modulation such as PCM and PPM which exchange bandwidth for signal-to-noise ratio has intensified the interest in a general theory of communication. A basis for such a theory is contained in the important papers of Nyquist[1] and Hartley[2] on this subject. In the present paper we will extend the theory to include a number of new factors, in particular the effect of noise in the channel, and the savings possible due to the statistical structure of the original message and due to the nature of the final destination of the information.



Information Theory



The Bell System Technical Journal

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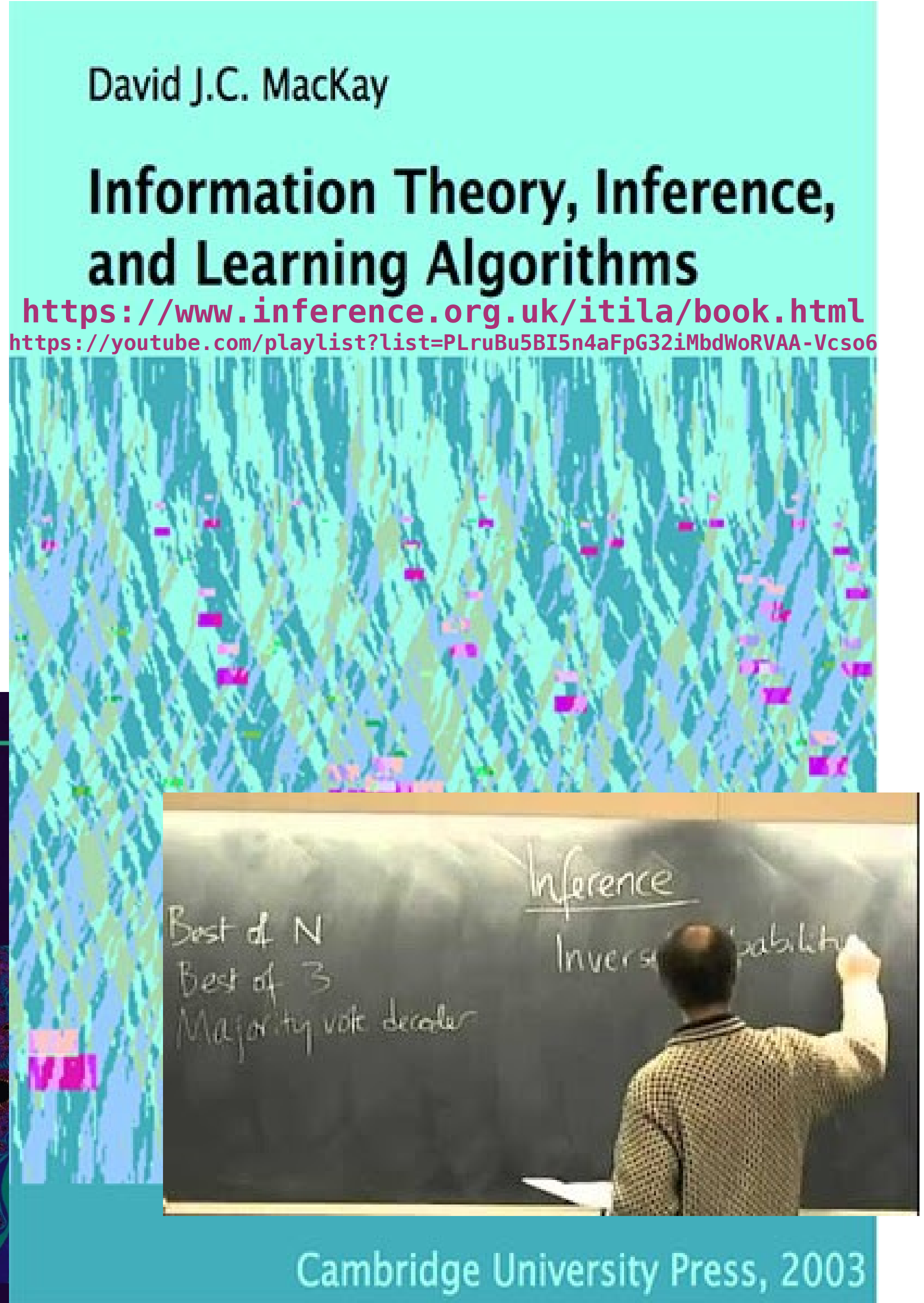
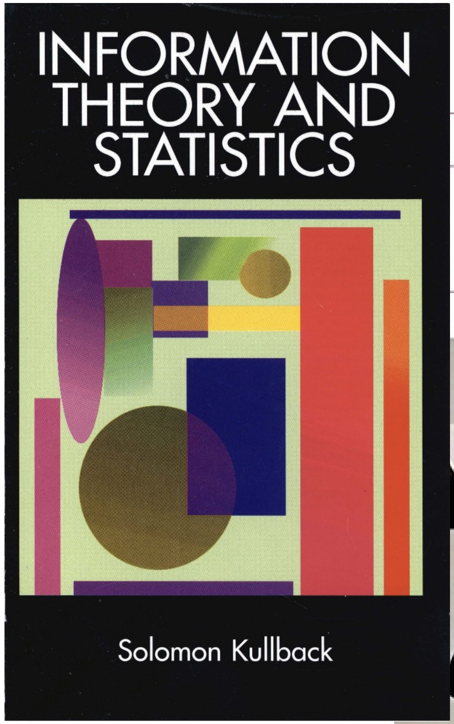
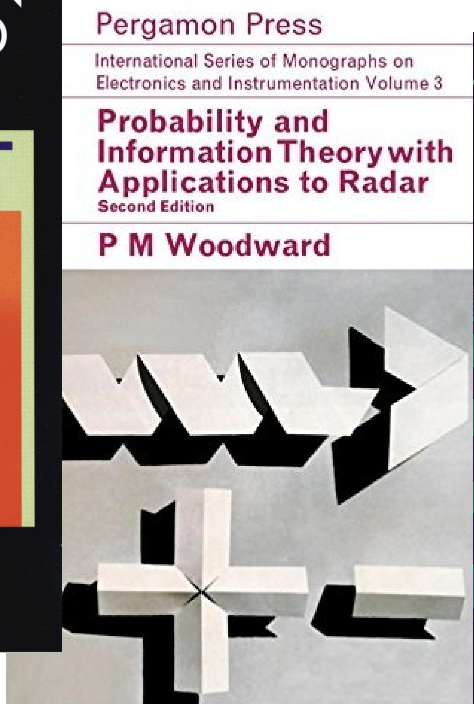
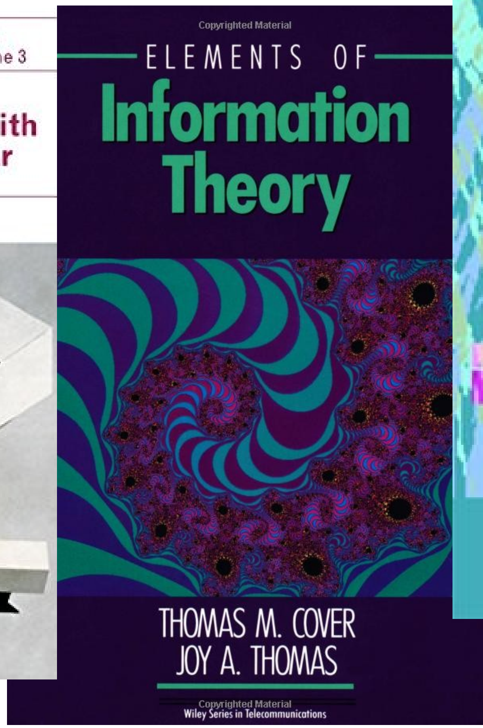
The fundamental problem of communication is that of reproducing at



https://www.inference.org.uk/itila/book.html
https://youtube.com/playlist?list=PLruBu5BI5n4aFpG32iMbdWoRVAA-Vcso6







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

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

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

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

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

IEC 80000-13

Edition 1.0 2008-03

INTERNATIONAL STANDARD

NORME INTERNATIONALE

Quantities and units –
Part 13: Information science and technology

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

IEC 80000-13

Edition 1.0 2008-03

INTERNATIONAL STANDARD

INFORMATION SCIENCE AND TECHNOLOGY — **QUANTITIES**

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

If Y is binary:

$$0\ \mathrm{Sh} \leq I(Y;X) \leq 1\ \mathrm{Sh}$$

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X and Y are independent

Using X is no better than flipping a coin

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Y is a deterministic function of X
X always yields perfect predictions

If Y is binary:

$$\underbrace{0 \text{ Sh}}_{\substack{X \text{ and } Y \text{ are independent} \\ \text{Using } X \text{ is no better than flipping a coin}}} \le I(Y;X) \le \underbrace{1 \text{ Sh}}_{\substack{Y \text{ is a deterministic function of } X \\ X \text{ always yields perfect predictions}}}$$

$$I(Y;X) = 0.22 \text{ Sh}$$

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In $N=100$ new prognoses:

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

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

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

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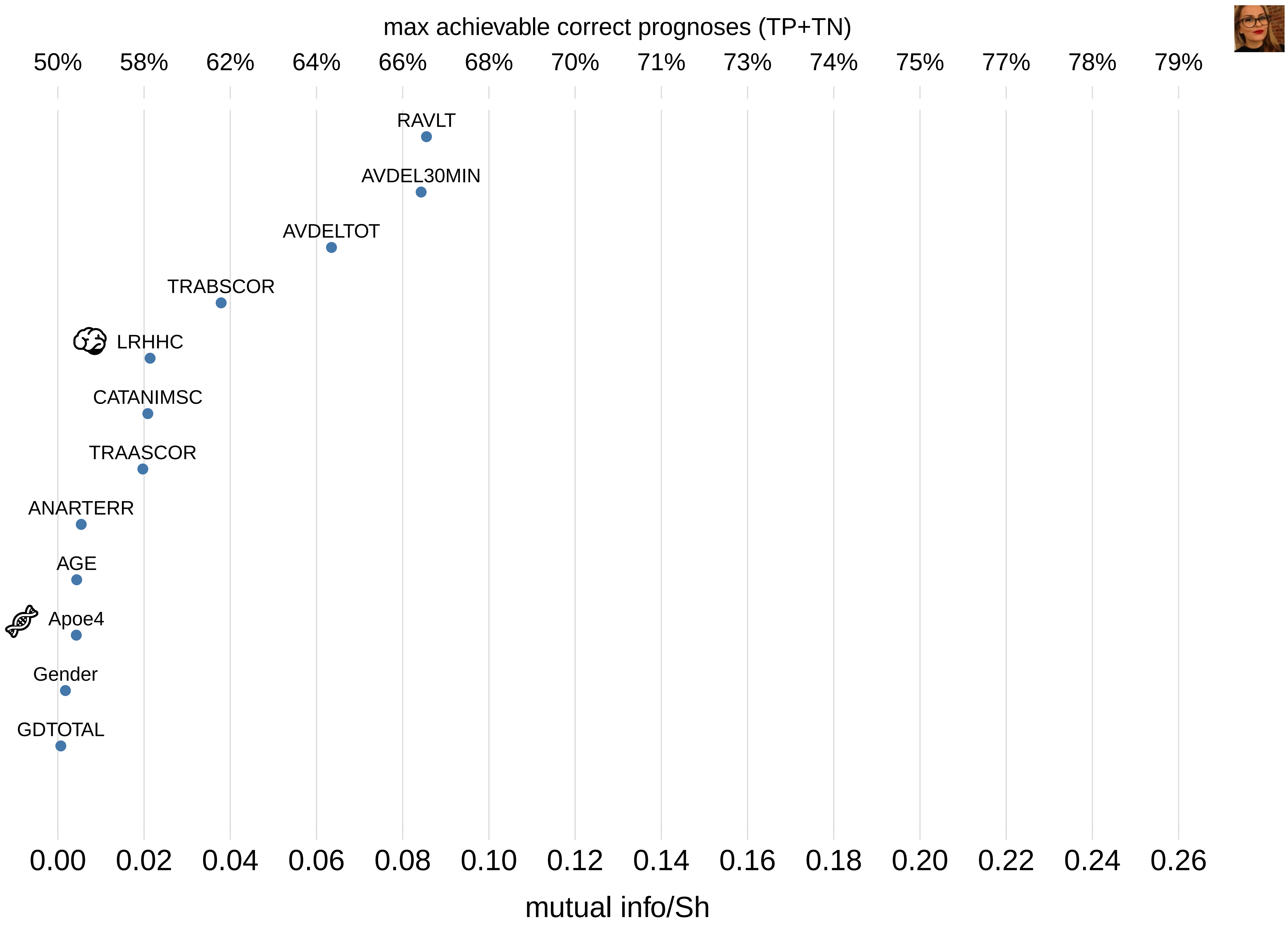
Maximum accuracy attainable
by *any* algorithm which uses only feature set X


max achievable correct prognoses (TP+TN)
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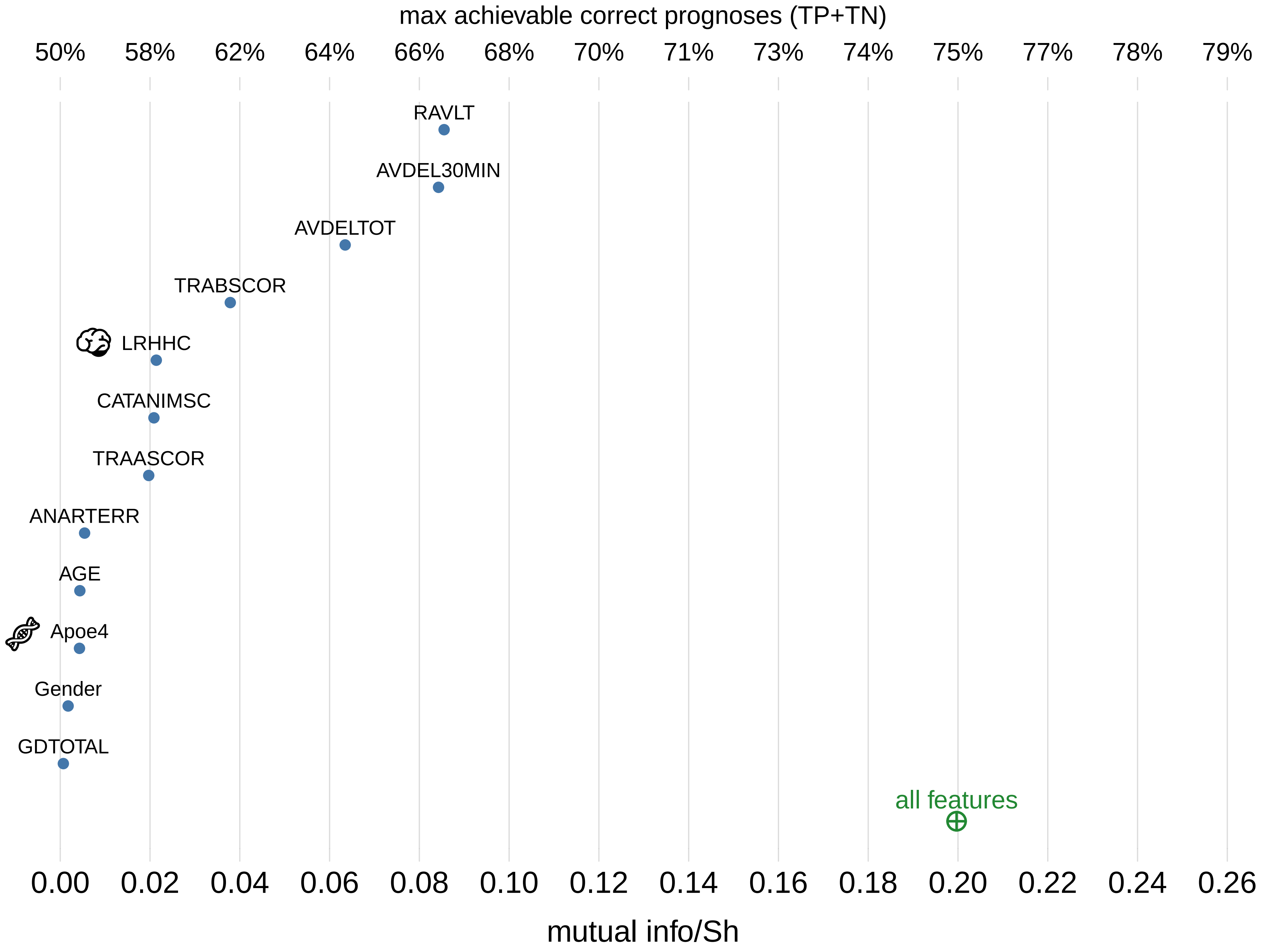
mutual info/Sh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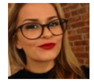

