

# Software for **Bayesian nonparametric population inference**

$P(Y | X \wedge I)$

*Luca Porta Mana & Håkon Mydland*

MMIV seminar, 24 October 2024

⚠ Warning! ⚠



This is an Emmental-seminar:  
there will be holes in the presentation!

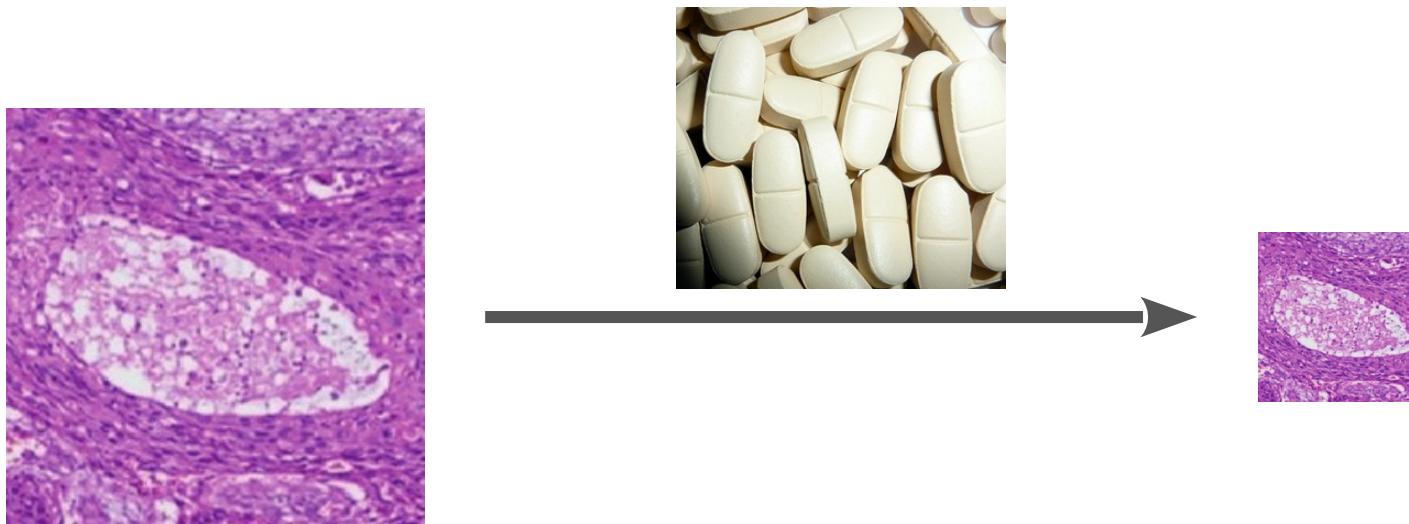
***Our purpose: making you curious & interested***

***Please get in touch!***

- ① Give you a picture of a powerful inference method
- ② Give you a picture of user-friendly software for it
- ③ Invite you to contribute with testing and feedback!

Hypothetical scenario:

New drug may reduce tumour mass



Hypothetical scenario:

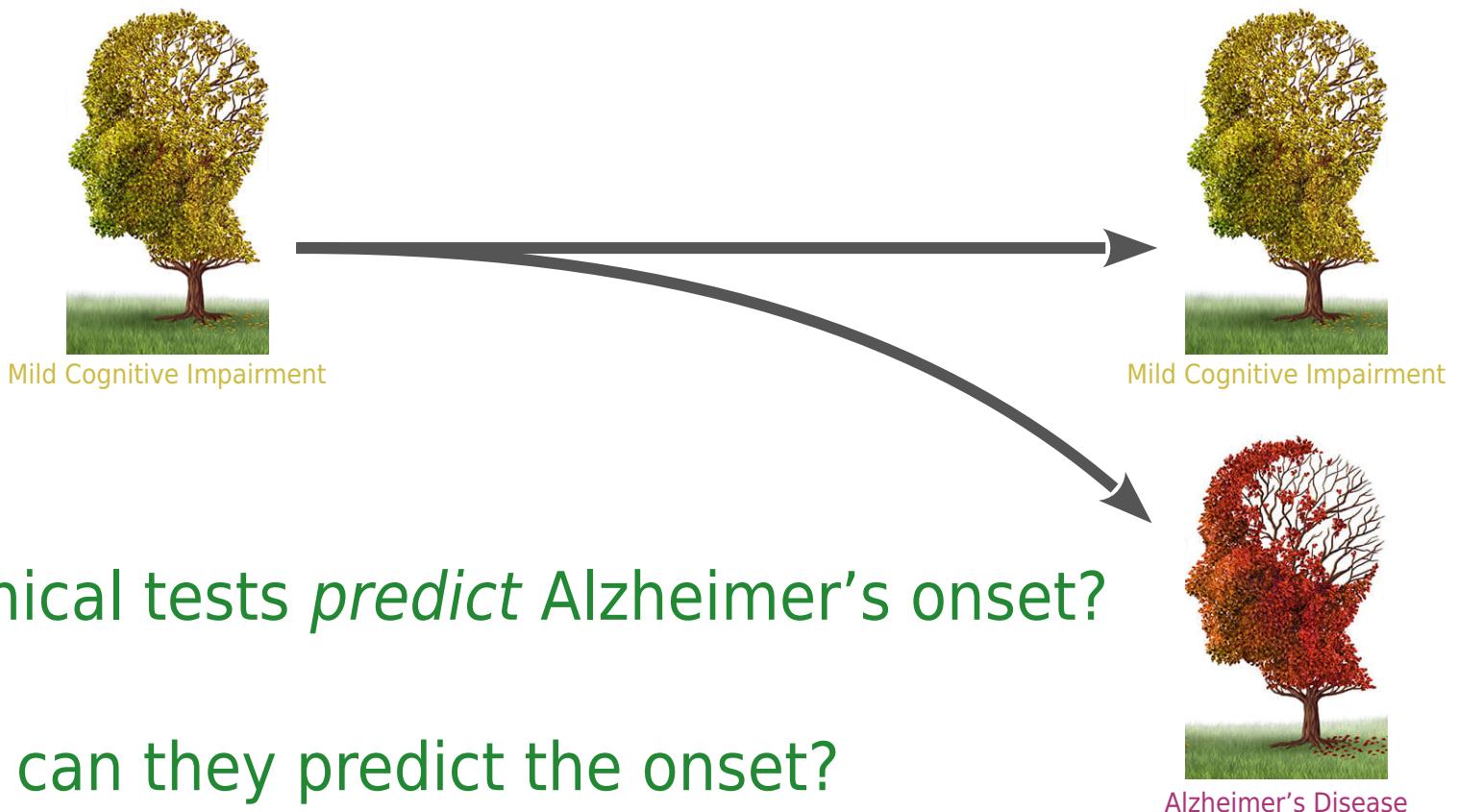
New drug may reduce tumour mass



- ➊ Does the drug have *some effect*?
- ➋ *How much* is the effect?
- ➌ Does the effect differ in different *subgroups*?
- ➍ ...

*Another hypothetical scenario:*

Can some clinical tests predict the conversion from MCI to AD?



- ① Can the clinical tests *predict* Alzheimer's onset?
- ② How surely can they predict the onset?
- ③ Does the predictive power differ in different *subgroups*?
- ④ ...

# Statistical Methods for Research Workers

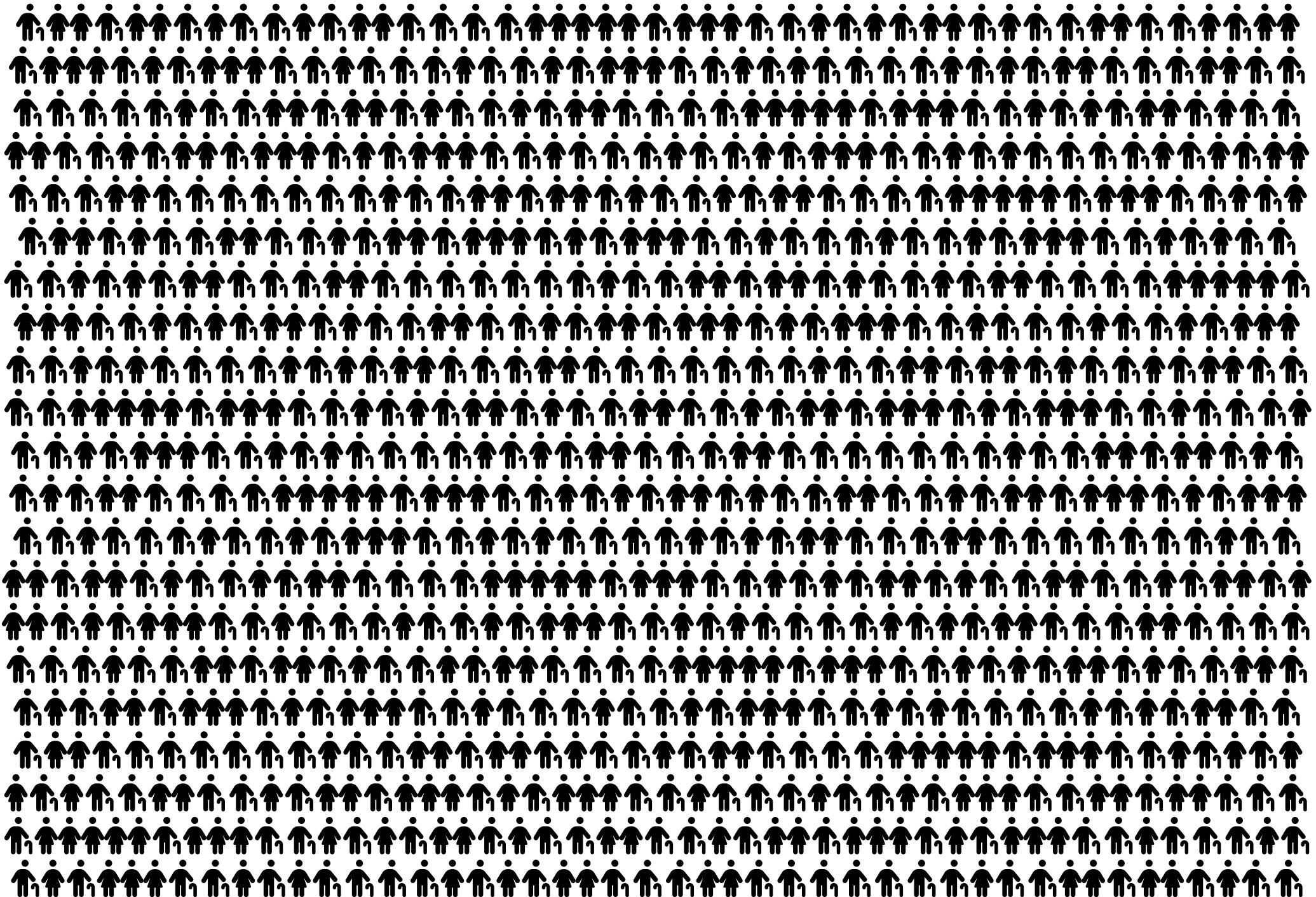
BY

SIR RONALD A. FISHER, SC.D., F.R.S.

mathematical language that are quite typical of problems arise in every case. Statistics may be regarded as (i) the study of populations, (ii) as the study



# What if we had the **whole** population?



## What if we had the **whole** population?



fraction

0.0



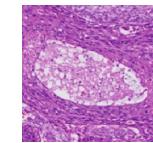
0.5

1.0

1.5

2.0

ratio of tumour mass increase



fraction

0.0



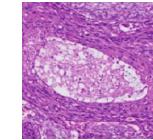
0.5

ratio of tumour mass increase

1.0

1.5

2.0



fraction

0.0



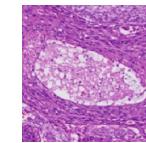
0.5

1.0

1.5

2.0

ratio of tumour mass increase



fraction

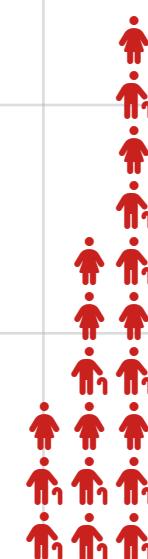
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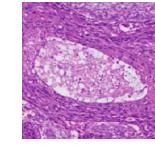
0.5

ratio of tumour mass increase

1.0



1.5



2.0

fraction

0.0



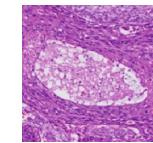
0.5

ratio of tumour mass increase

1.0

1.5

2.0



fraction

0.0



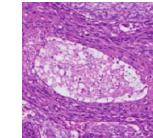
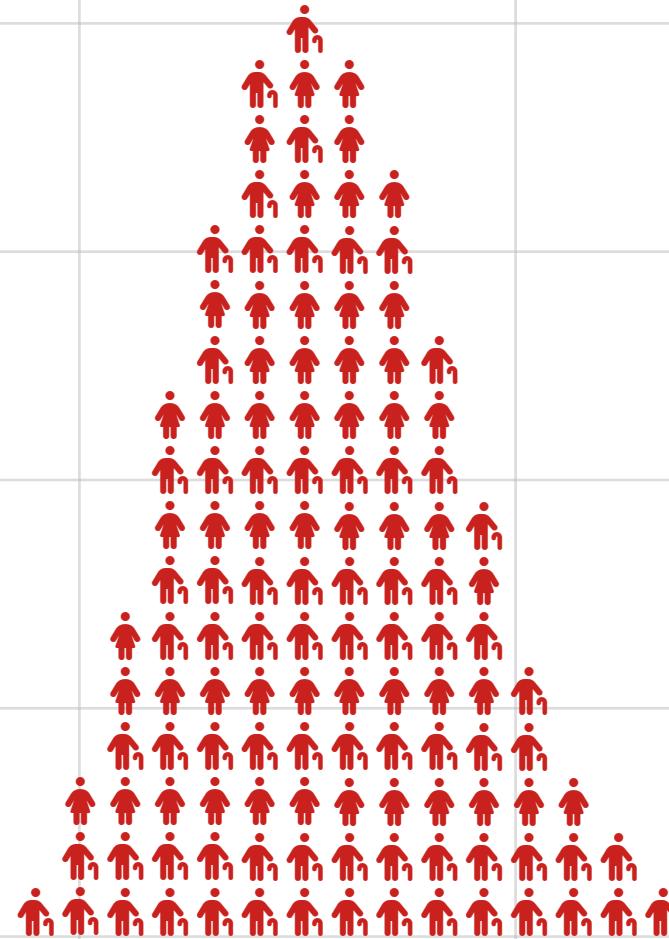
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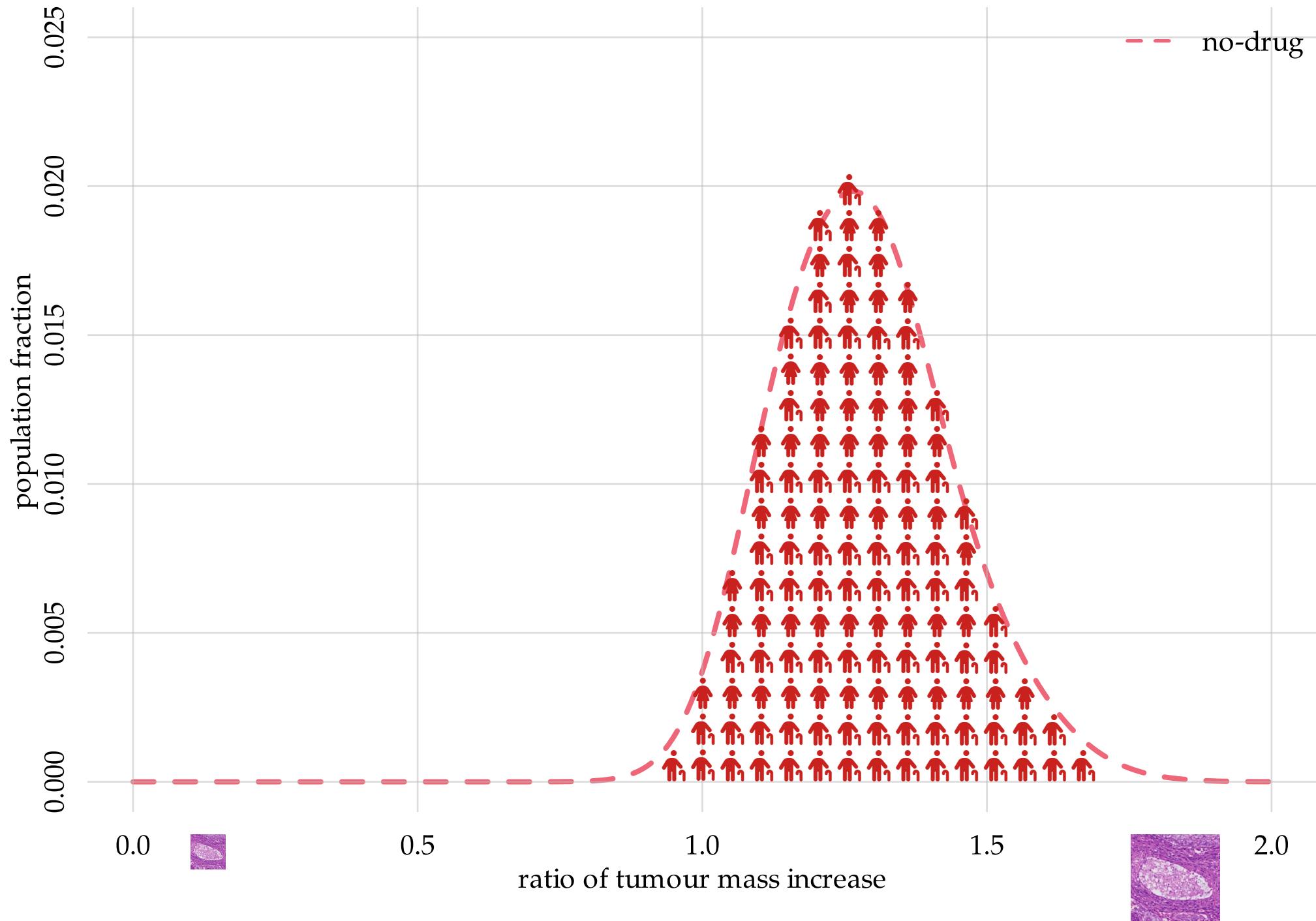
ratio of tumour mass increase