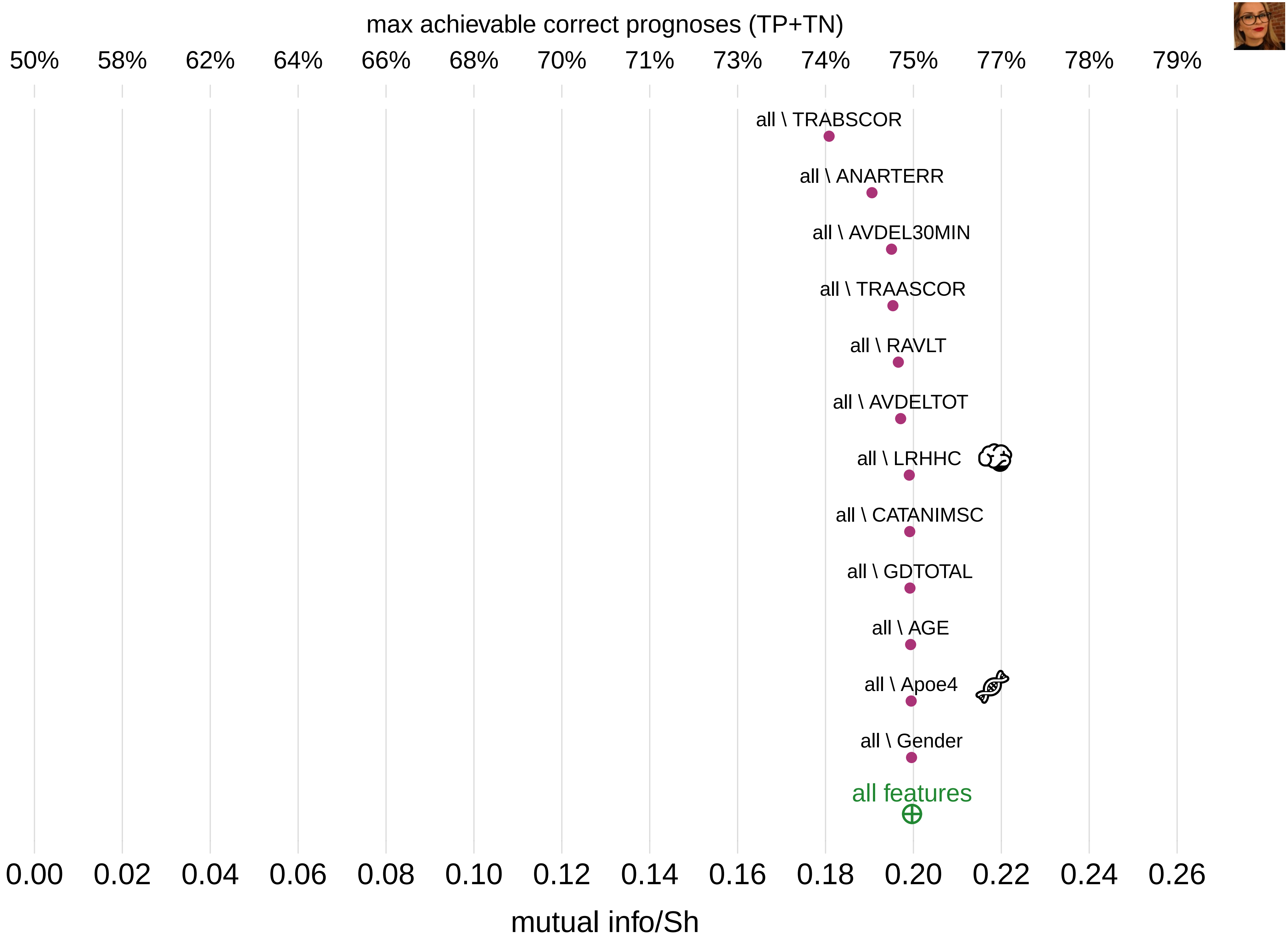
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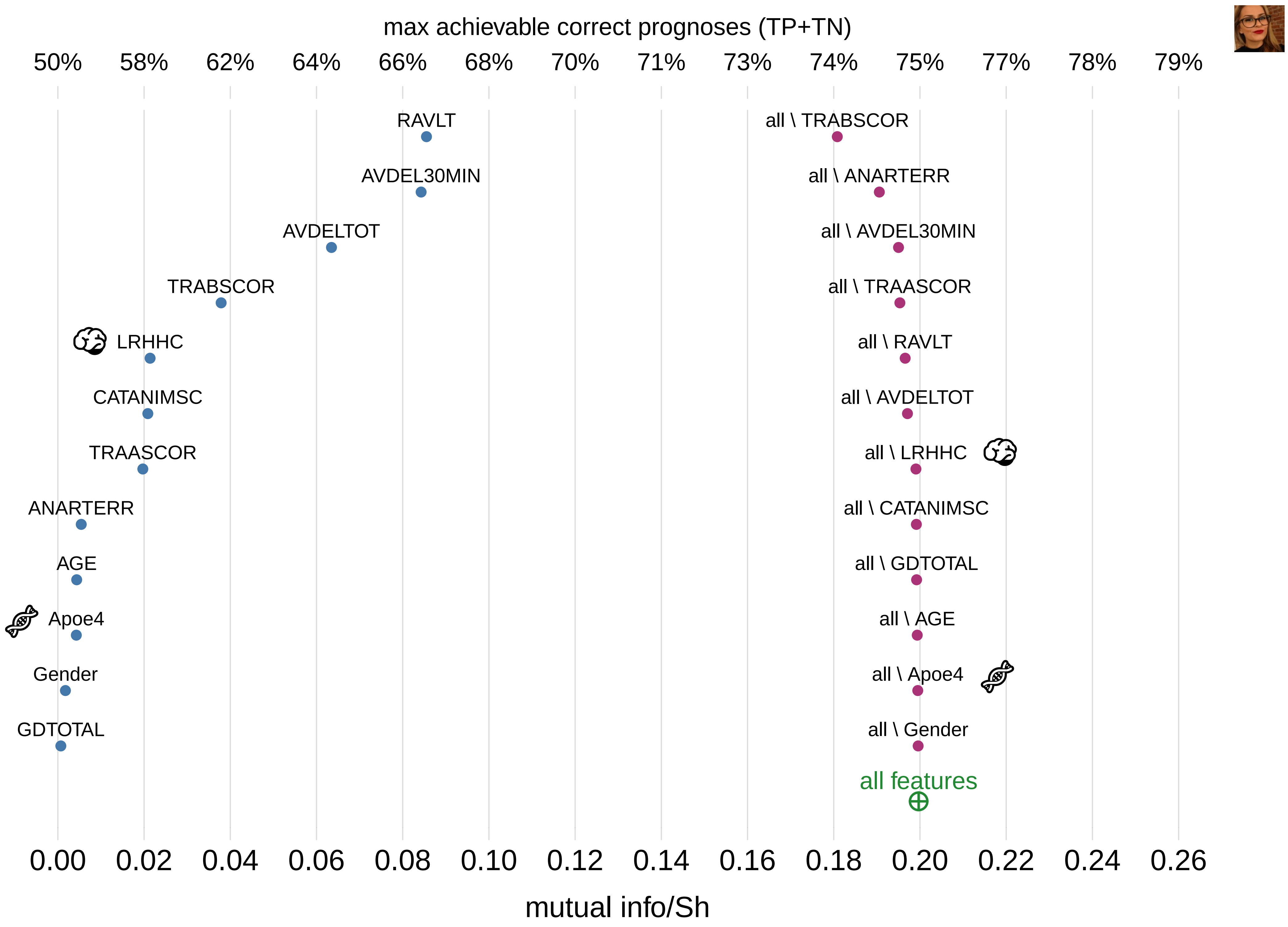

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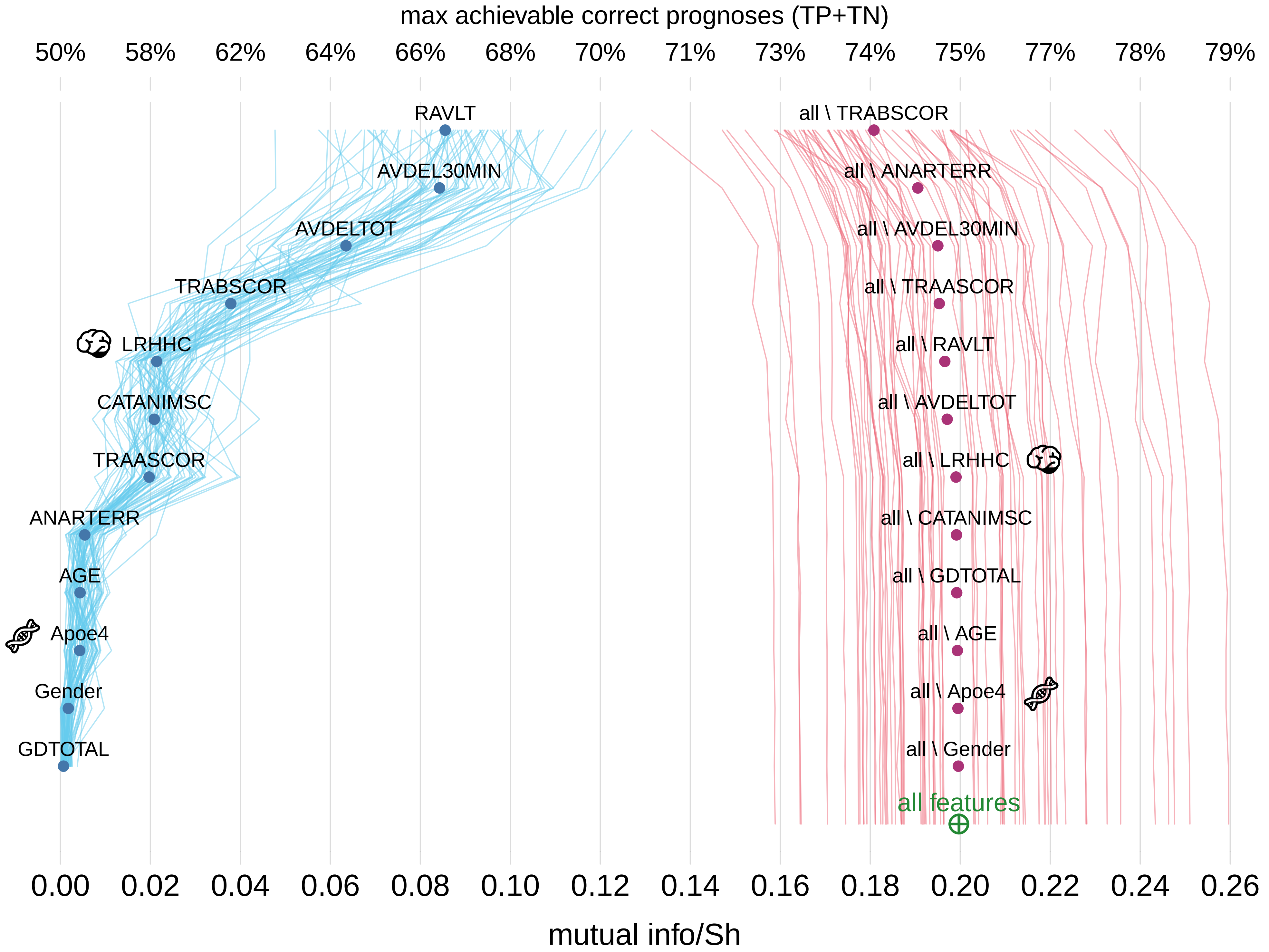
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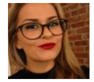

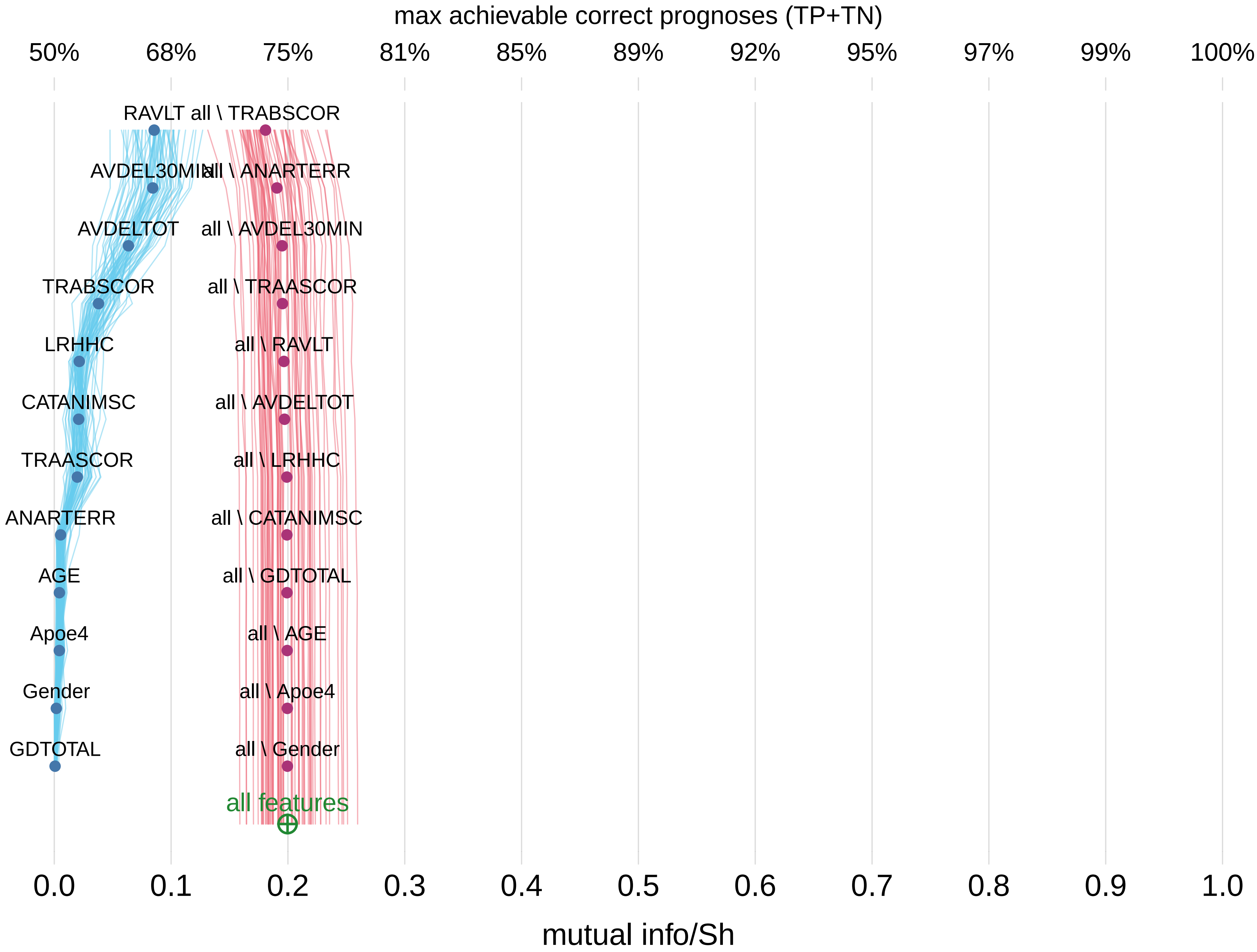

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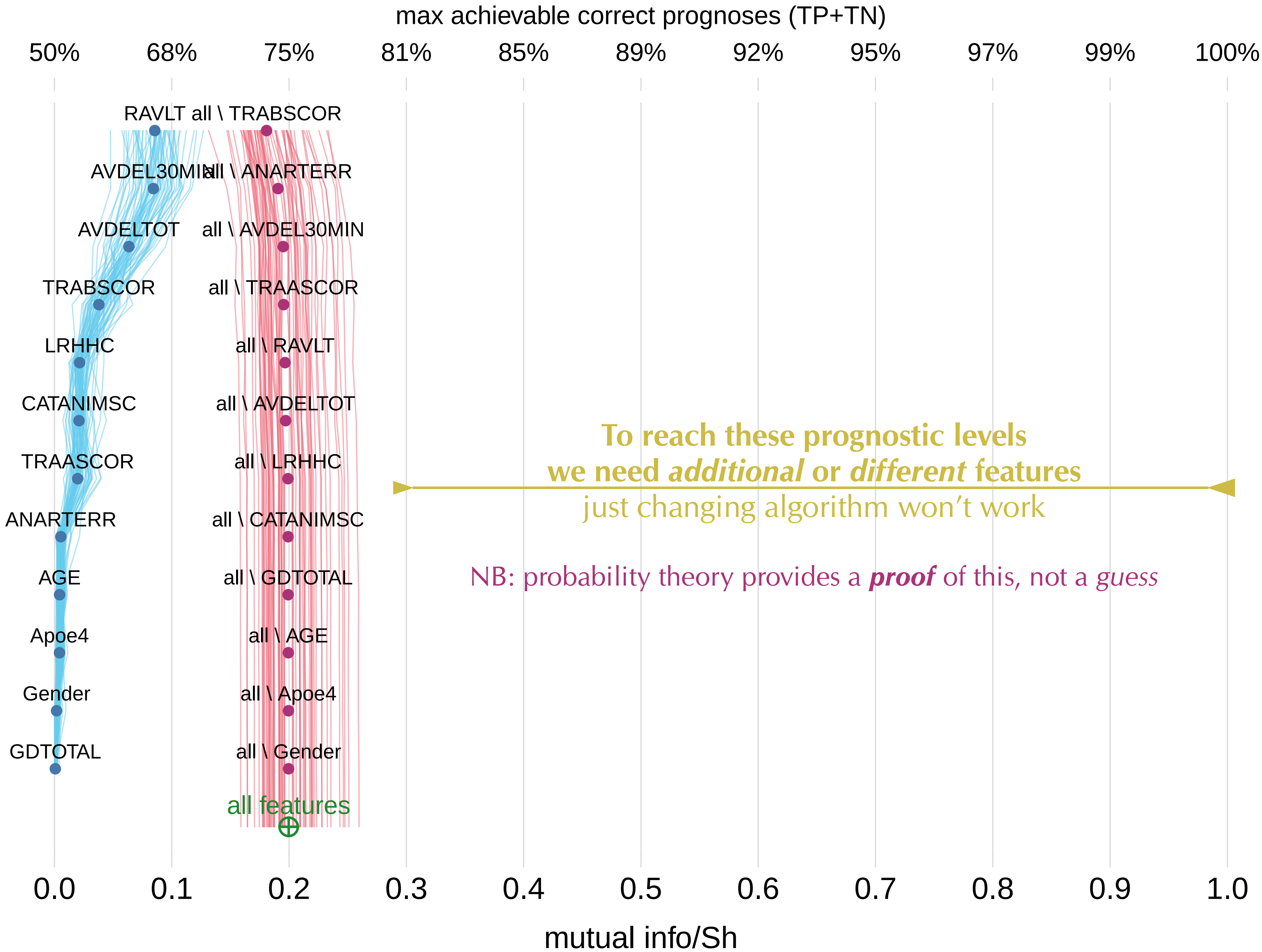