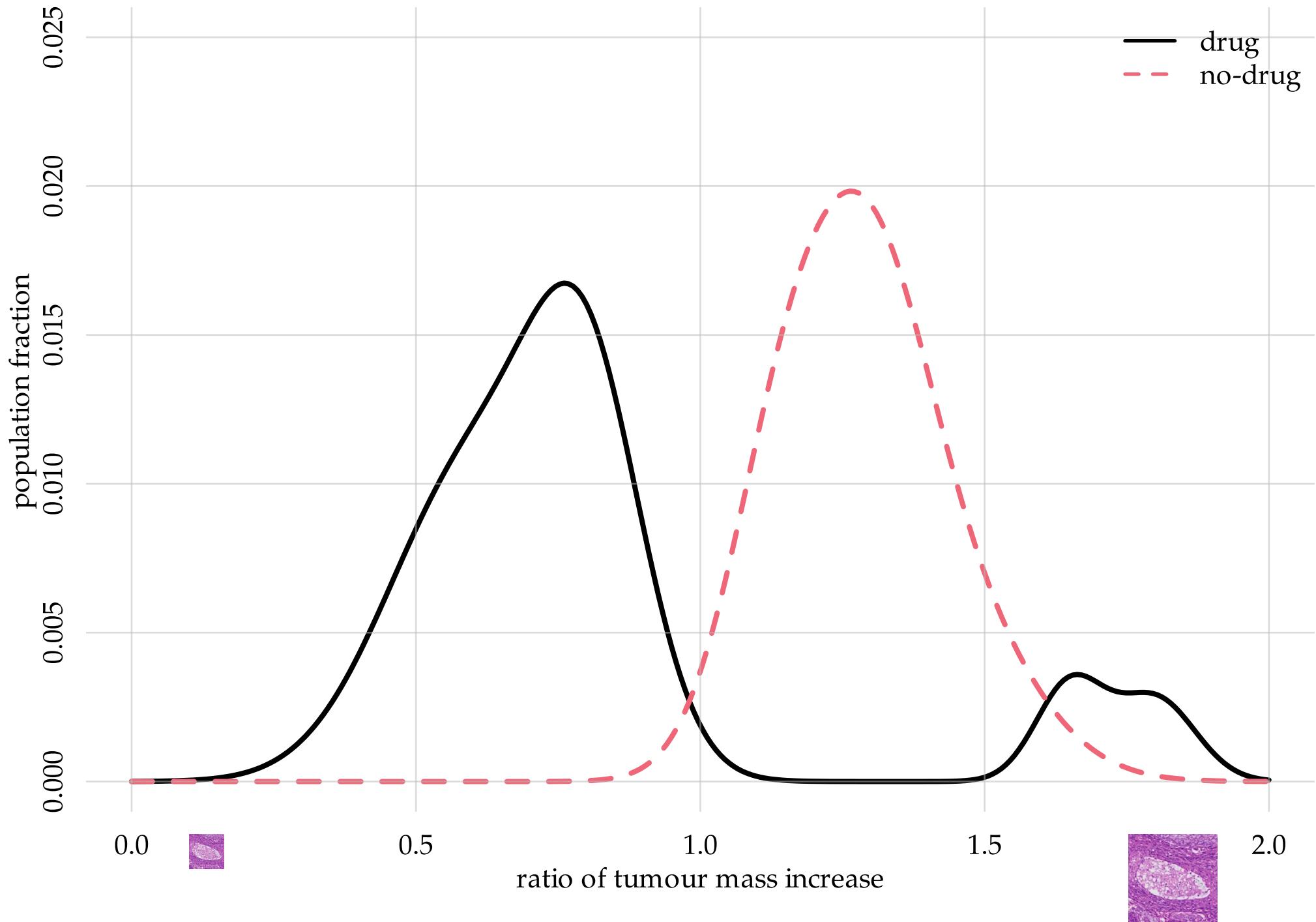
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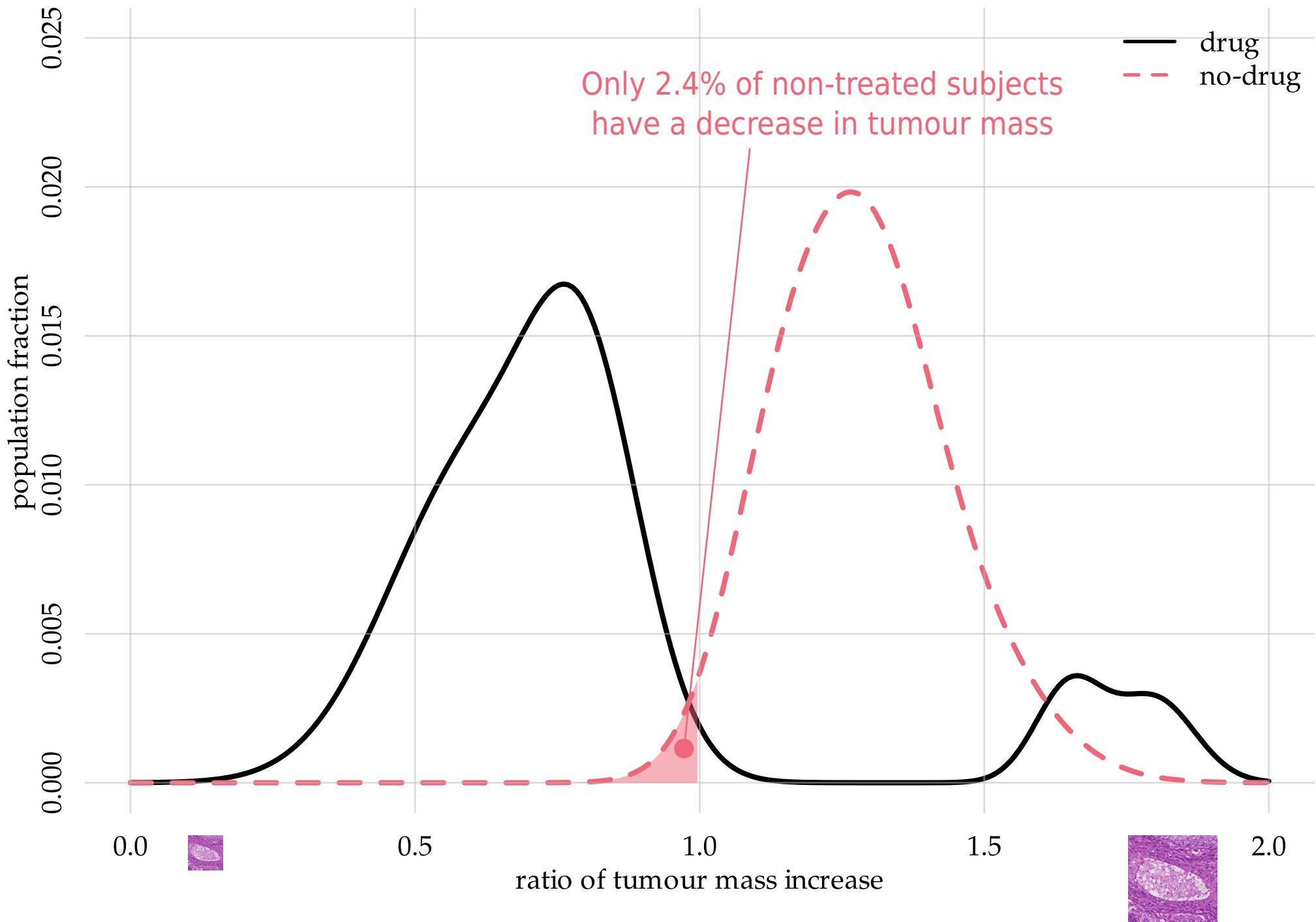
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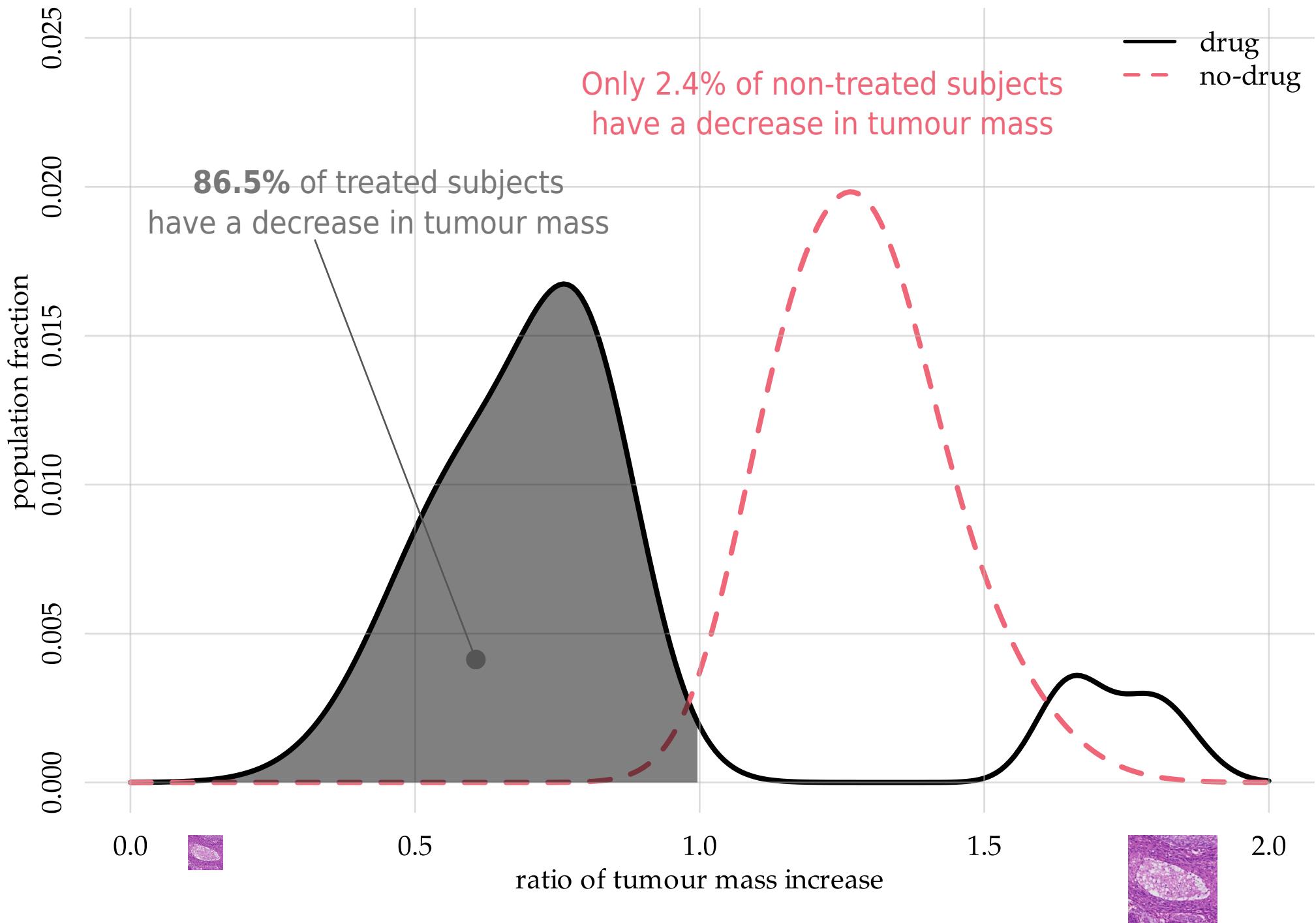
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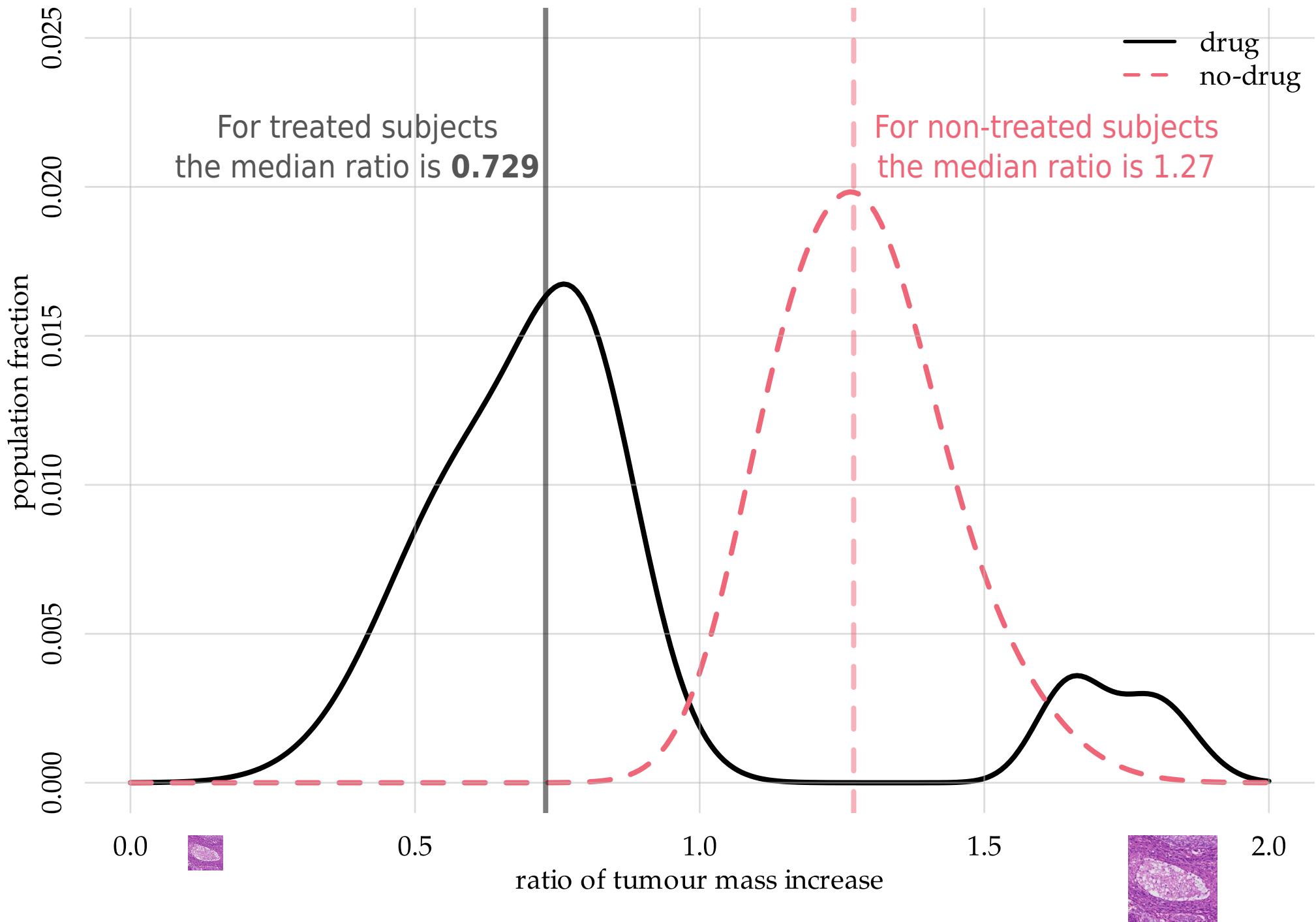


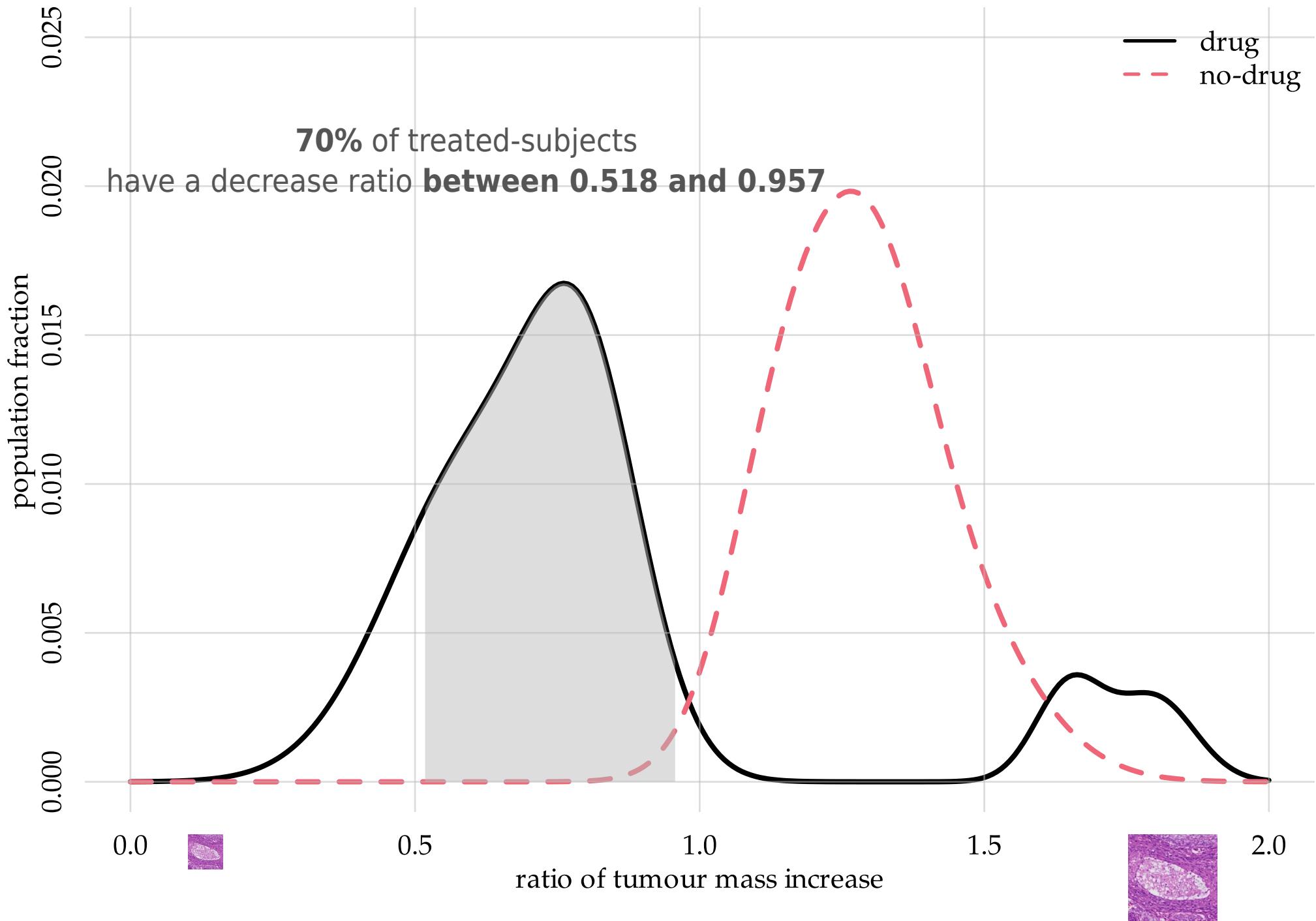


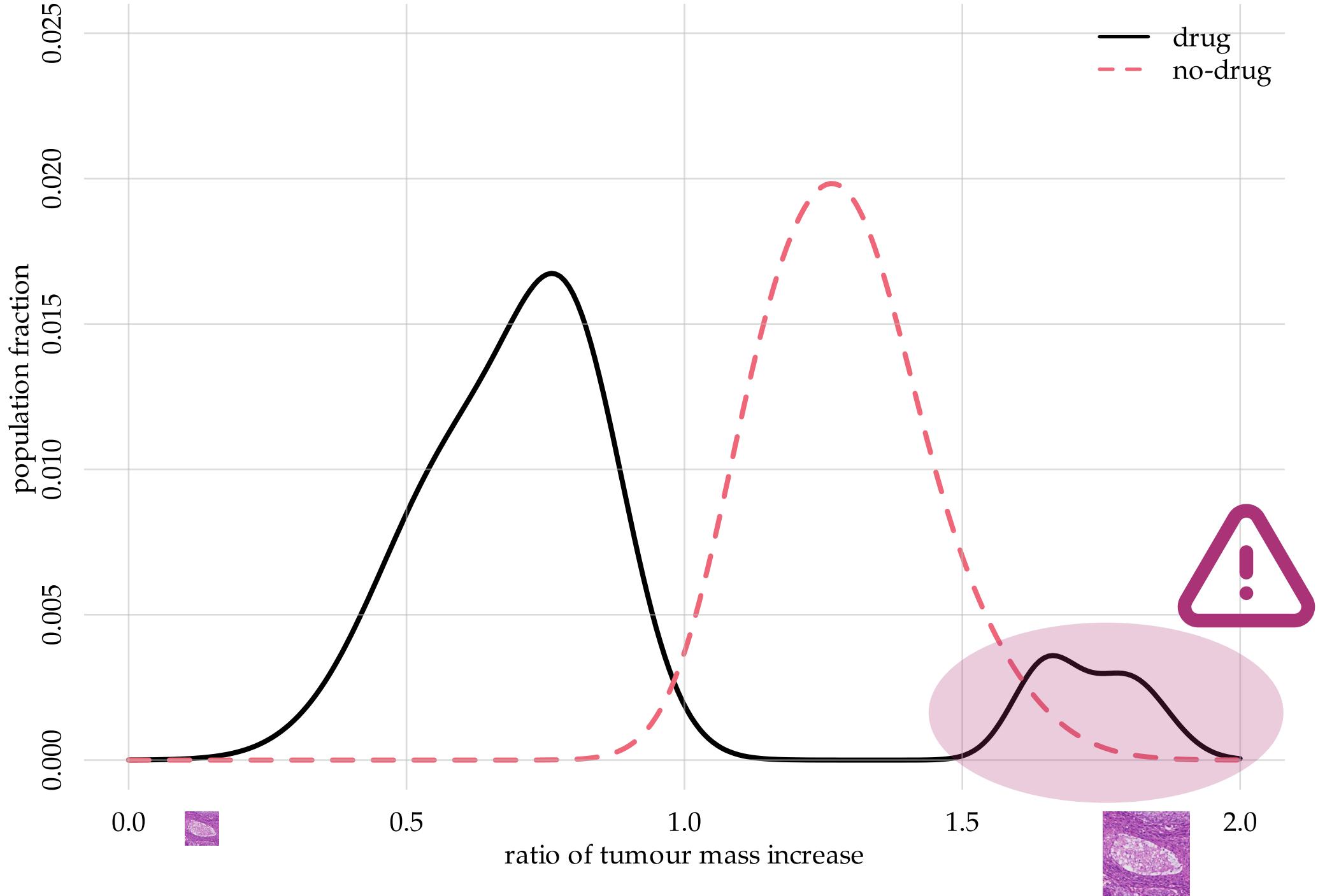












# Population

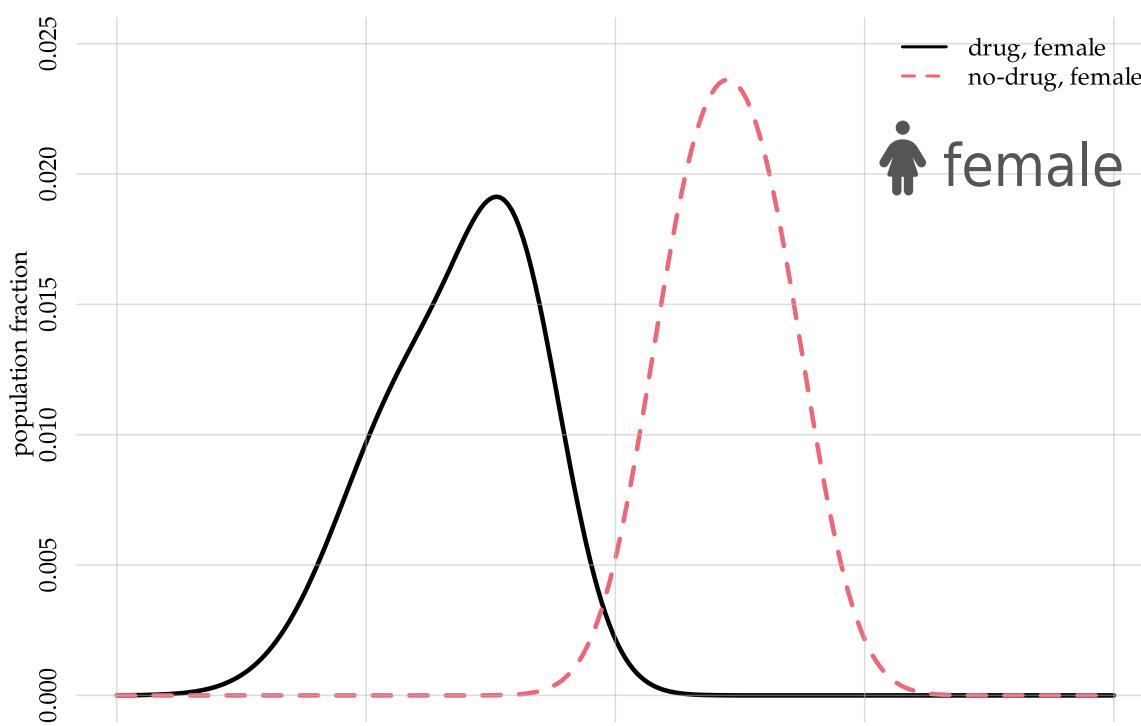


## Female subpopulation

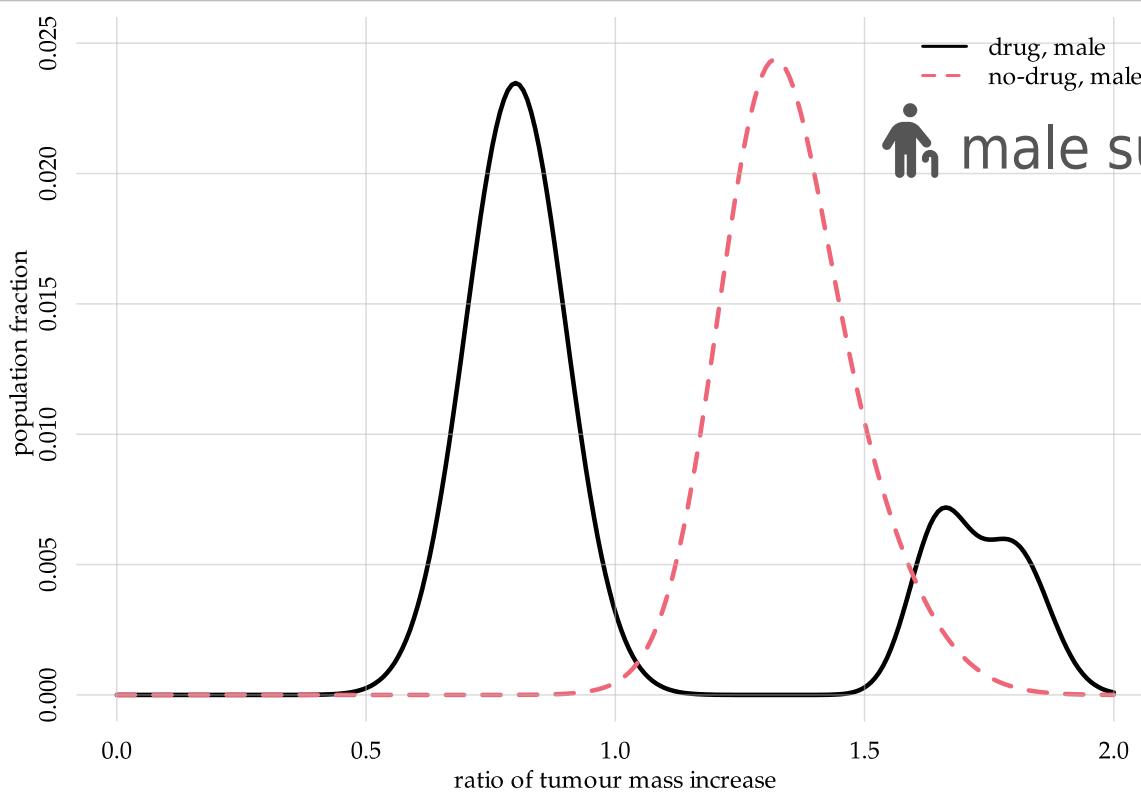


## Male subpopulation

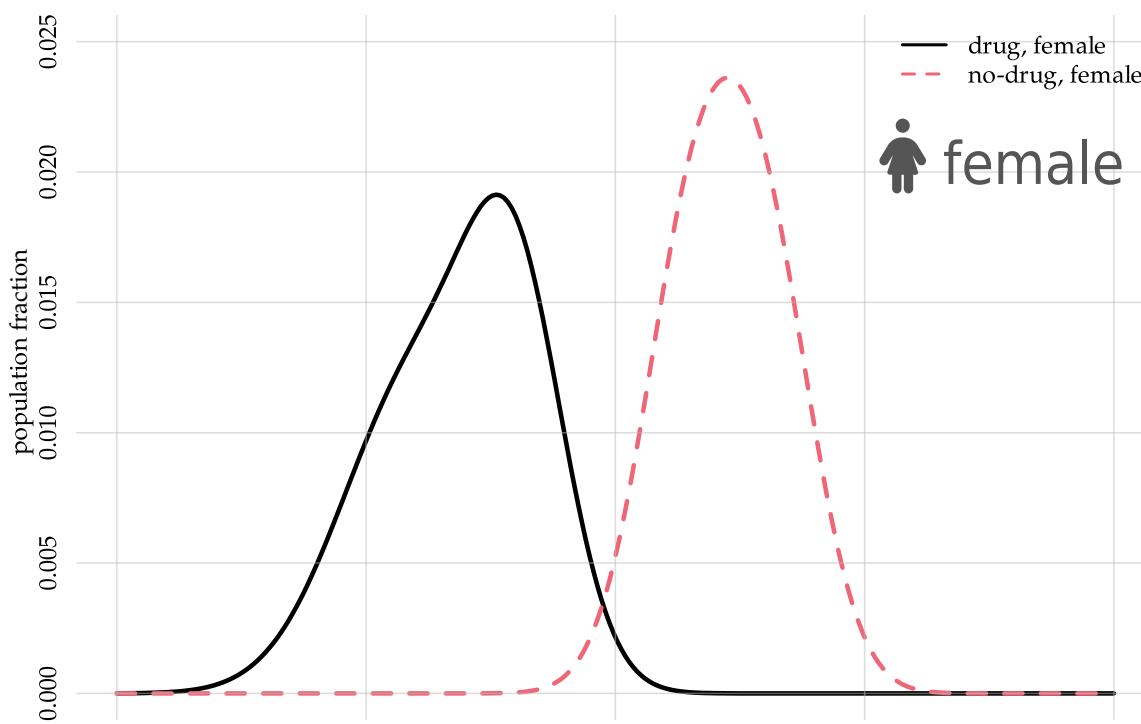




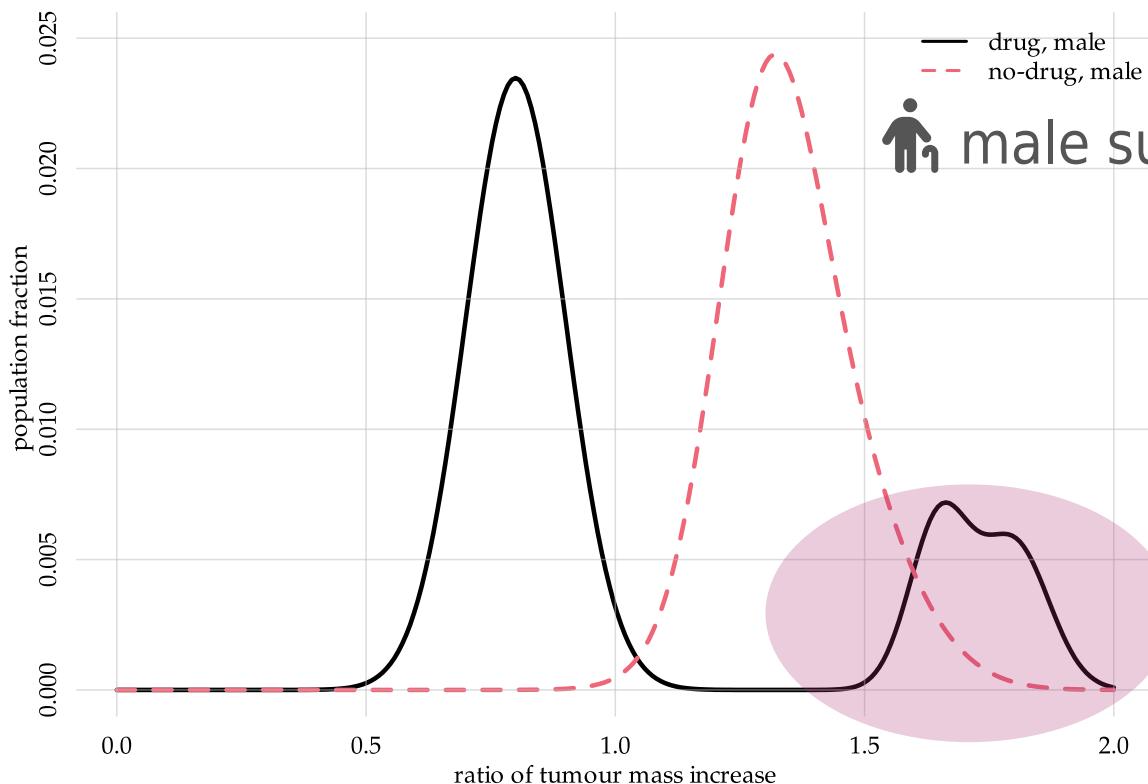
❸ female subpopulation



❹ male subpopulation



⌚ female subpopulation



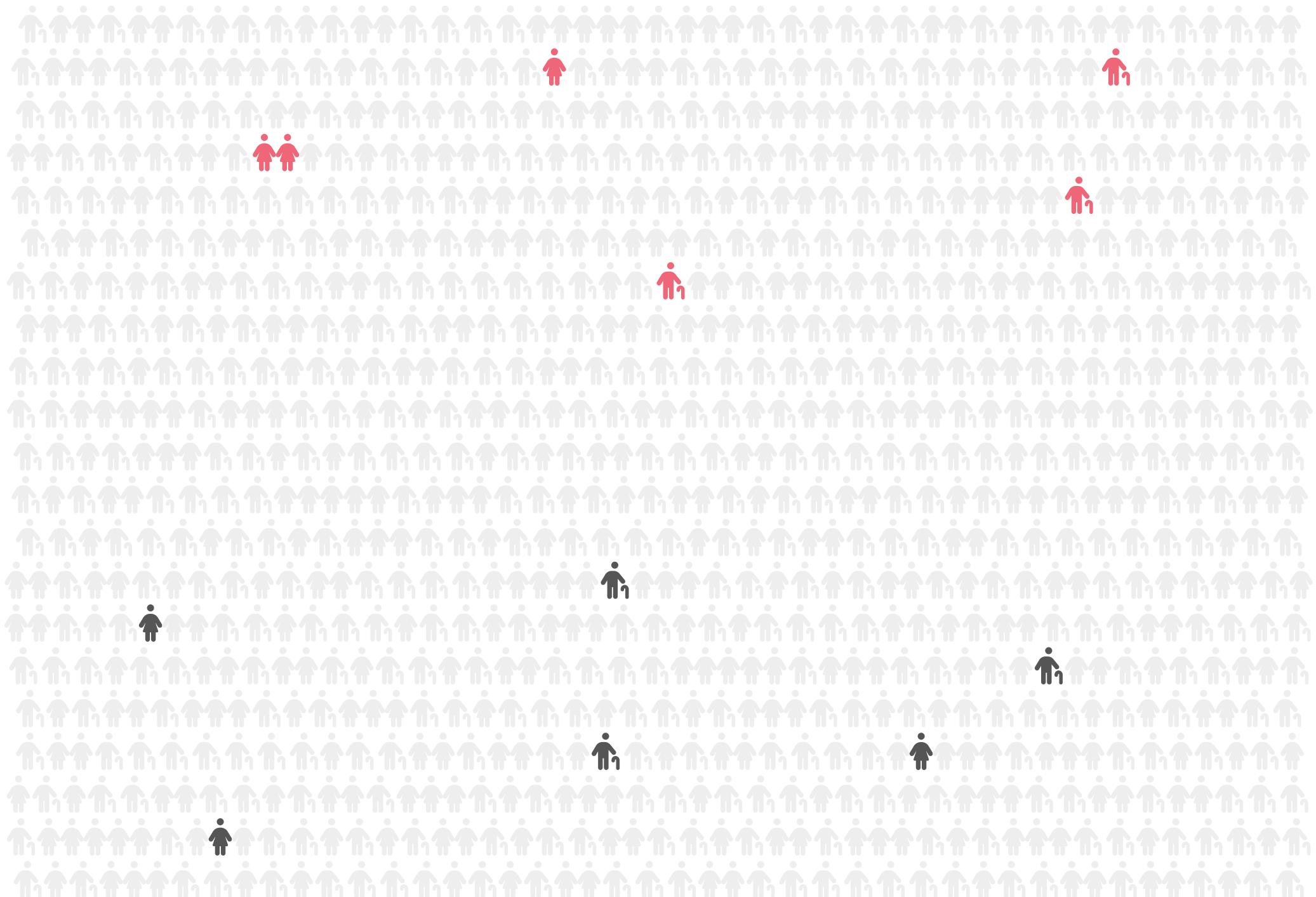
⌚ male subpopulation

The drug has adverse effects on males:  
**25.0%** of the male subpopulation  
has an increase ratio **larger than 1.2**

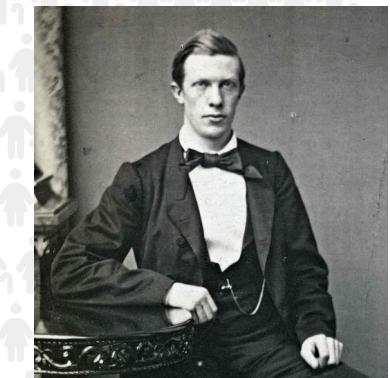
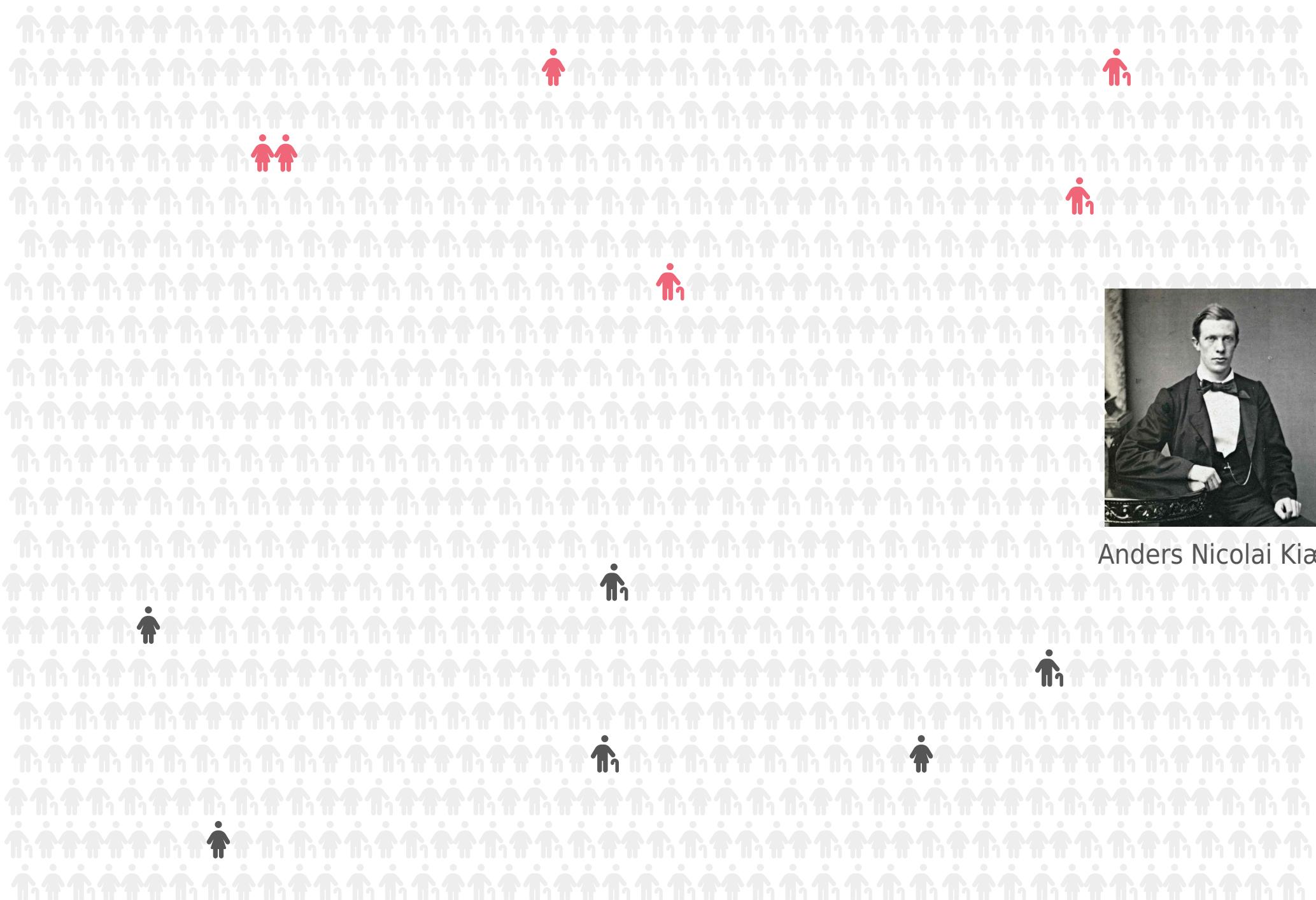
Our fundamental problem: we don't have the **whole** population