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To reach these prognostic levels
we need *additional* or *different* features
just changing algorithm won't work
NB: probability theory provides a ***proof*** of this, not a *guess*
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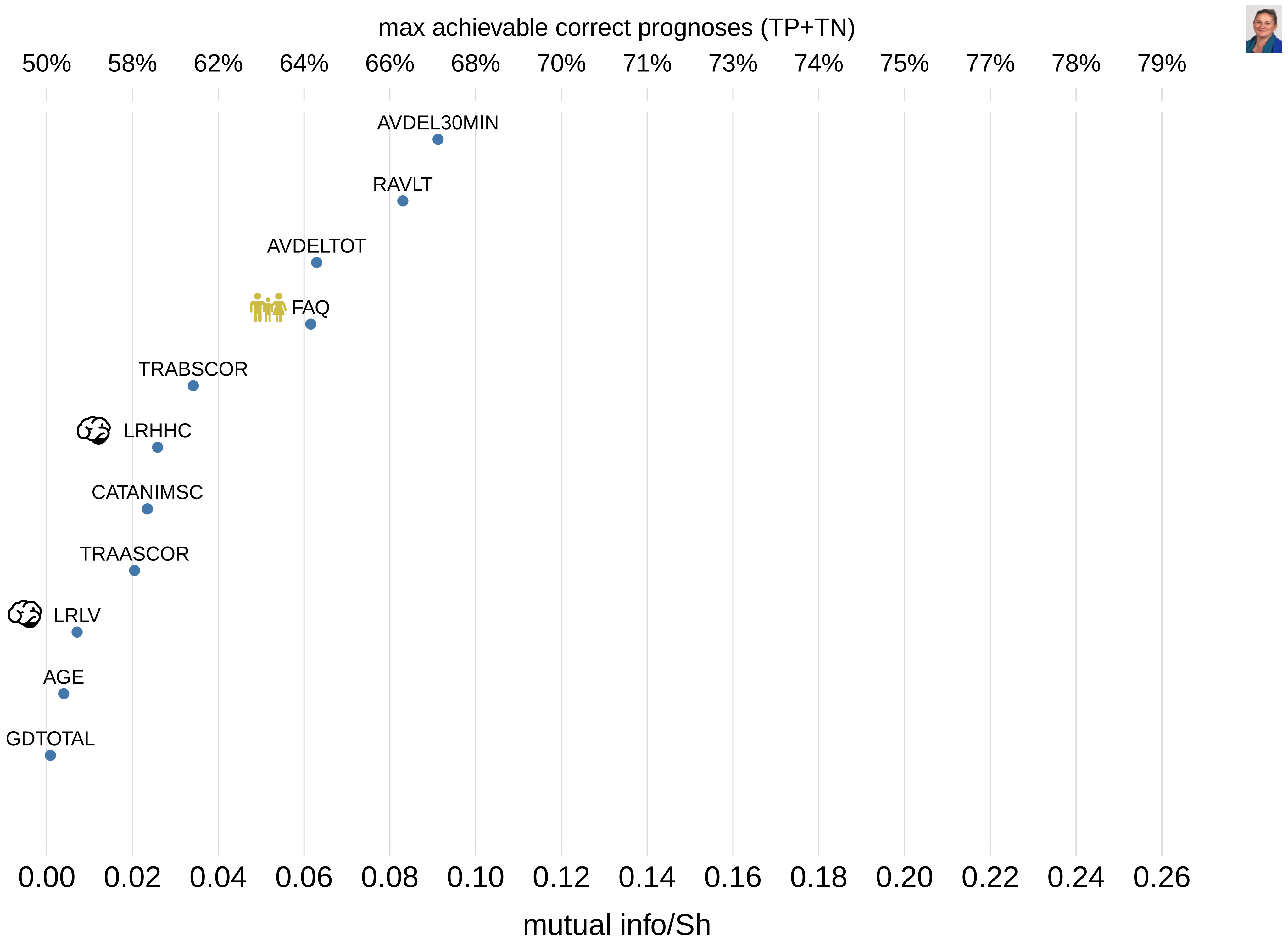
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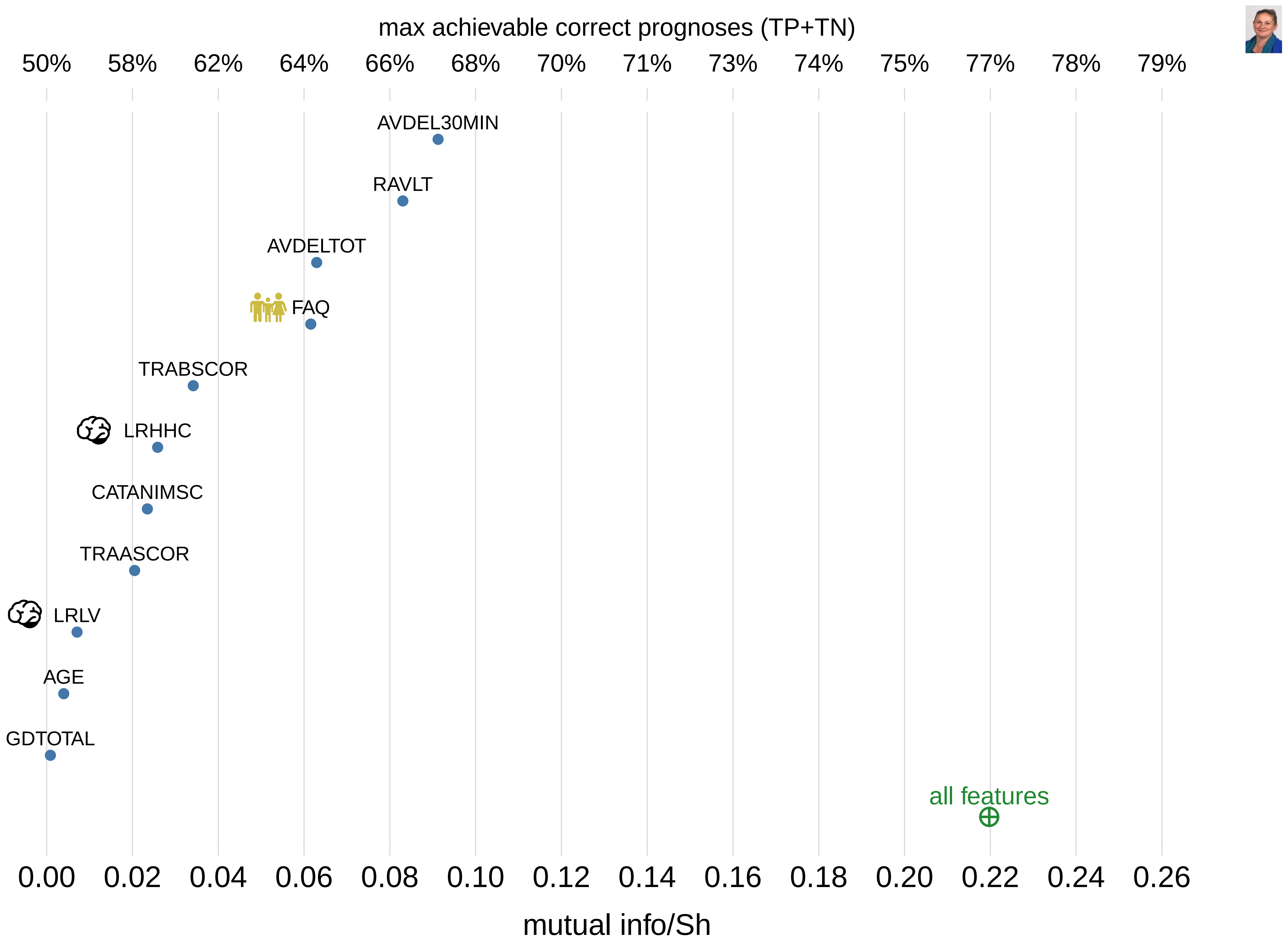
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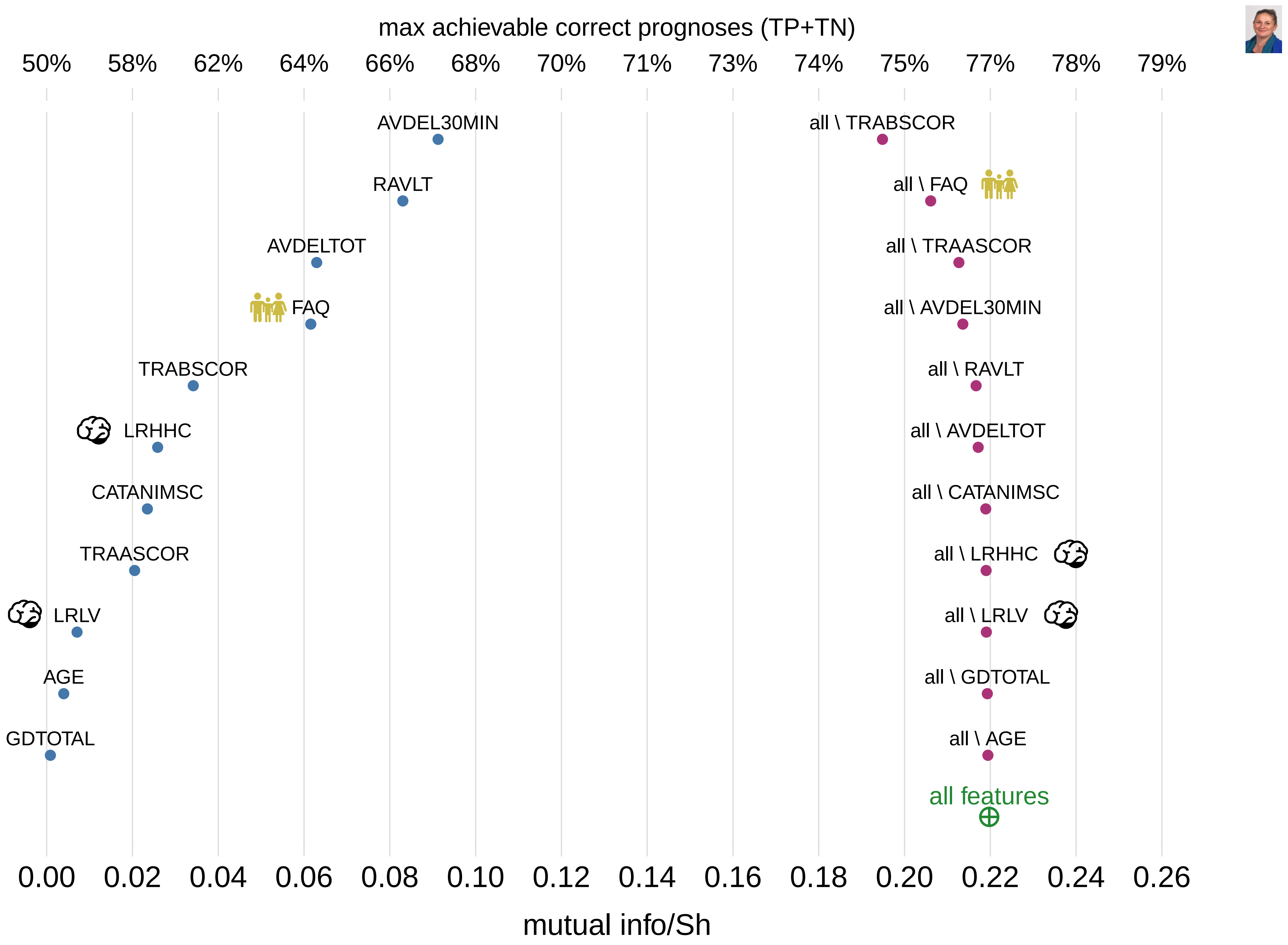
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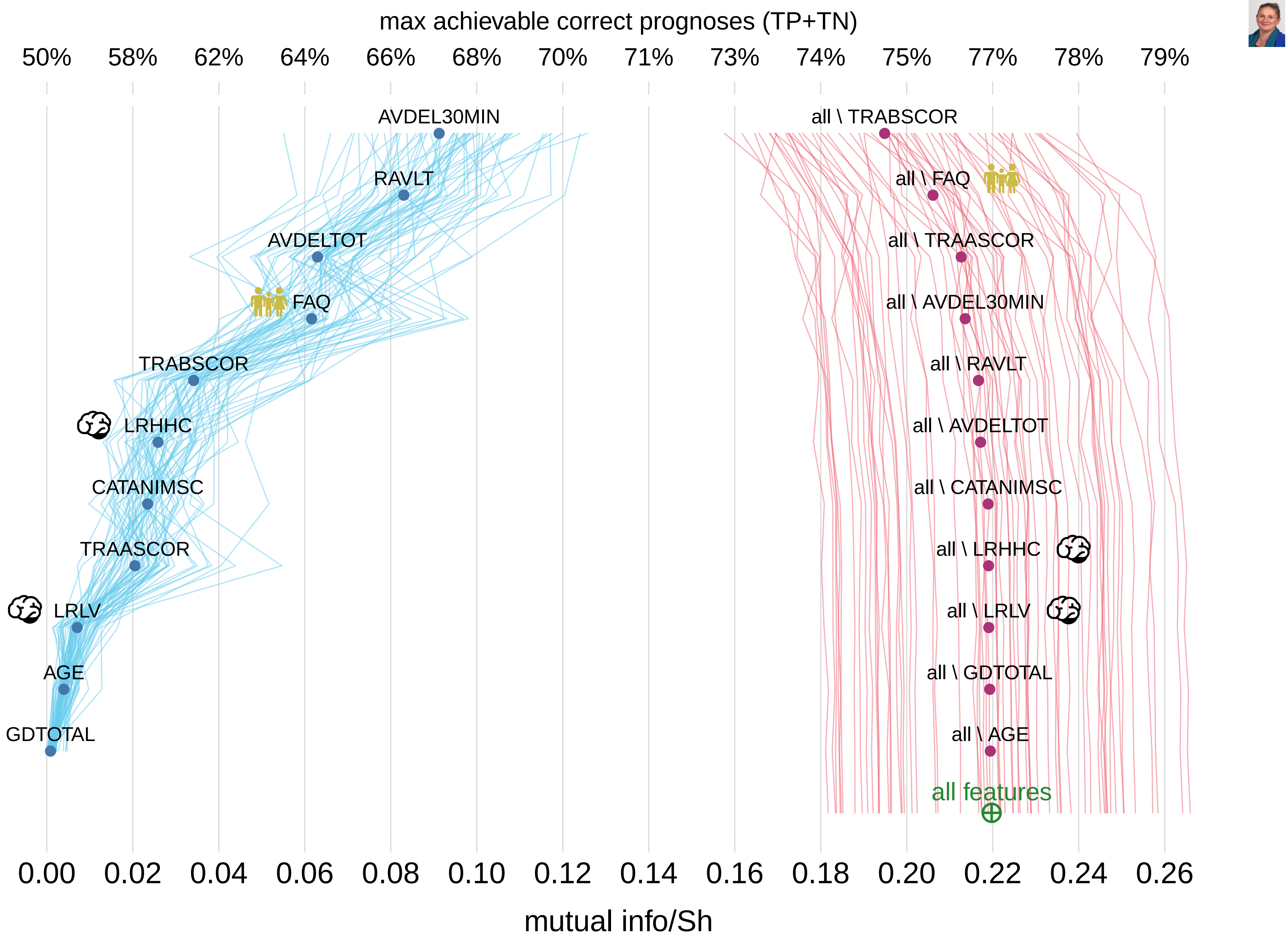