# Our fundamental problem: we only have a **sample**!

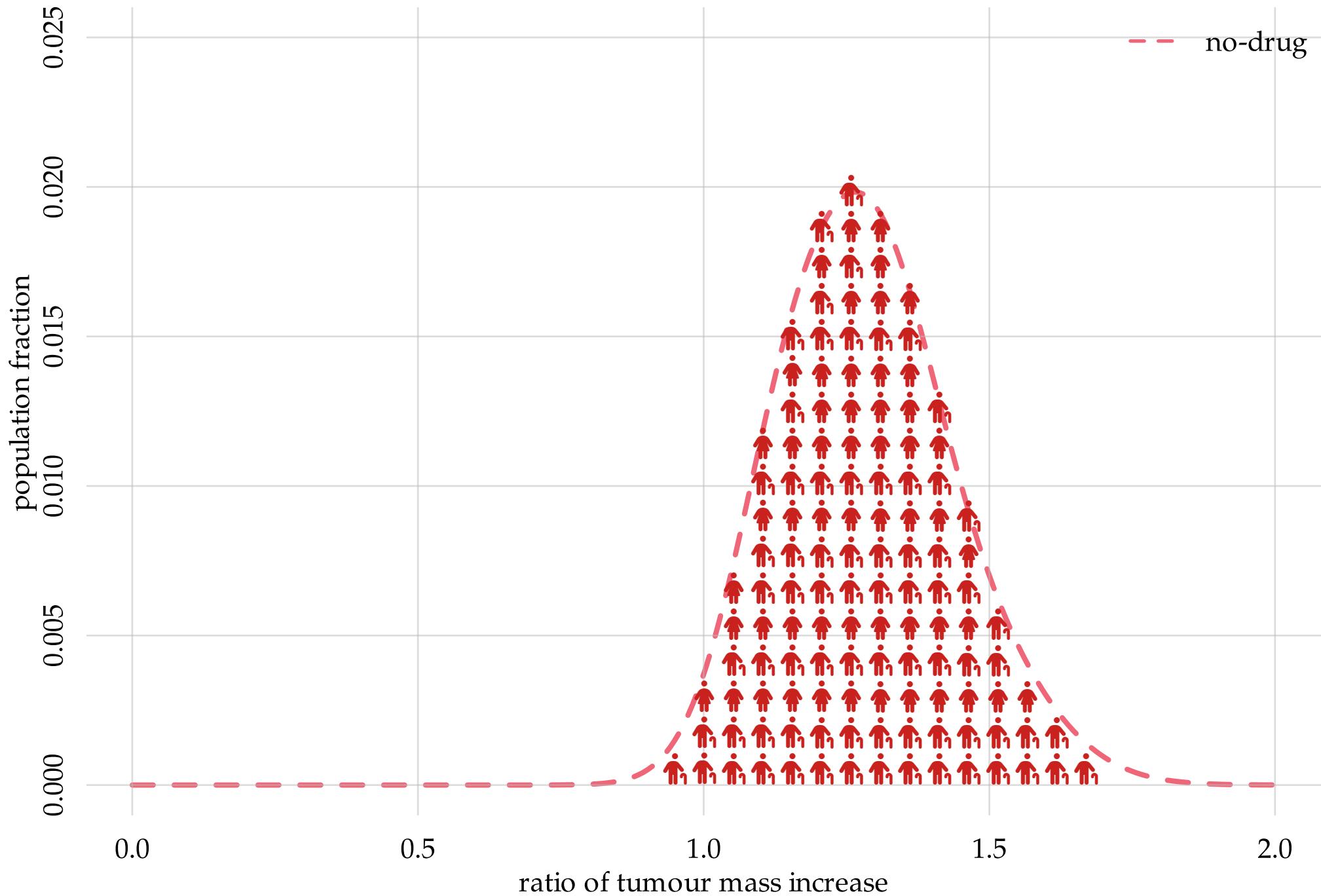


# Our fundamental problem: we only have a **sample**!

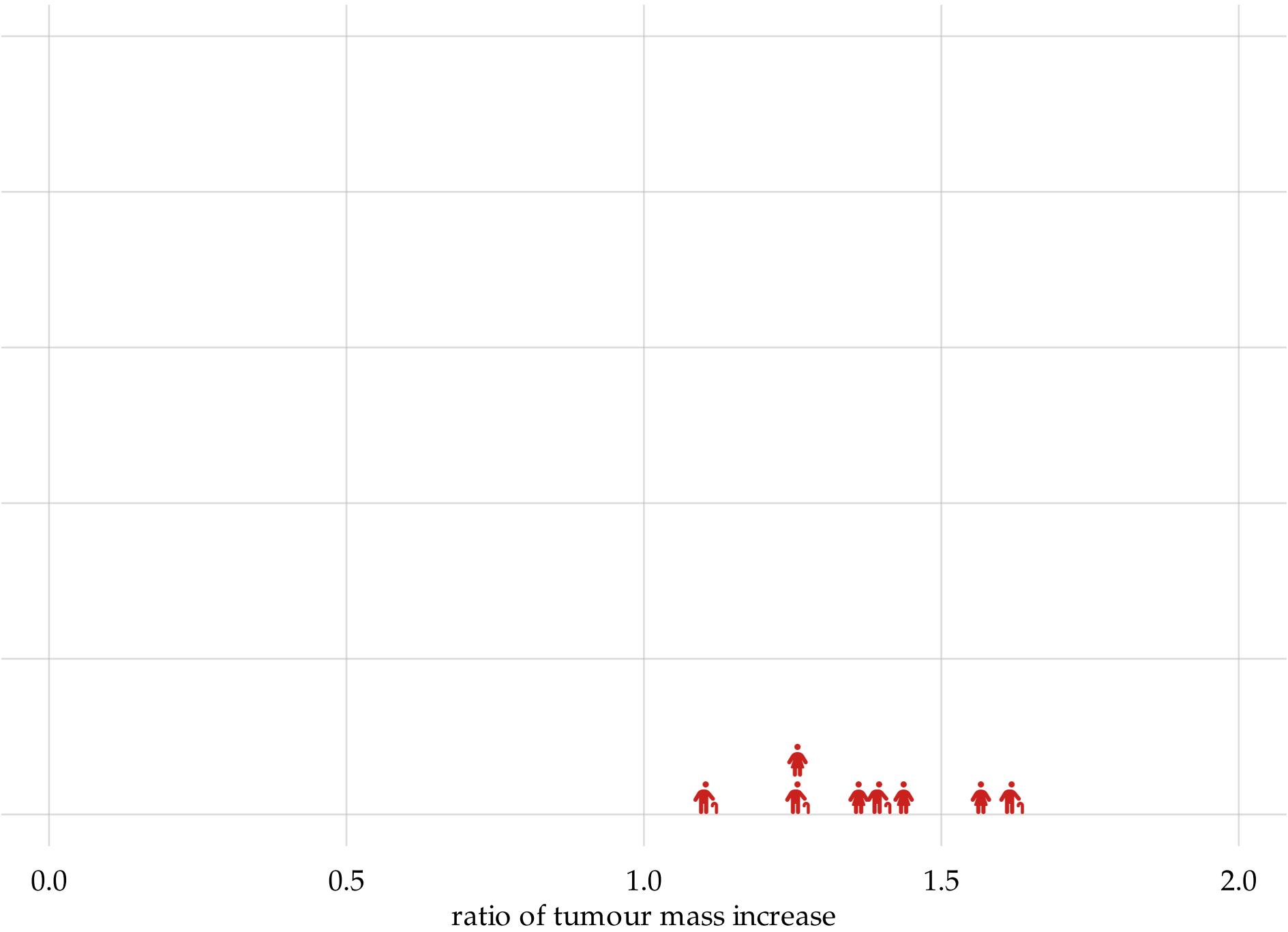


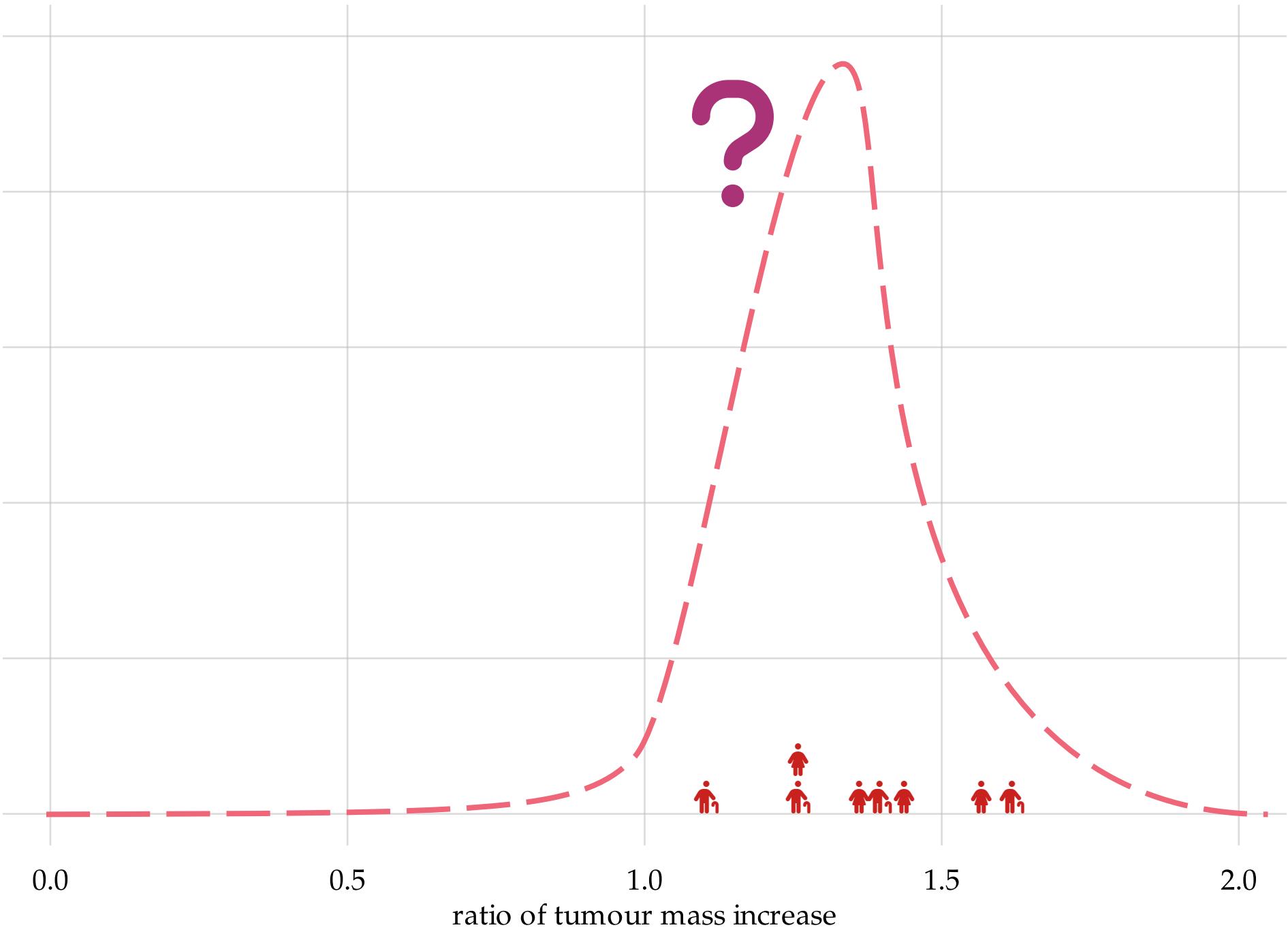
Anders Nicolai Kiær

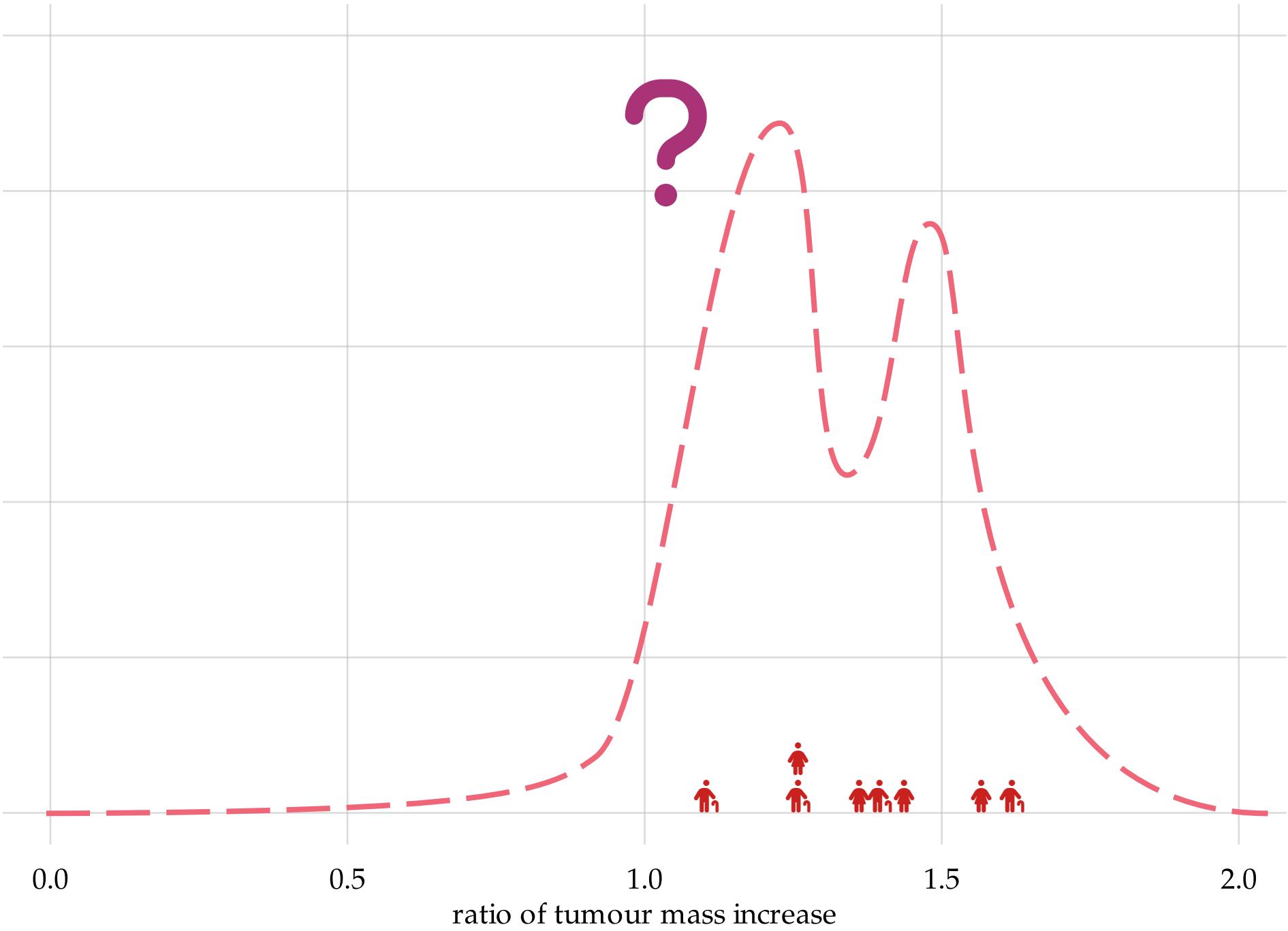
## Our fundamental problem: we don't have the **whole** population

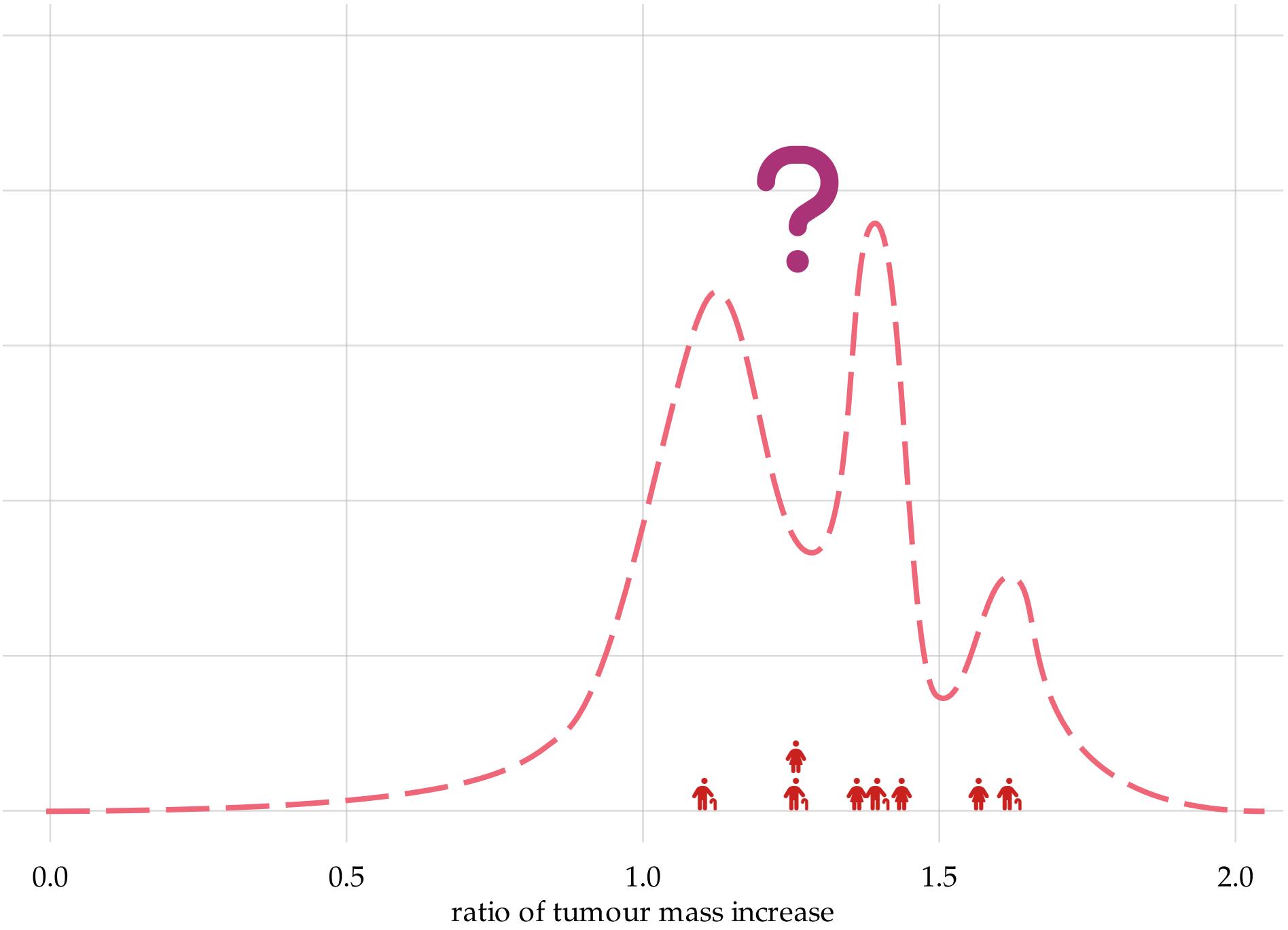


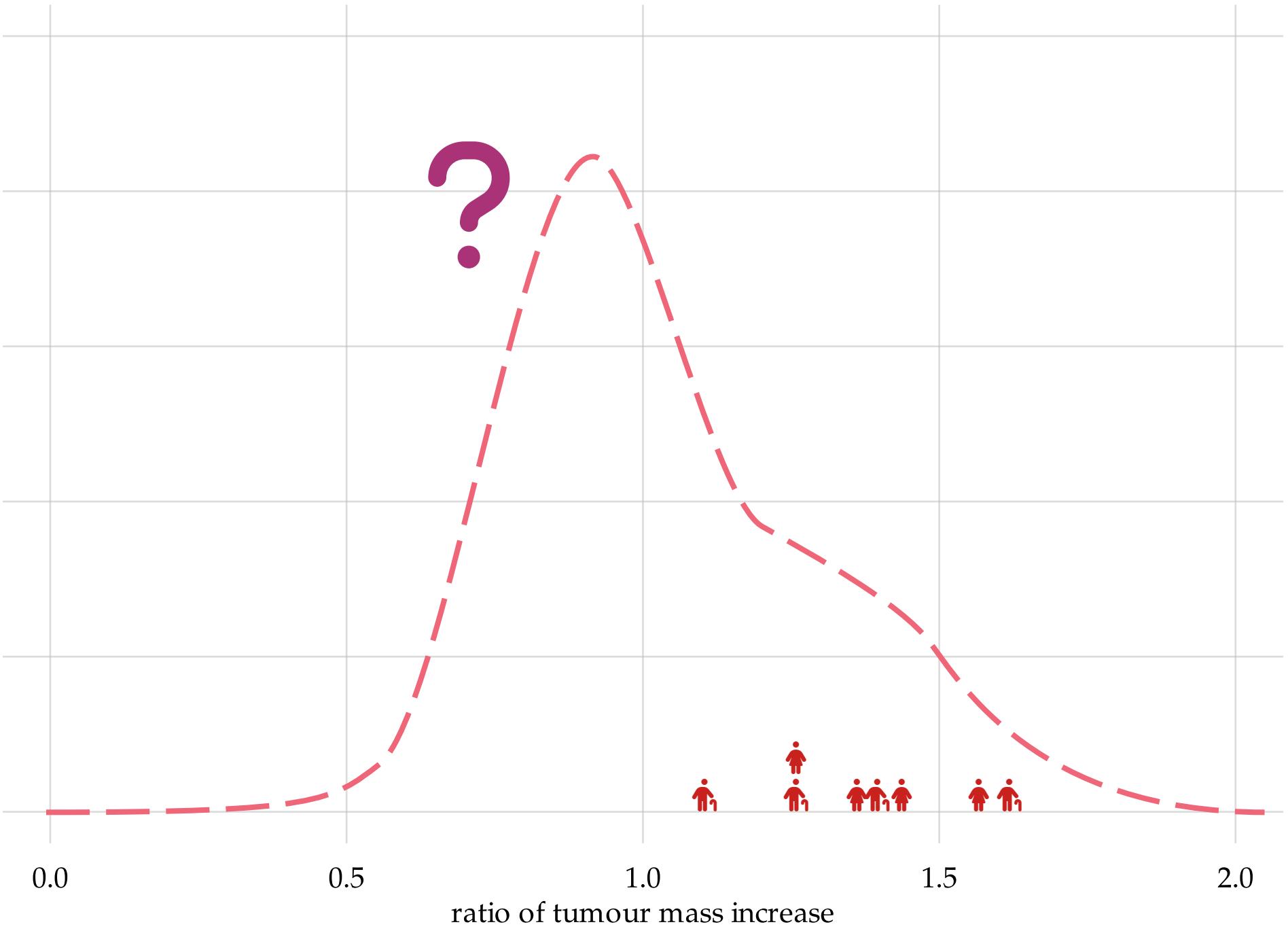
## Our fundamental problem: we only have a **sample**!











## The fundamental problem: we only have a **sample**

- Uncertainty in results
- “Tests” (t-test, ANOVA, F-test, . . .)
- *p*-values
- Confidence intervals
- Statistical models (Gaussian, . . .)

# Bayesian nonparametric population inference

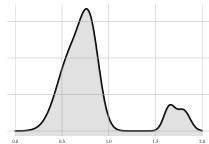
# Bayesian nonparametric population inference

*uses **probabilities**  
to represent & quantify uncertainty*

*does not make  
distribution assumptions*

*focuses on  
whole-population properties*

# Bayesian nonparametric population inference



- 🏆 No Gaussian assumptions, linear assumptions, etc (“model-free”)

$\Pr(H_0 \mid \text{data}) = 78\%$

- 🏆 Direct probabilities about hypotheses



- 🏆 Quantifies uncertainty of generalizing sample → whole population



- 🏆 Immediate integration with Clinical Decision Making



ratio = 0.3  
age = ?  
sex = male

- 🏆 Automatic, principled imputation of missing data

~~Bonferroni~~

- 🏆 No corrections for sample size, multiple hypotheses, etc



- 🏆 Insensitive to “stopping rules”

- 🏆 Can be used with nominal, ordinal, interval, censored variates

- 🏆 Can correct base-rate fallacies and similar biases

**INTRODUCTION  
TO  
MEDICAL DECISION MAKING**

*By*

LEE B. LUSTED, M.D.

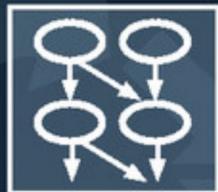
*Professor and Chairman  
Department of Radiology  
Stritch School of Medicine  
Loyola University Medical Center  
Hines, Illinois*



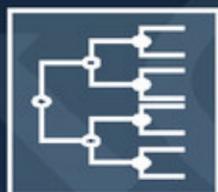
CHARLES C THOMAS • PUBLISHER  
• Springfield • Illinois • U.S.A.

# Decision Making in Health and Medicine

Integrating Evidence and Values



SECOND  
EDITION



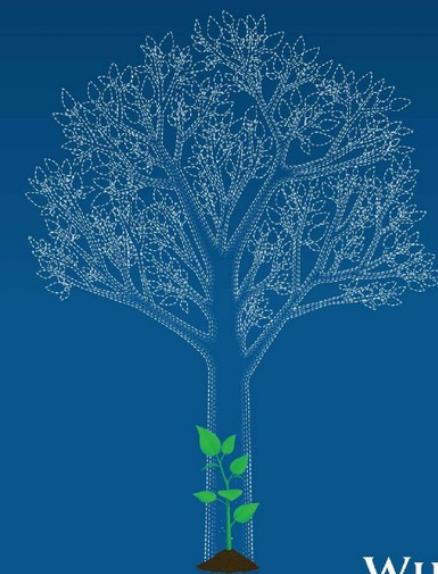
M. G. Myriam Hunink  
Milton C. Weinstein  
Eve Wittenberg  
Michael F. Drummond  
Joseph S. Pliskin  
John B. Wong  
Paul P. Glasziou

CAMBRIDGE  
Medicine

THIRD EDITION

# MEDICAL DECISION MAKING

HAROLD C. SOX • MICHAEL C. HIGGINS  
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WILEY Blackwell

# KENDALL'S ADVANCED THEORY OF STATISTICS

SECOND EDITION

VOLUME

**2B**

*Bayesian  
Inference*

ANTHONY O'HAGAN AND JONATHAN FORSTER

# ASA Section on Bayesian Statistical Science

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## What is SBSS?

The Section on Bayesian Statistical Science (SBSS) of the ASA provides a forum for statisticians and people who have interest in the Bayesian paradigm. The broad objectives of the Section are: to encourage research on theory and methods of statistical inference and decision making associated with Bayes' theorem and to encourage the application and proper use of Bayesian procedures in the behavioral, biological, managerial, engineering, environmental, legal, medical, pharmaceutical, physical, and social sciences.

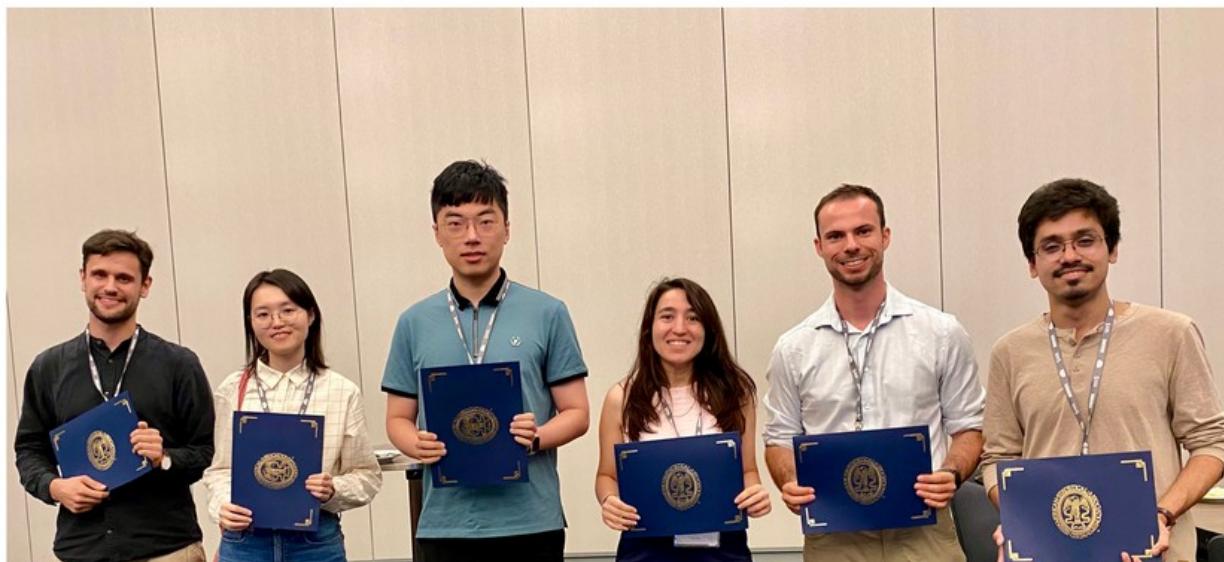
## Upcoming deadlines

We hope you can take part in [JSM 2025!](#)

- The deadline for the SBSS student paper competition is November 15th, 2024. Please see the [Awards page](#) for more details.



## 2024 ASA SBSS student paper competition





Home > Training > Public courses > Introduction to statistics > Introduction to Bayesian Statistics  
> Online, Wednesday 12 March 2025, 5.00PM

## Introduction to Bayesian Statistics - Virtual Classroom

**Date:** Tuesday 11 March 2025 9.30AM - Wednesday 12 March 2025 5.00PM

**Location:** Online

**CPD:** 12.0 hours

[Book now](#)[Share this event](#)

### RSS Training

[!\[\]\(7ebdaa8f61b993ca25383c4de194b122\_img.jpg\) Event overview](#)[!\[\]\(f4b4e05c6bbd31fcb2bfc8a326c17544\_img.jpg\) Full event information](#)[!\[\]\(7daa1f9006d8cf9d319d4492e24b39fc\_img.jpg\) Speakers](#)[!\[\]\(1accaf637325c70743f4b5e9d84df397\_img.jpg\) Event costs](#)

**Level:** Intermediate (I)

This virtual course aims to provide a working knowledge of Bayesian statistics for interested researchers.

Bayesian statistics has become a standard approach for many applied statisticians across a wide variety of fields due to its conceptual unity, clarity and practical benefits. However, because training in Bayesian methods is often not a standard part of research curricula, the benefits of Bayesian statistics have been slower to reach applied researchers.



# Trial of a Preferential Phosphodiesterase 4B Inhibitor for Idiopathic Pulmonary Fibrosis

**Authors:** Luca Richeldi, M.D., Ph.D., Arata Azuma, M.D., Ph.D., Vincent Cottin, M.D., Ph.D. , Christian Hesslinger, Ph.D., Susanne Stowasser, M.D., Claudia Valenzuela, M.D., Marlies S. Wijsenbeek, M.D., Ph.D. , Donald F. Zoz, M.D., Florian Voss, Ph.D., and Toby M. Maher, M.D., Ph.D., for the 1305-0013 Trial Investigators\* [Author Info & Affiliations](#)

Published May 15, 2022 | N Engl J Med 2022;386:2178-2187 | DOI: 10.1056/NEJMoa2201737 | VOL. 386 NO. 23

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## EFFICACY

On the basis of the Bayesian analysis, the median change in the FVC was 5.7 ml (95% credible interval, -39.1 to 50.5) in the BI 101550 group and -81.7 ml (95% credible interval, -133.5 to -44.8) in the placebo group among patients without background antifibrotic use (median difference, 88.4 ml; 95% credible interval, 29.5 to 154.2; probability that BI 101550 was superior to placebo, 0.998). Among patients with background antifibrotic use, the respective FVC changes were 2.7 ml (95% credible interval, -32.8 to 38.2) and -59.2 ml (95% credible interval, -111.8 to -17.9) (median difference, 62.4 ml; 95% credible interval, 6.3 to 125.5; probability that BI 101550 was superior to placebo, 0.986) ([Figure 2](#) and [Table S2](#)).

	2646	2835	2869	2411
Median — ml				
Percent of predicted value	80.4±16.0	82.1±17.7	75.8±17.9	71.7±12.3
Percent of predicted DLCO, corrected for the hemoglobin level	52.0±16.7	48.3±12.1	49.0±18.3	47.2±14.8
L-PF questionnaire total score§	33.9±18.3	32.4±16.1	25.8±16.7	26.1±15.7

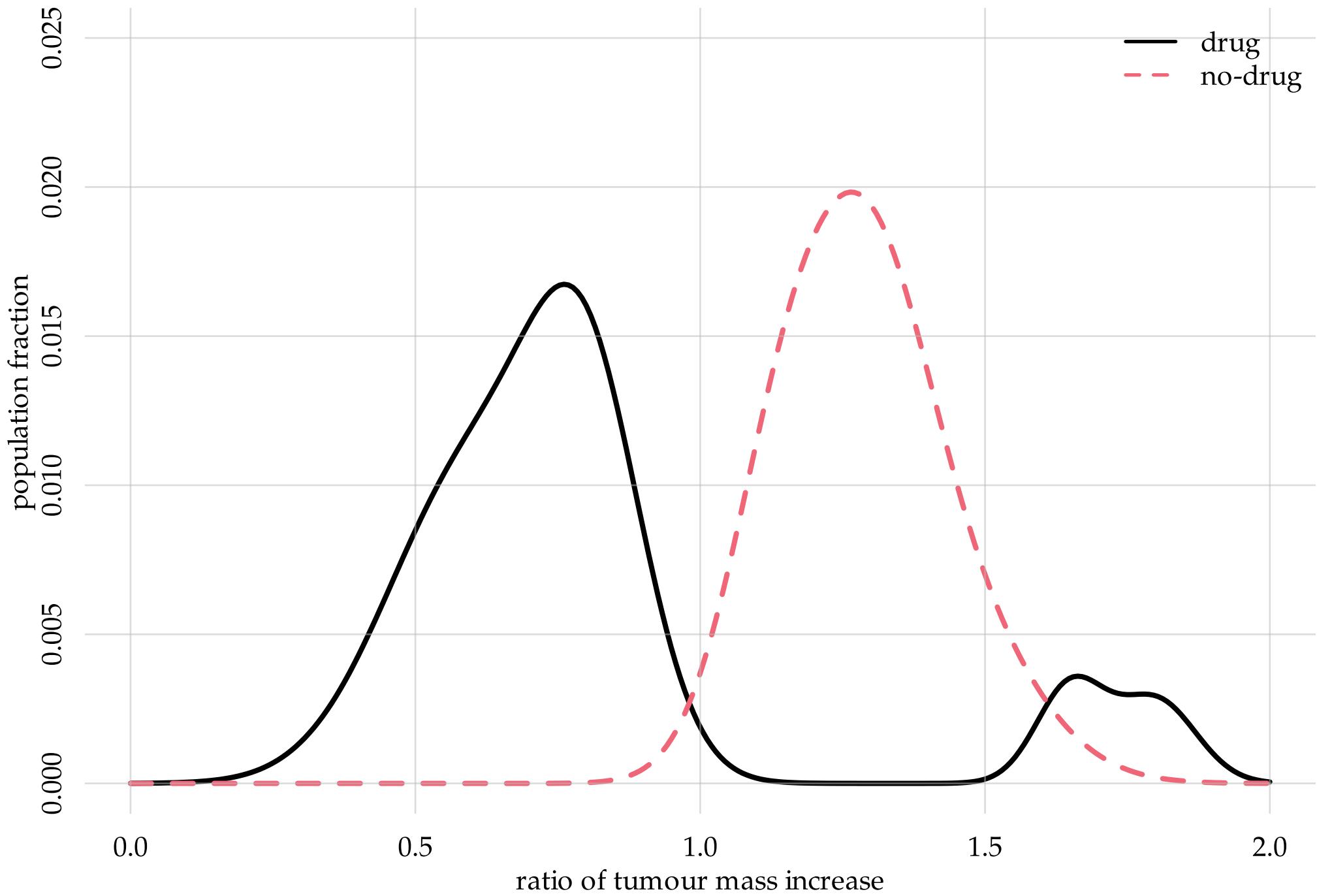
\* Plus-minus values are means ±SD. DLCO denotes diffusing capacity of the lung for carbon monoxide, and FVC forced vital capacity.

† Race was noted in the electronic case-report form by the trial site staff. There were no explicit instructions regarding patient report or investigator determination of race.

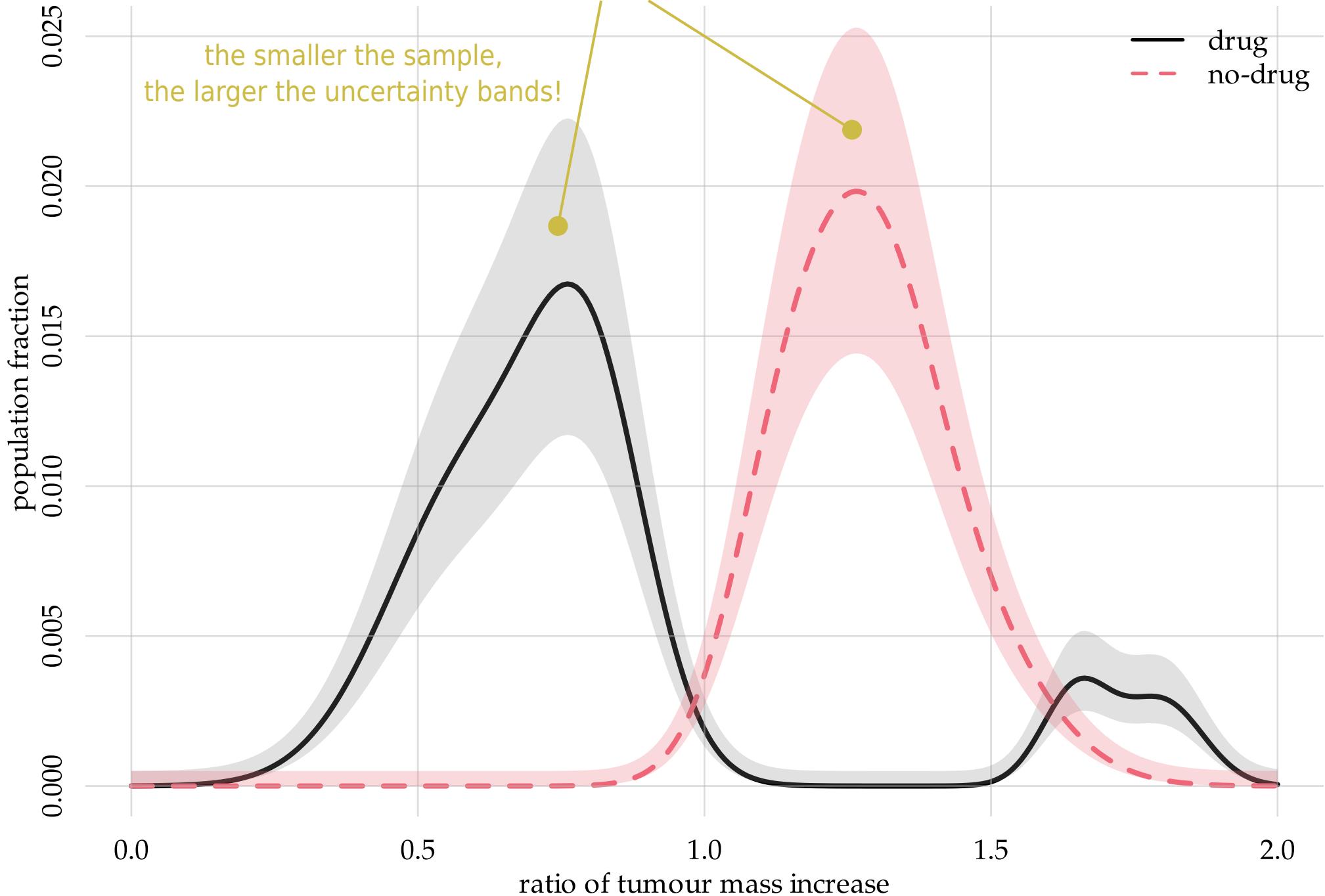
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.