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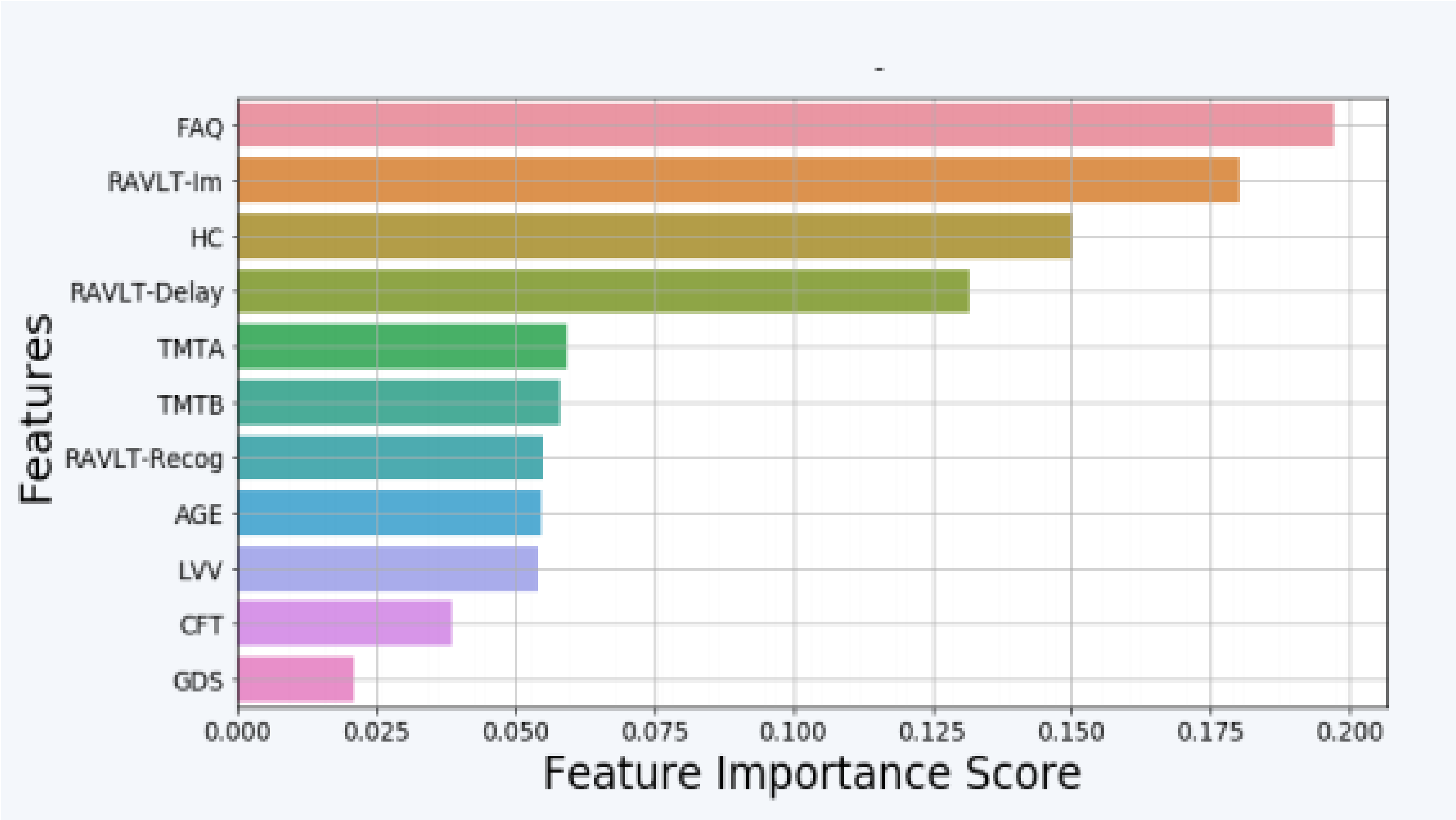
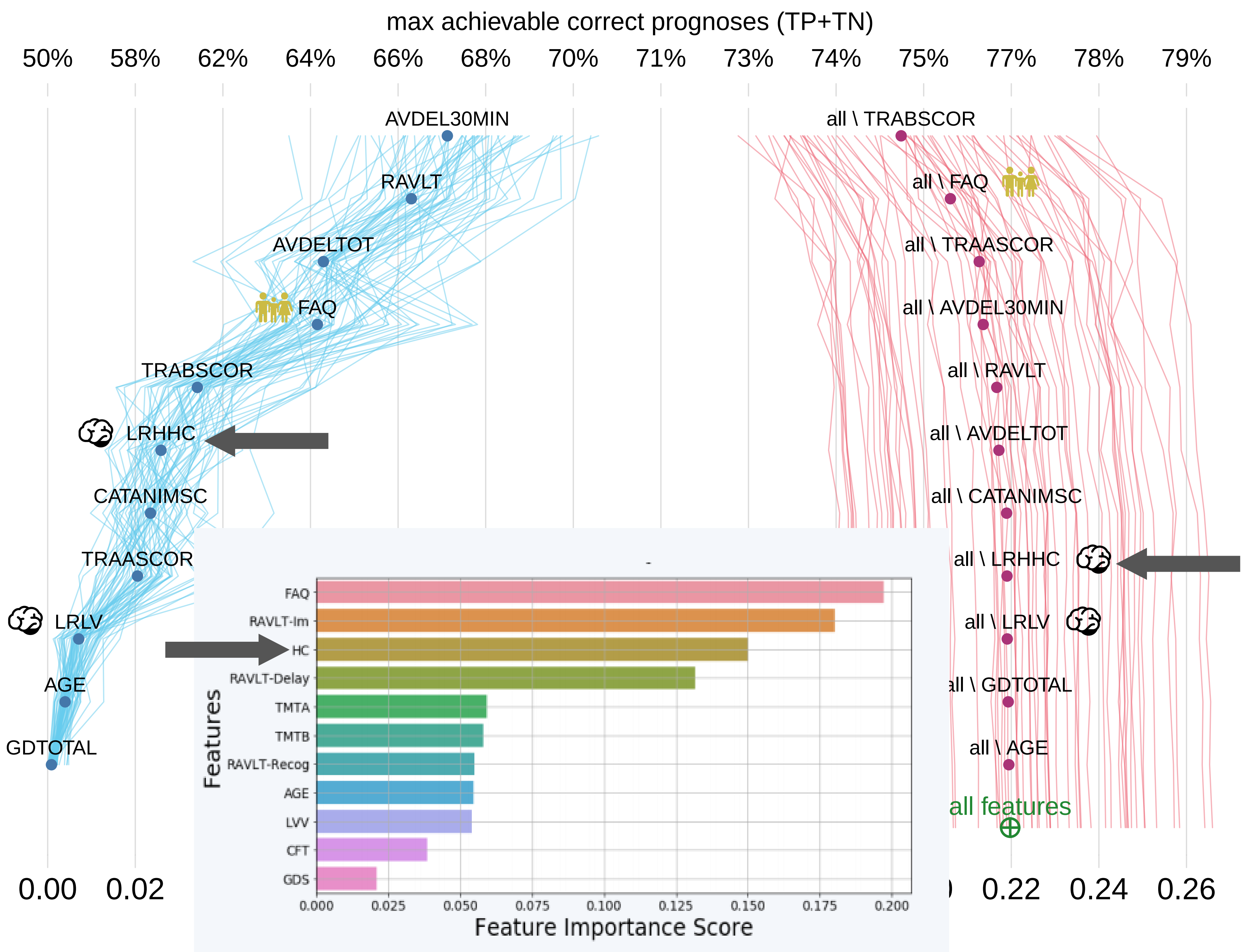
mutual info/Sh