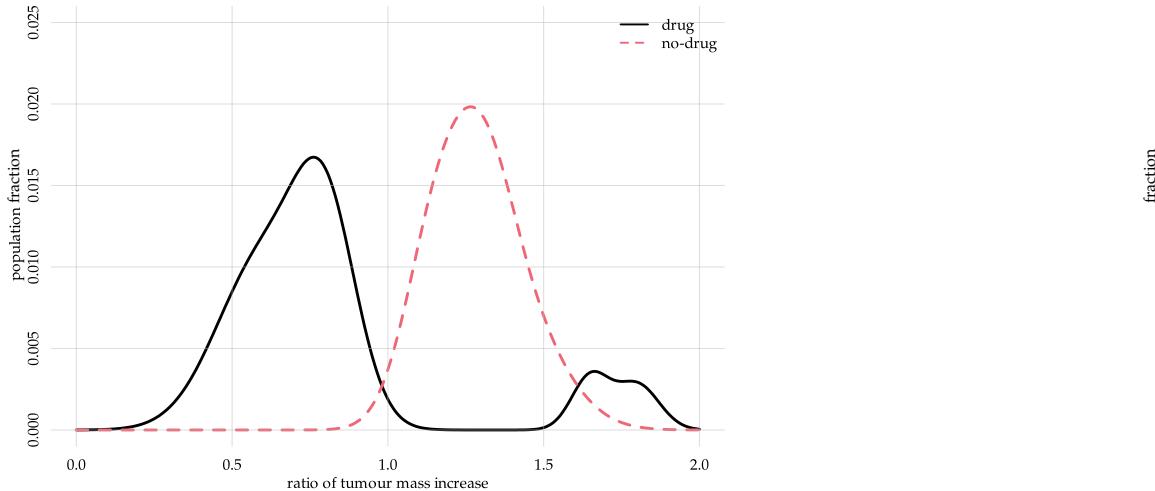
§ The Living with Pulmonary Fibrosis (L-PF) questionnaire is a 44-item questionnaire with two modules: Symptoms and Impacts.<sup>22</sup> Scores in the Symptoms and Impacts modules are summed to yield a total L-PF score. Summary scores range from 0 to 100, with higher scores indicating greater impairment.

*Characteristics of the Patients at Baseline, According to Cohort.*



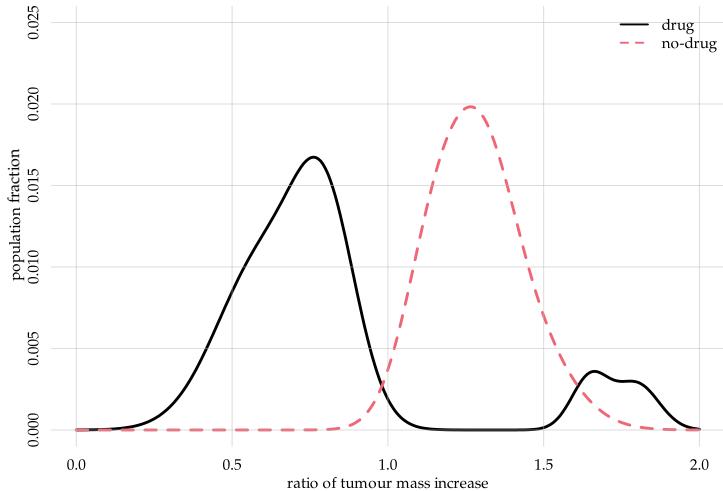
## 90%-uncertainty bands





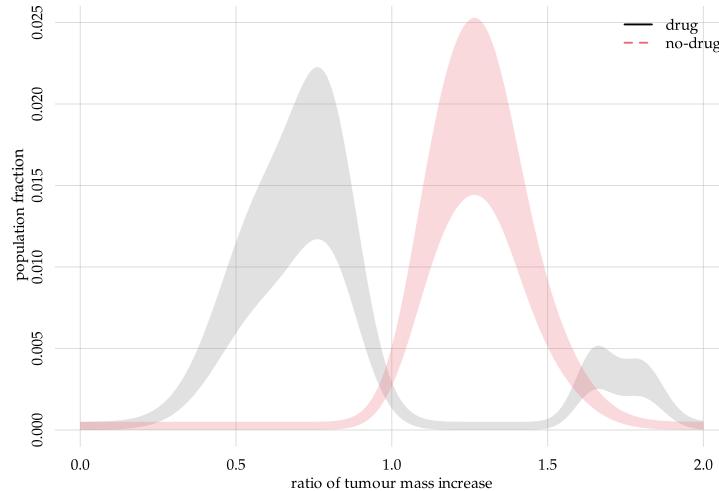
**86.5%** of treated subjects  
have a decrease in tumour mass

2.4% of non-treated subjects  
have a decrease in tumour mass



**86.5%** of treated subjects  
have a decrease in tumour mass

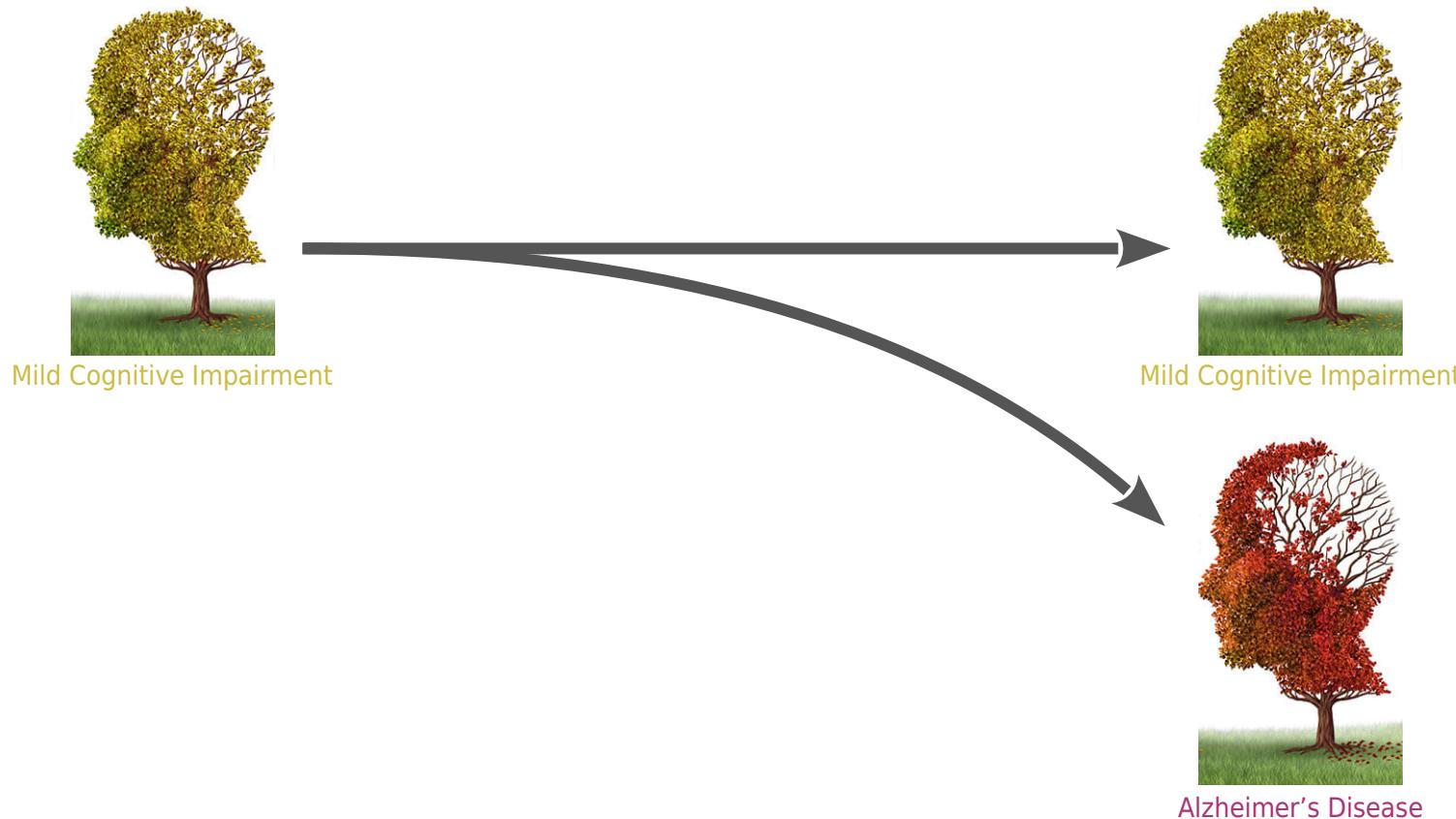
2.4% of non-treated subjects  
have a decrease in tumour mass



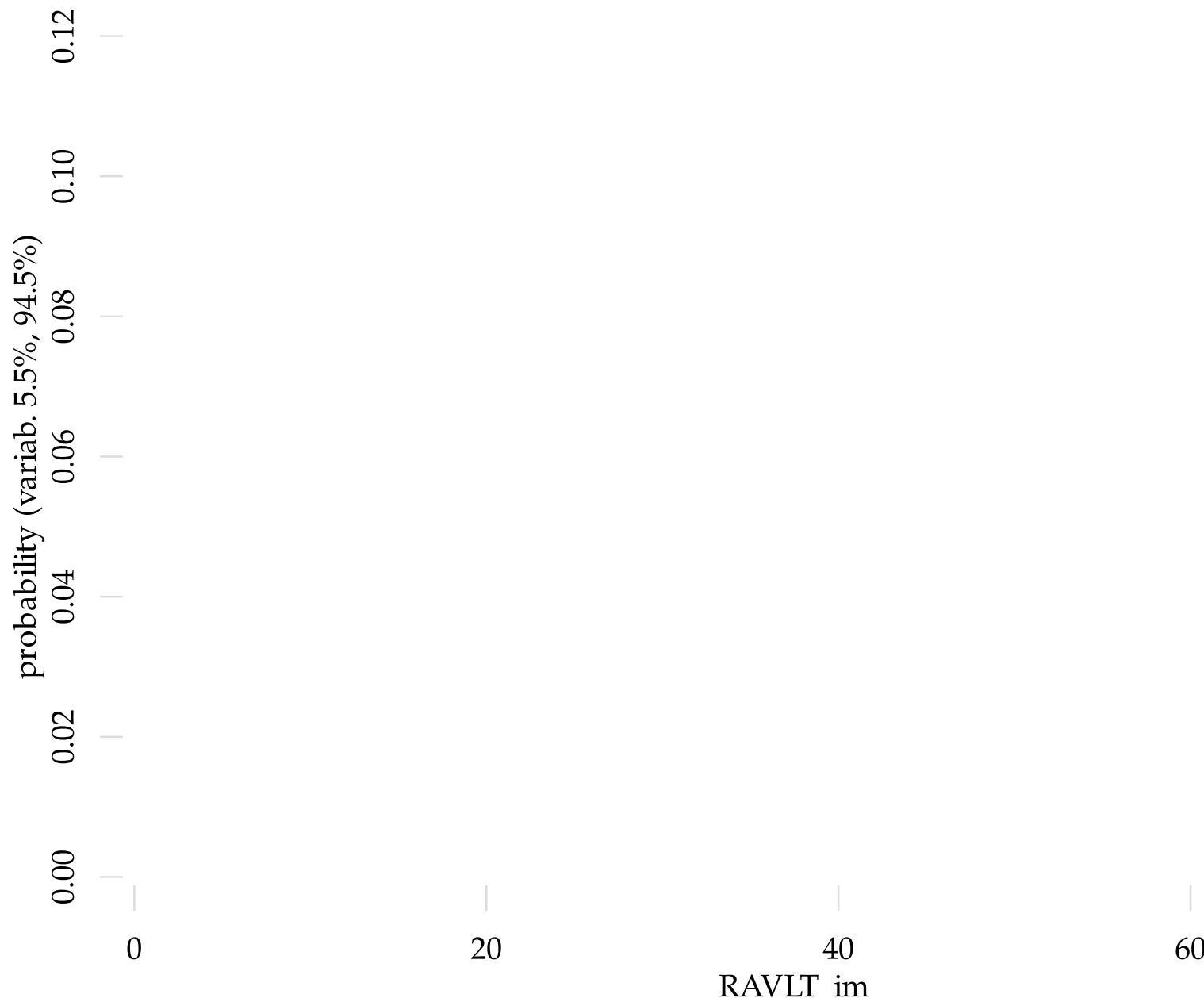
Fraction of treated subjects  
with a decrease in tumour mass:  
**between 72% and 93%**  
with a **90% probability**

Fraction of non-treated subjects  
with a decrease in tumour mass:  
**between 0.1% and 4.3%**  
with a **90% probability**

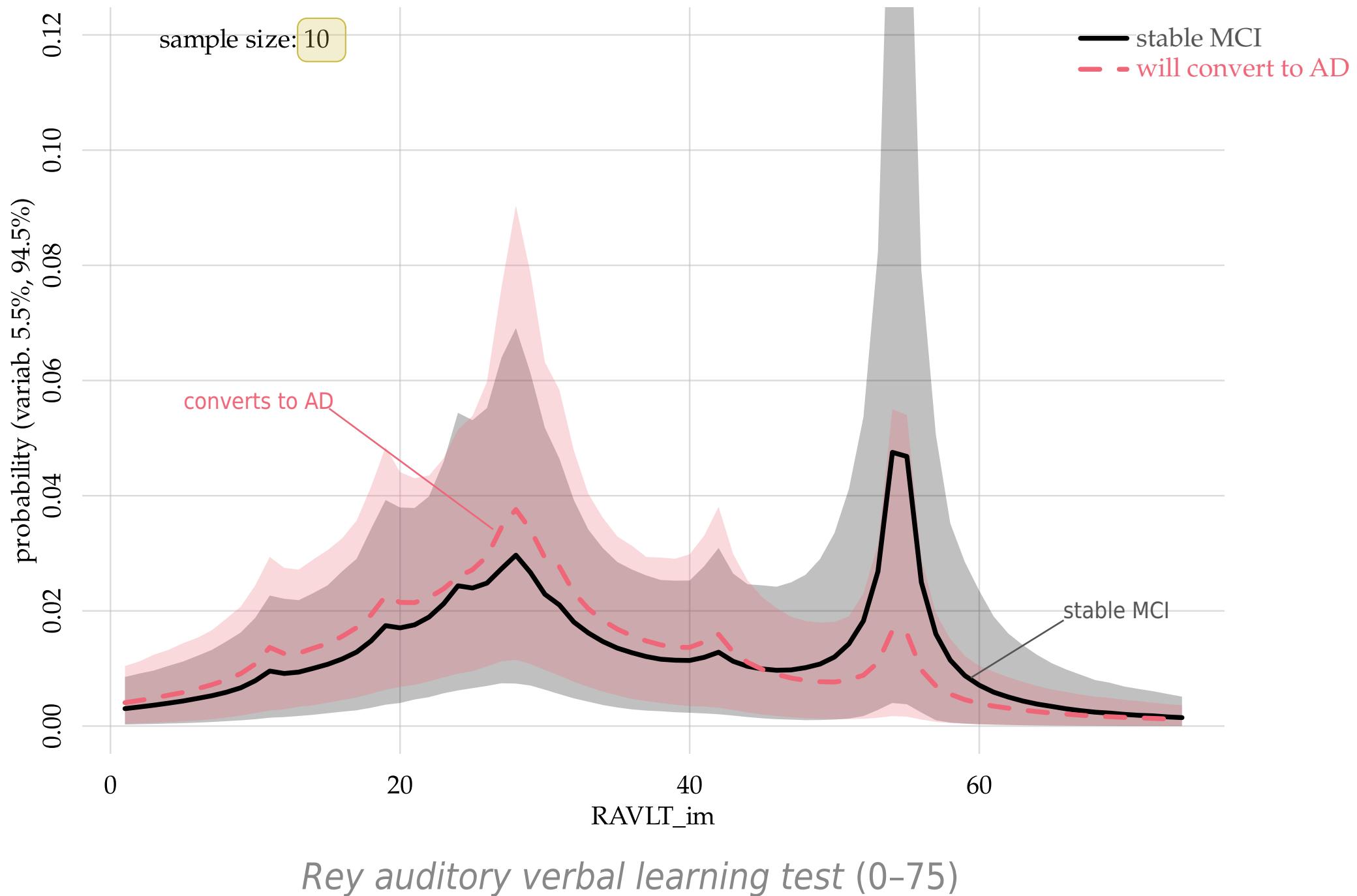
## Real example: **prognosing** conversion to Alzheimer's Disease

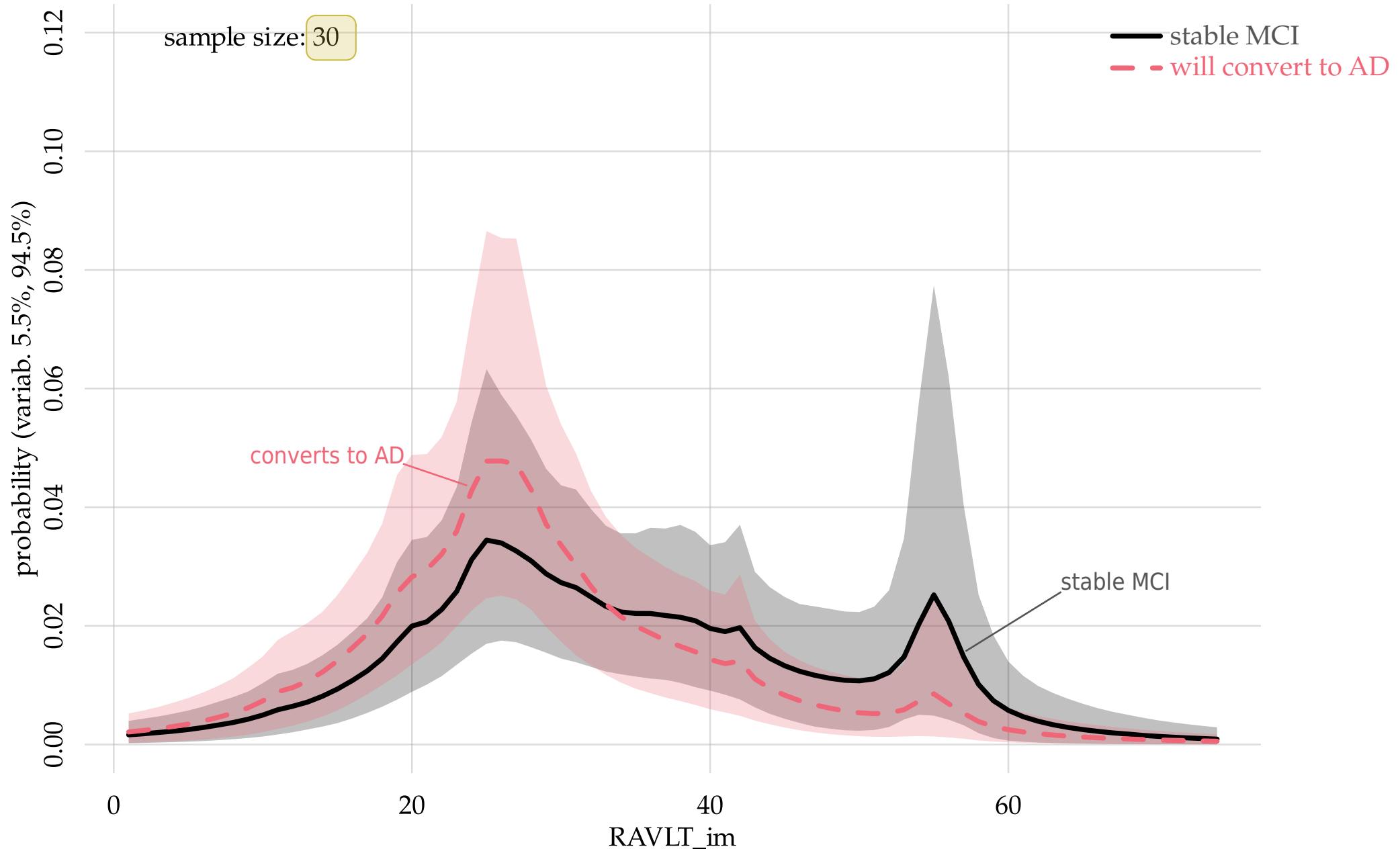


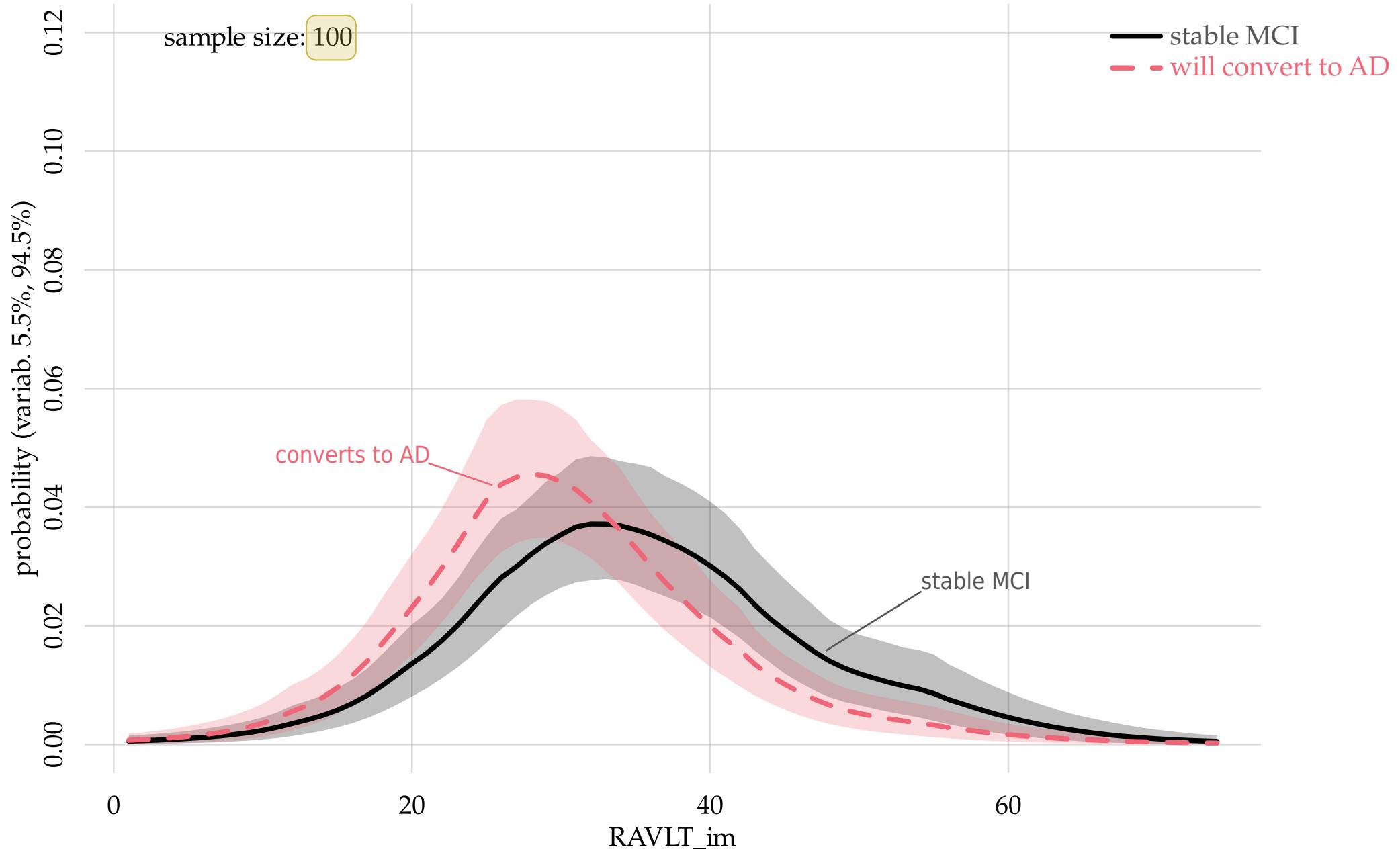
- Sample: 704 patients
- 13 variates (demographics, genetic, cognitive tests, Hippoc. volume)
- Some missing data

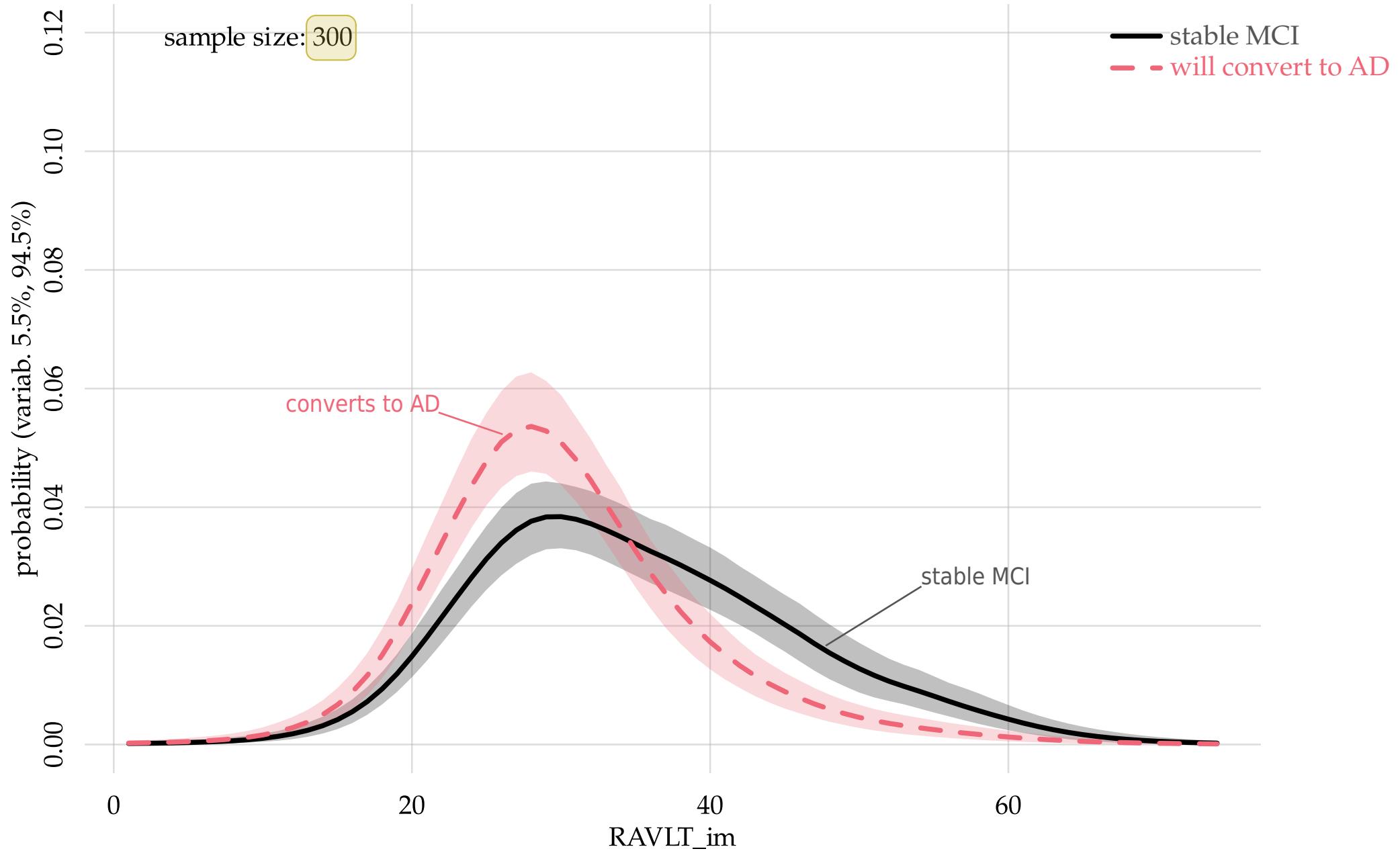


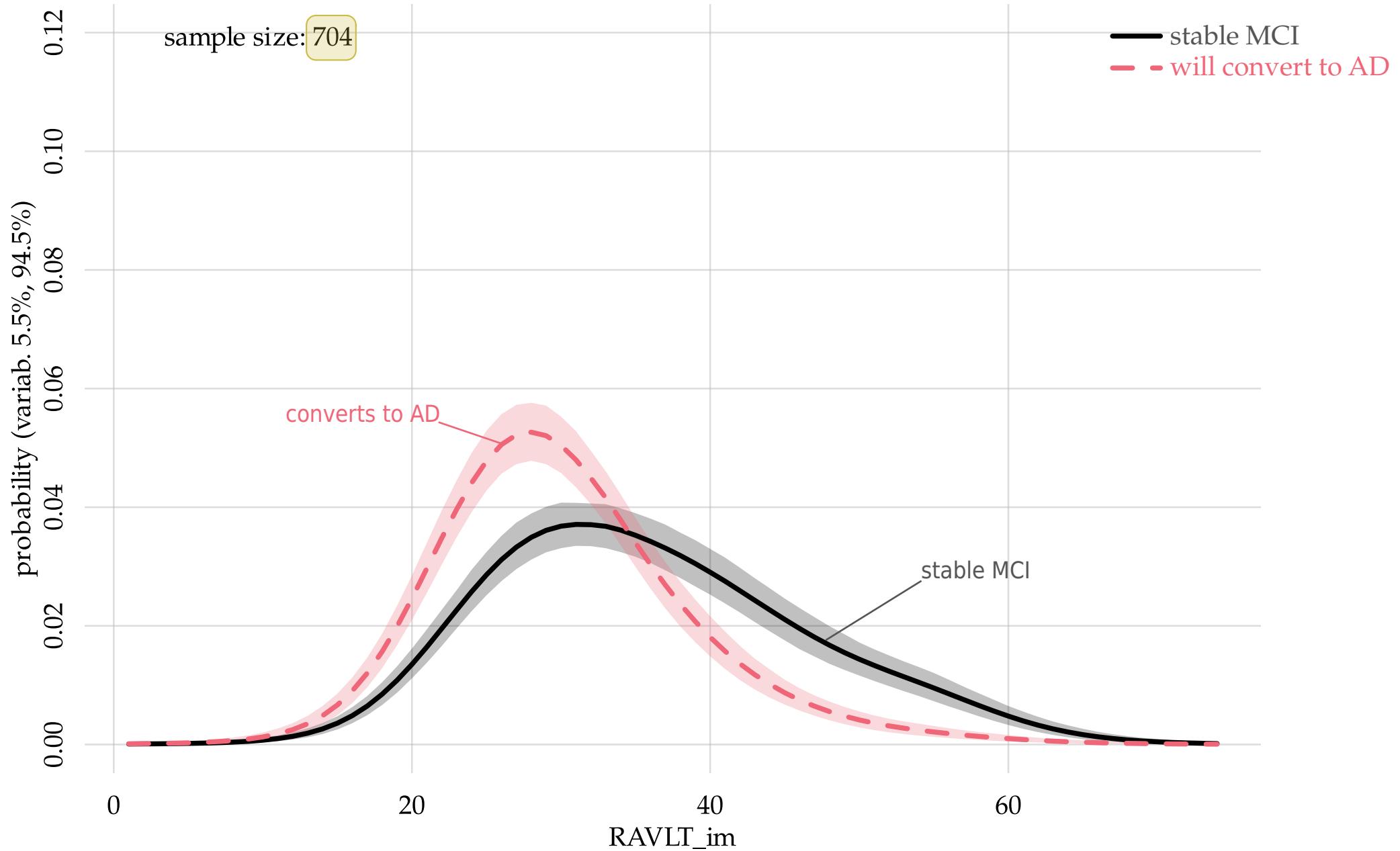
*Rey auditory verbal learning test (0-75)*







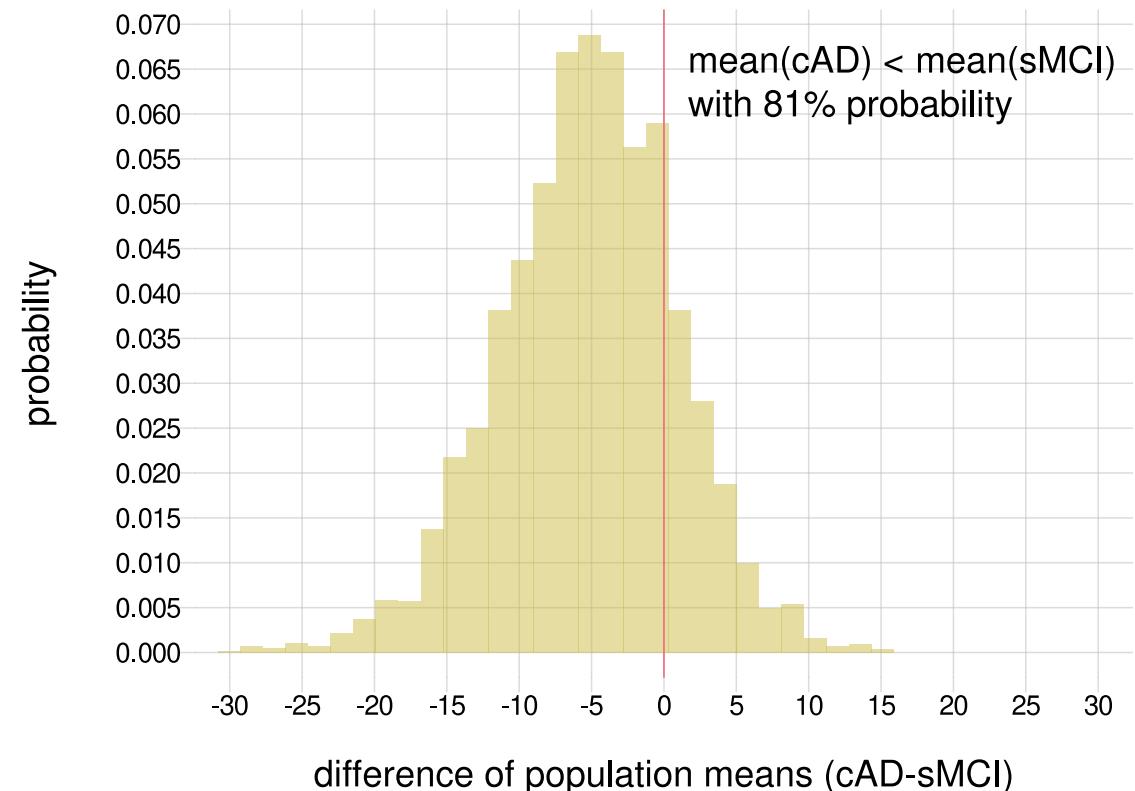
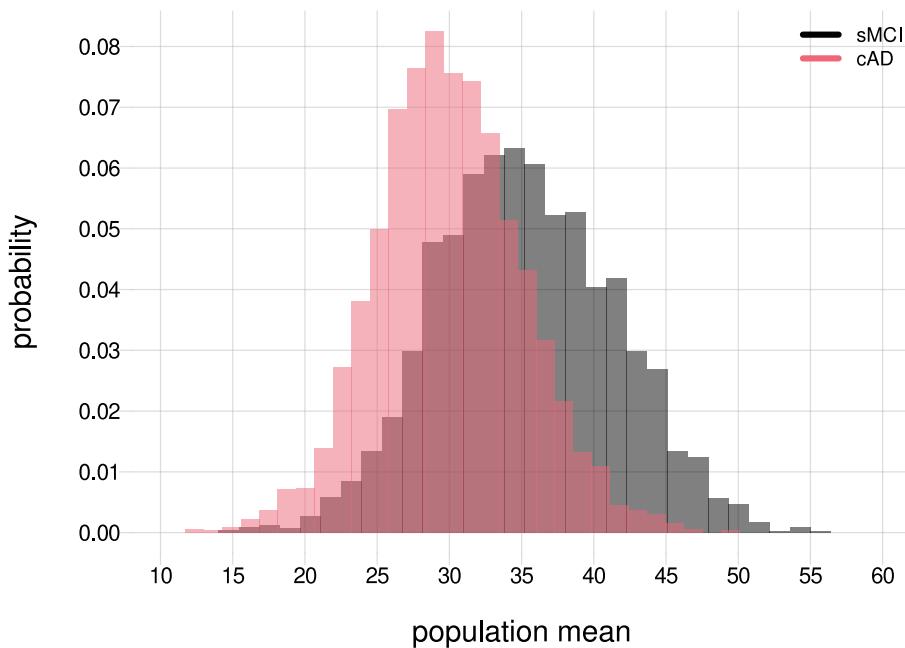




# *Are the means of the stable-MCI and convert-AD different? how much?*

sample size: 10

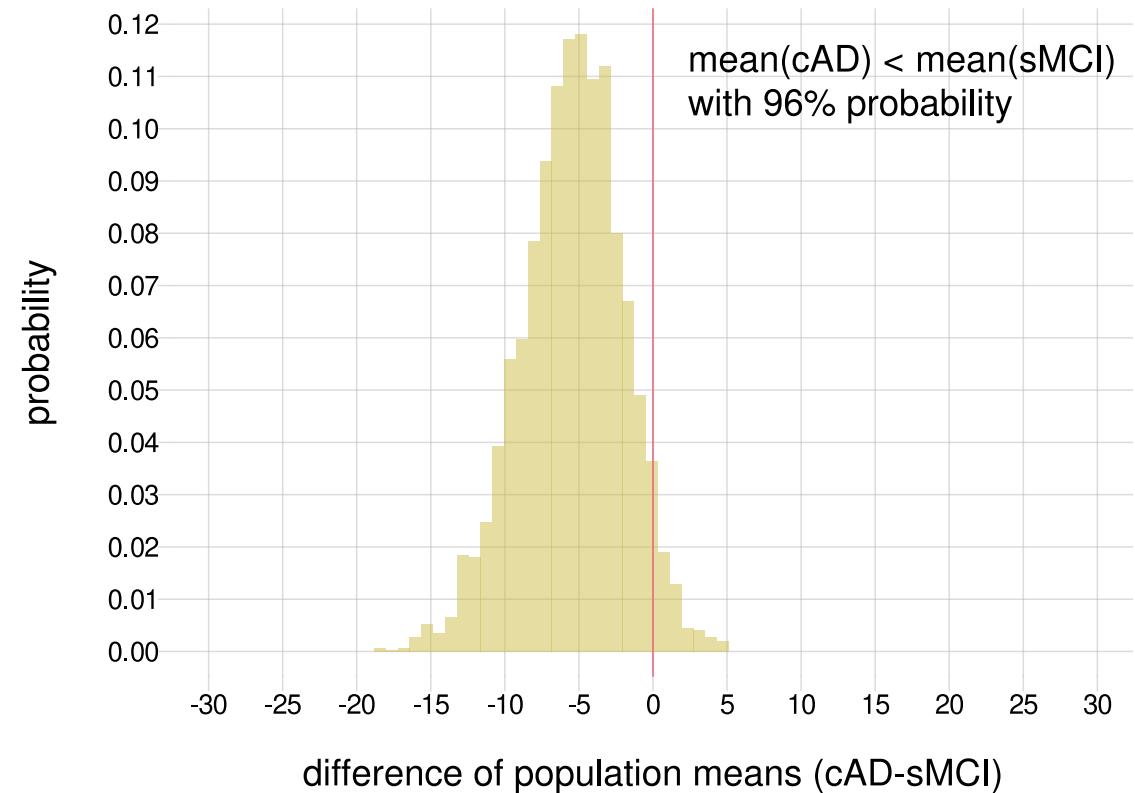
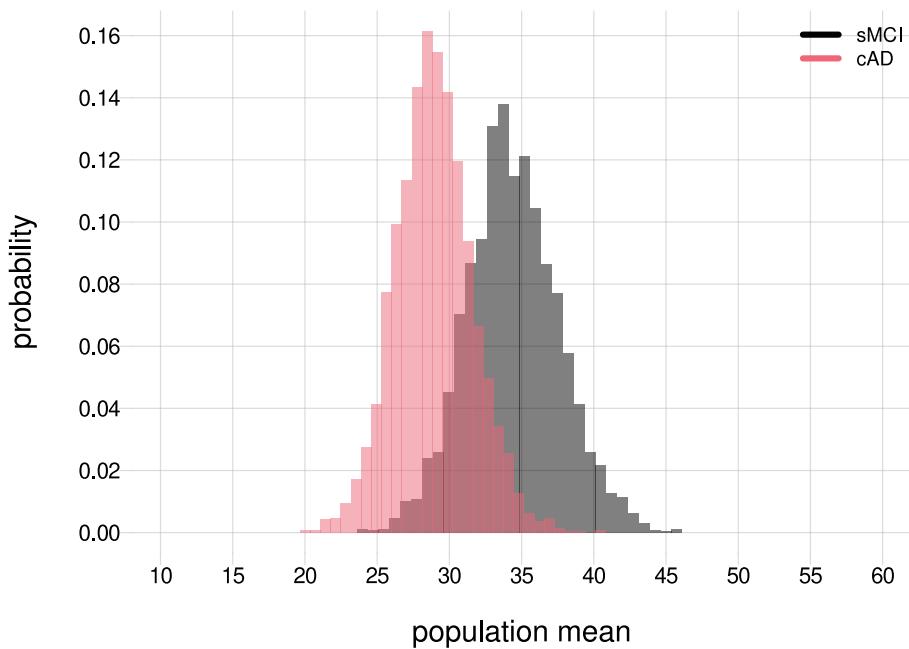
81% probability that  $\text{mean}(\text{sMCI}) < \text{mean}(\text{cAD})$