Alexandra's results





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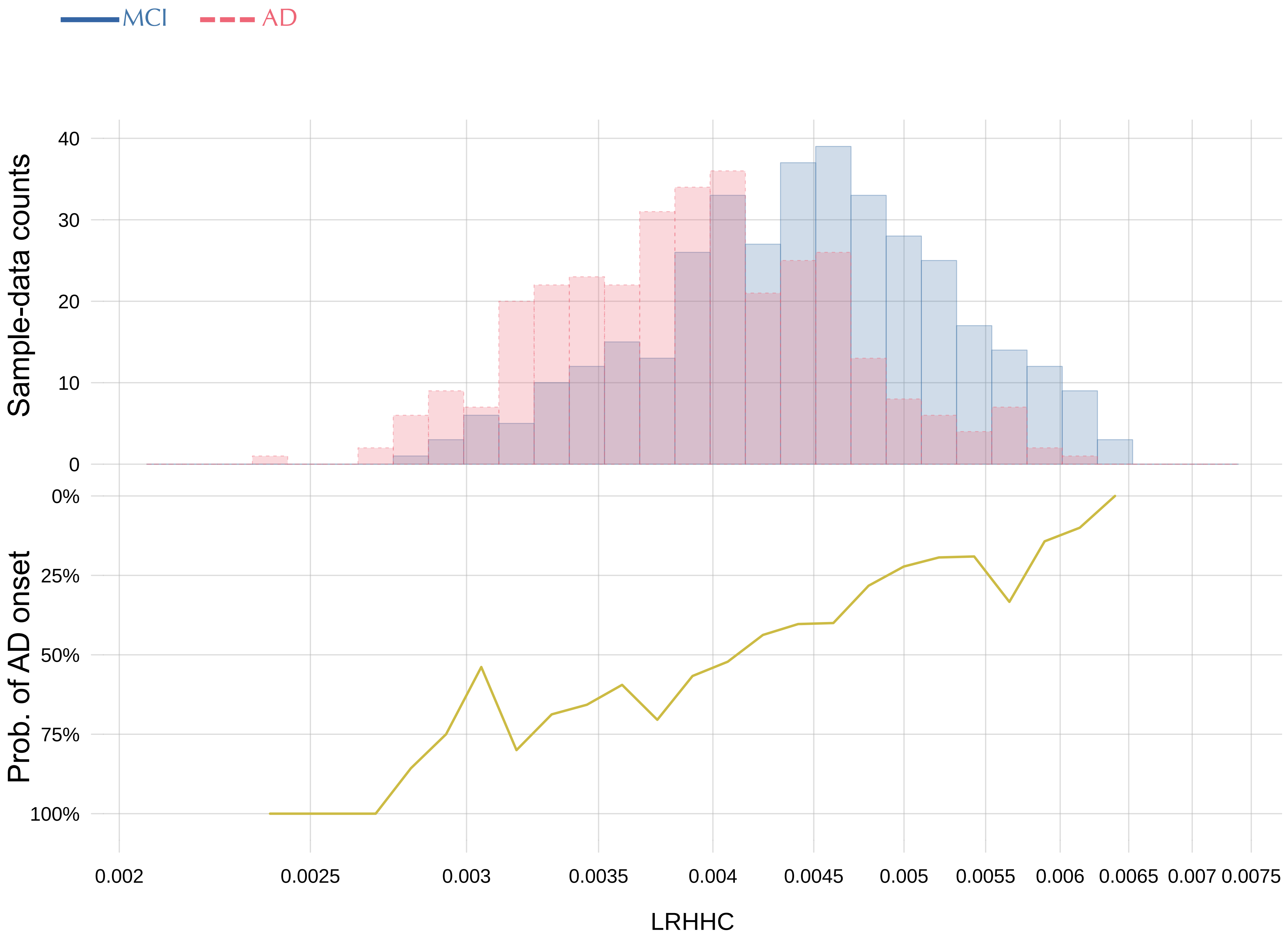
Feature Importance Score



MCI
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Sample-data counts
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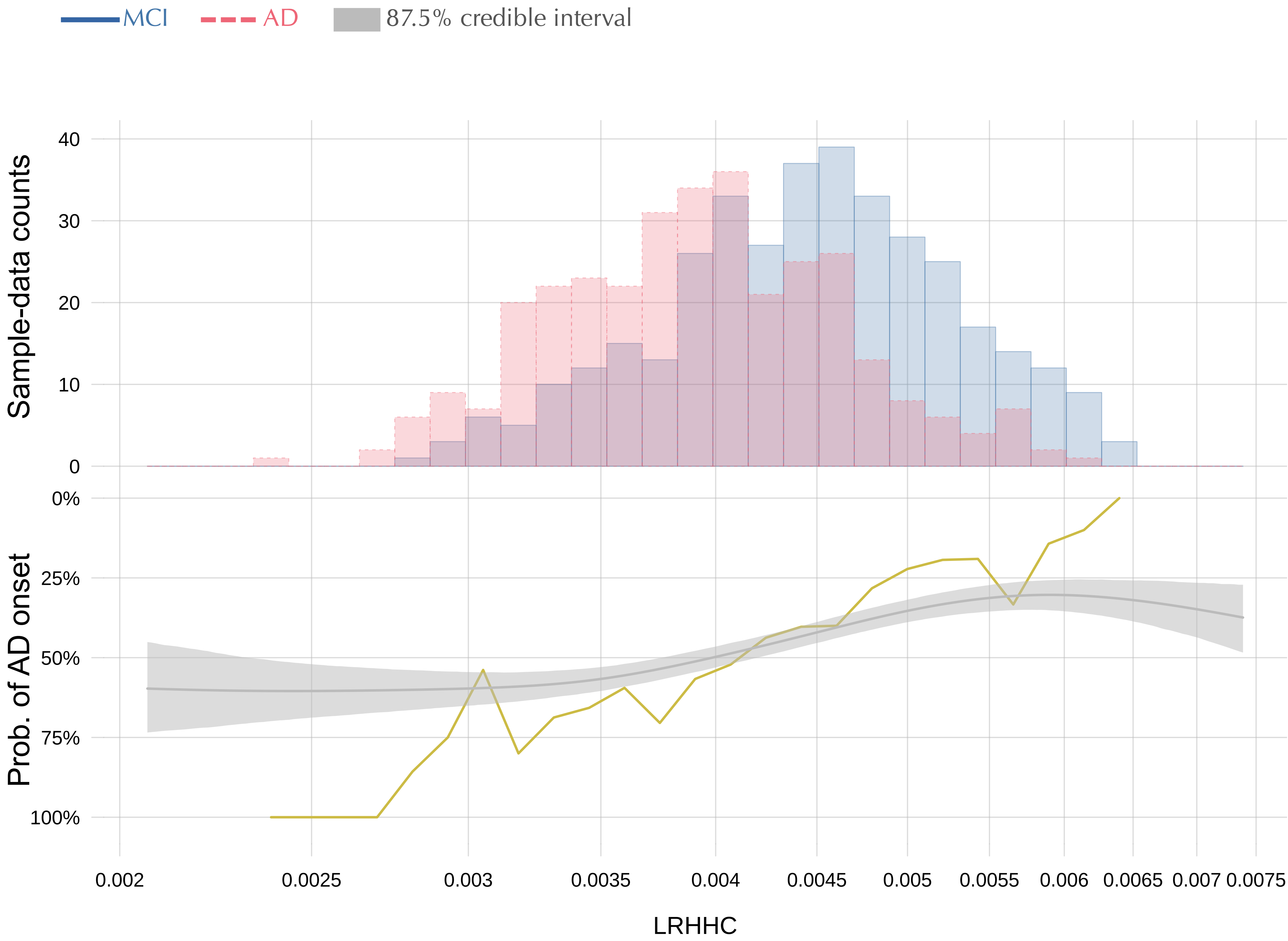
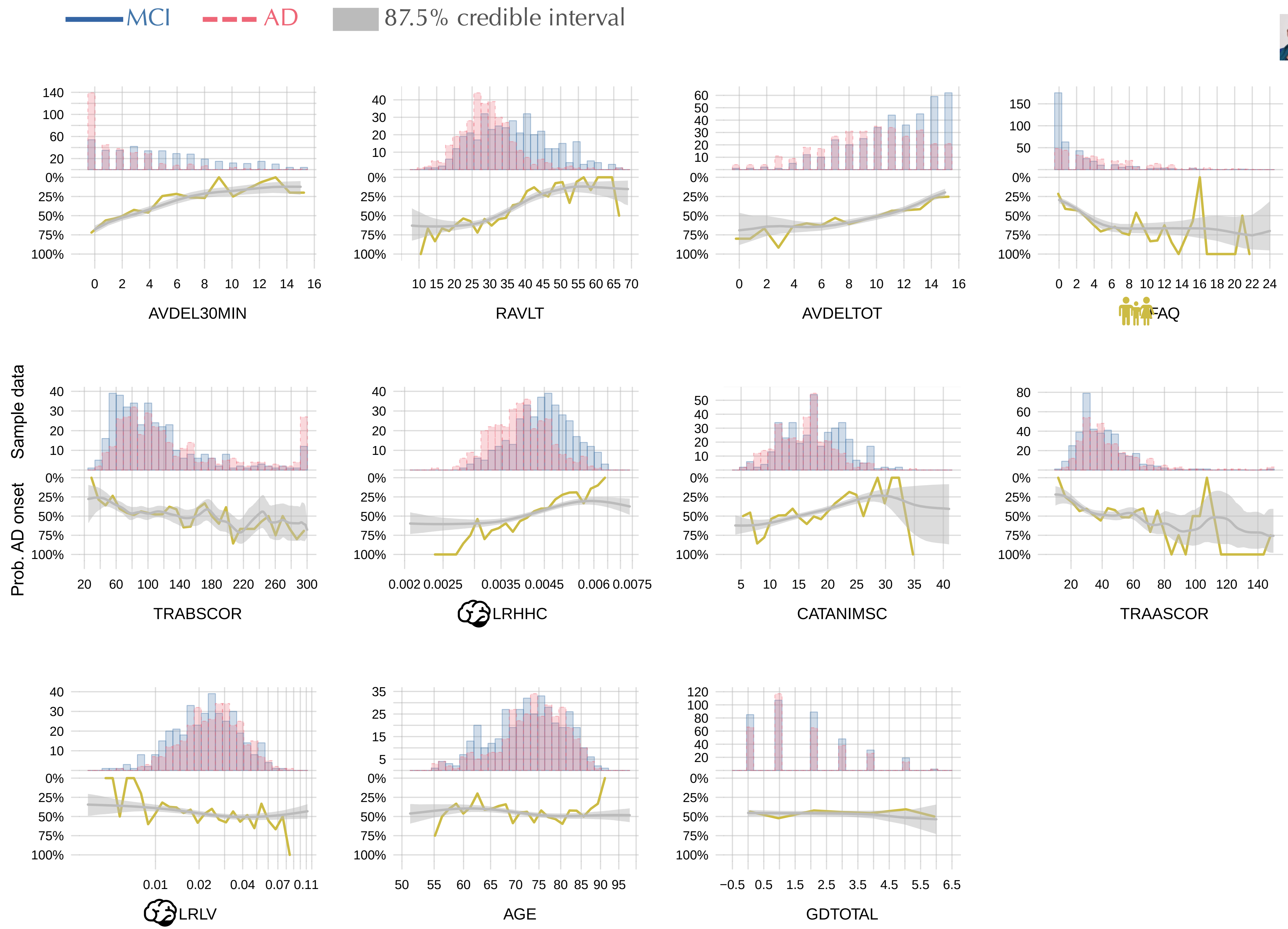
30
20
10
0
0%
25%
50%
75%
100%
Prob. of AD onset
0.002
0.0025
0.003
0.0035
0.004
0.0045
0.005
0.0055
0.006
0.0065
0.007
0.0075
LRHHC



MCI
AD
87.5% credible interval
Sample-data counts
40
30
20
10
0
Prob. of AD onset
0%
25%
50%
75%
100%
0.002
0.0025
0.003
0.0035
0.004
0.0045
0.005
0.0055
0.006
0.0065
0.007
0.0075
LRHHC


MCI
AD
Sample data
Prob. AD onset
AVDEL30MIN
RAVLT
AVDELTOT
FAQ
TRABSCOR
LRHHC
CATANIMSC
TRAASCOR
LRLV
AGE
GDTOTAL


MCI
AD
87.5% credible interval
Sample data
Prob. AD onset
AVDEL30MIN
RAVLT
AVDELTOT
FAQ
TRABSCOR
LRHHC
CATANIMSC
TRAASCOR
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AGE
GDTOTAL