# *Are the means of the stable-MCI and convert-AD different? how much?*

sample size: 30

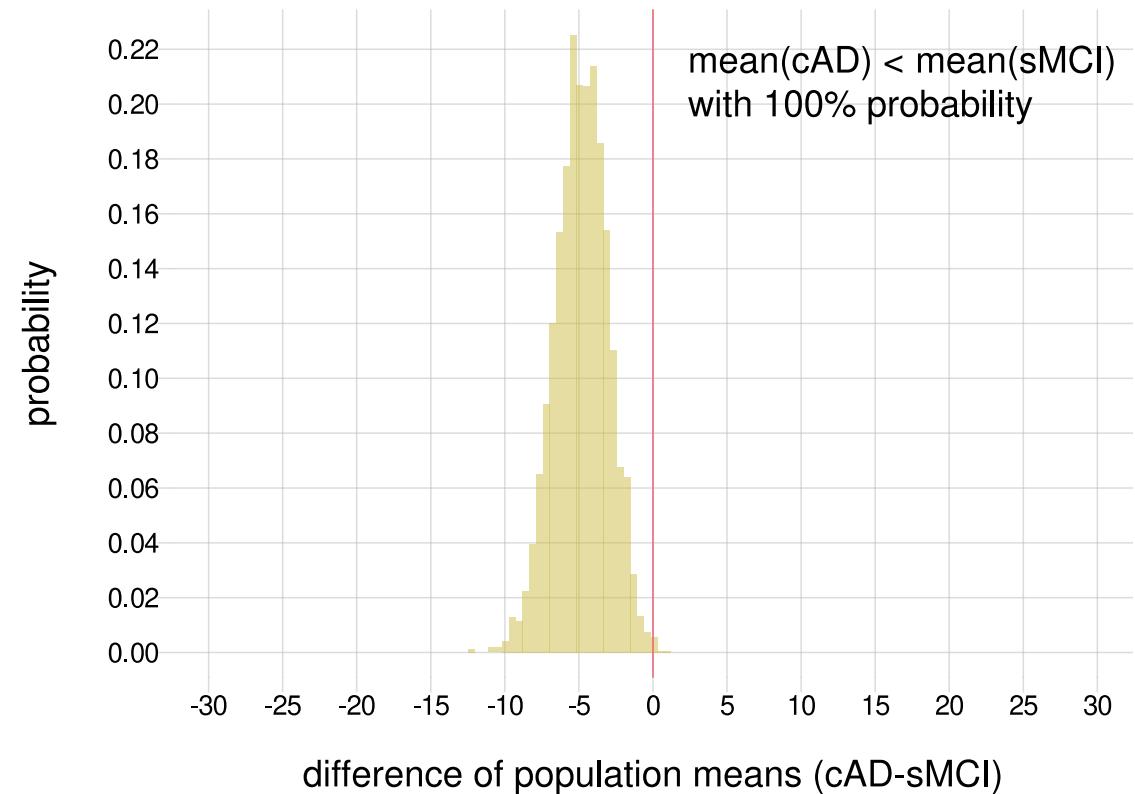
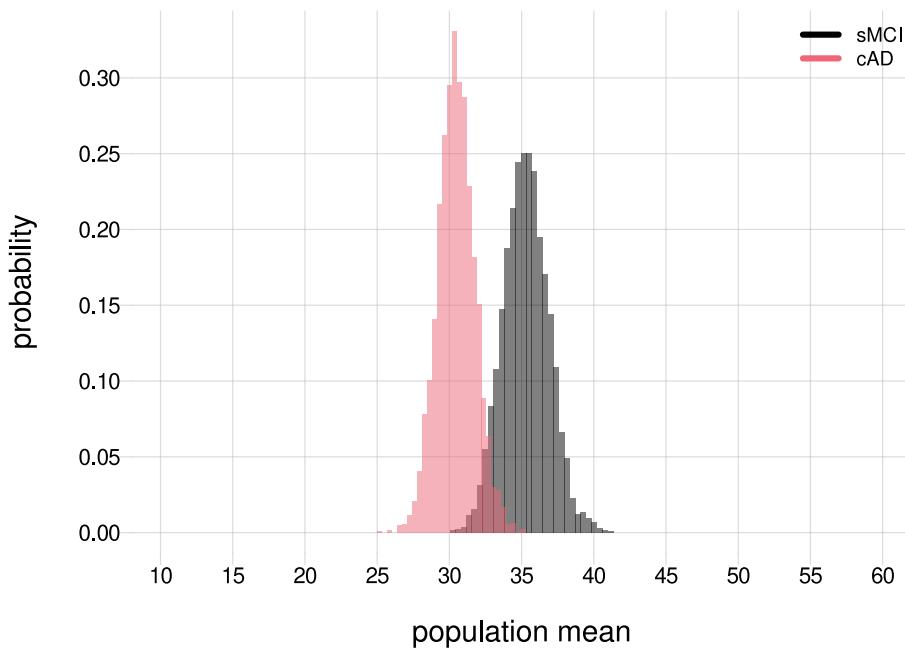
96% probability that  $\text{mean}(\text{sMCI}) < \text{mean}(\text{cAD})$



## *Are the means of the stable-MCI and convert-AD different? how much?*

sample size: 100

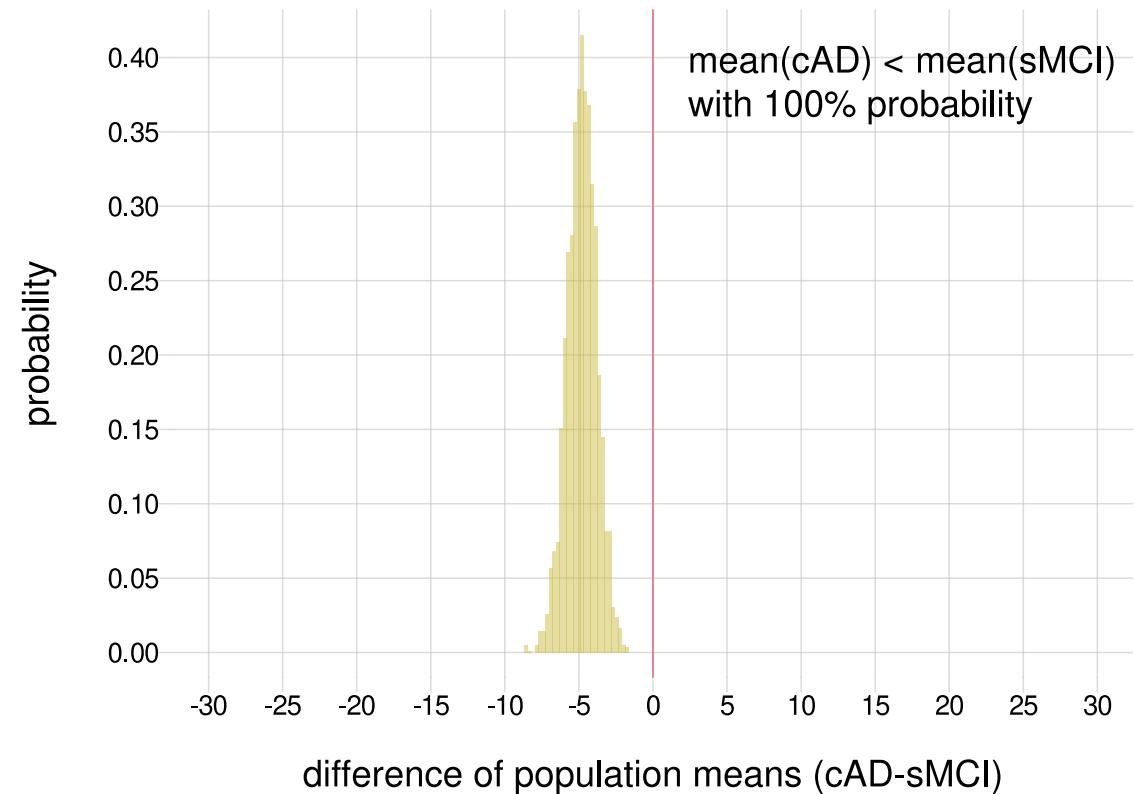
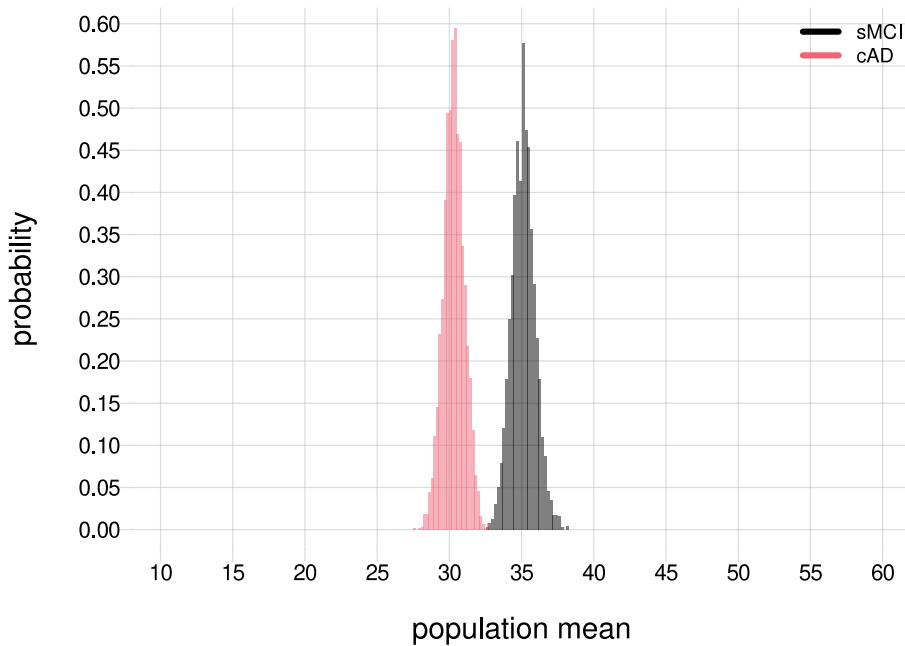
100% probability that  $\text{mean}(\text{sMCI}) < \text{mean}(\text{cAD})$



## *Are the means of the stable-MCI and convert-AD different? how much?*

sample size: 300

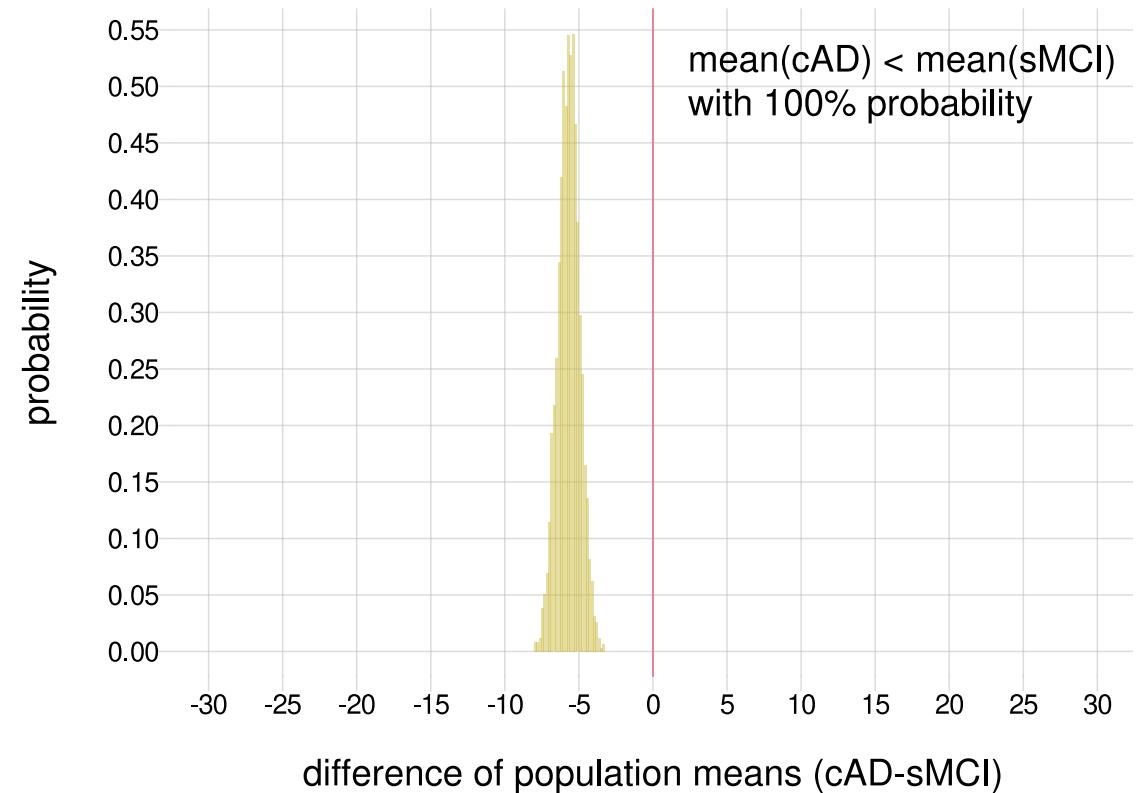
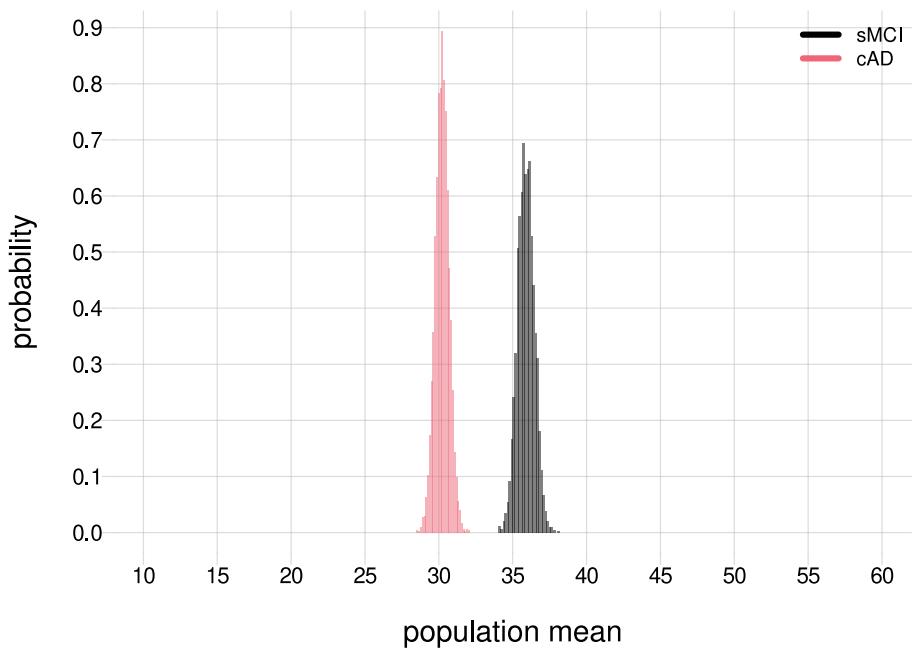
100% probability that  $\text{mean}(\text{sMCI}) < \text{mean}(\text{cAD})$



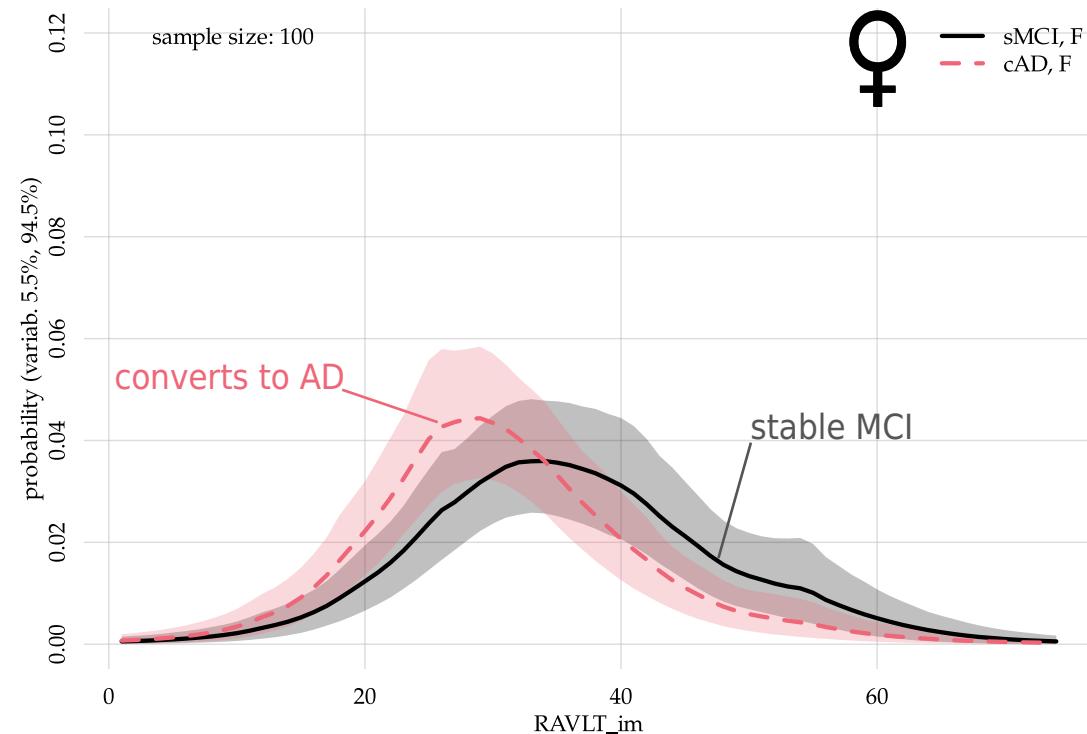
## *Are the means of the stable-MCI and convert-AD different? how much?*

sample size: 704

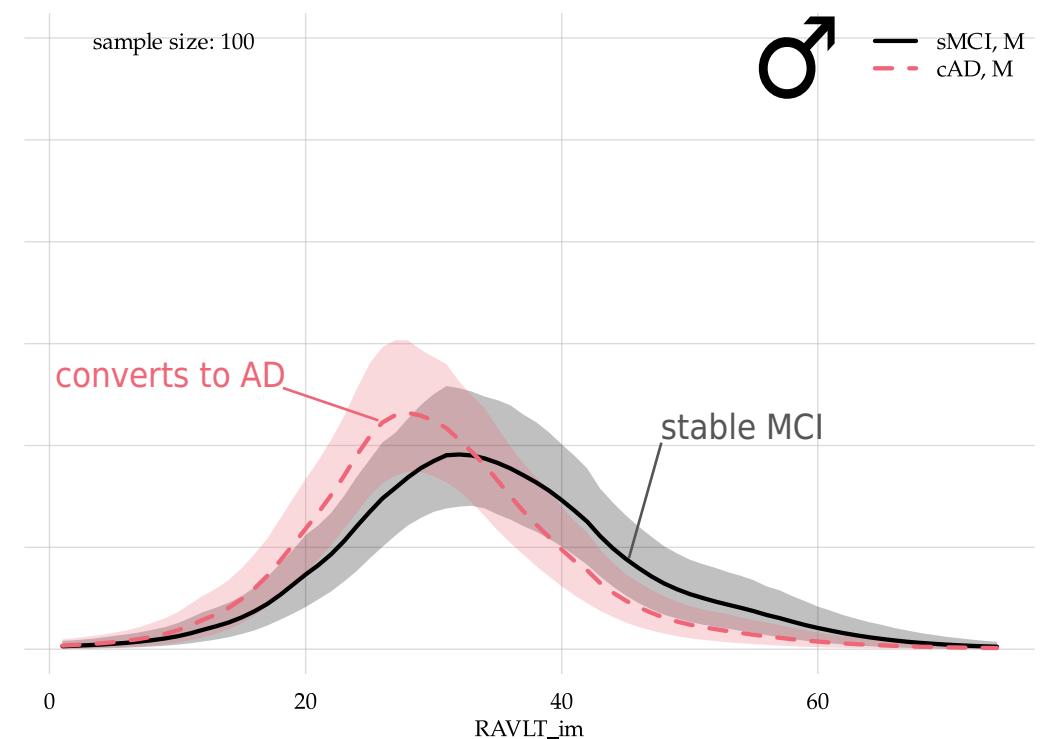
100% probability that  $\text{mean}(\text{sMCI}) < \text{mean}(\text{cAD})$



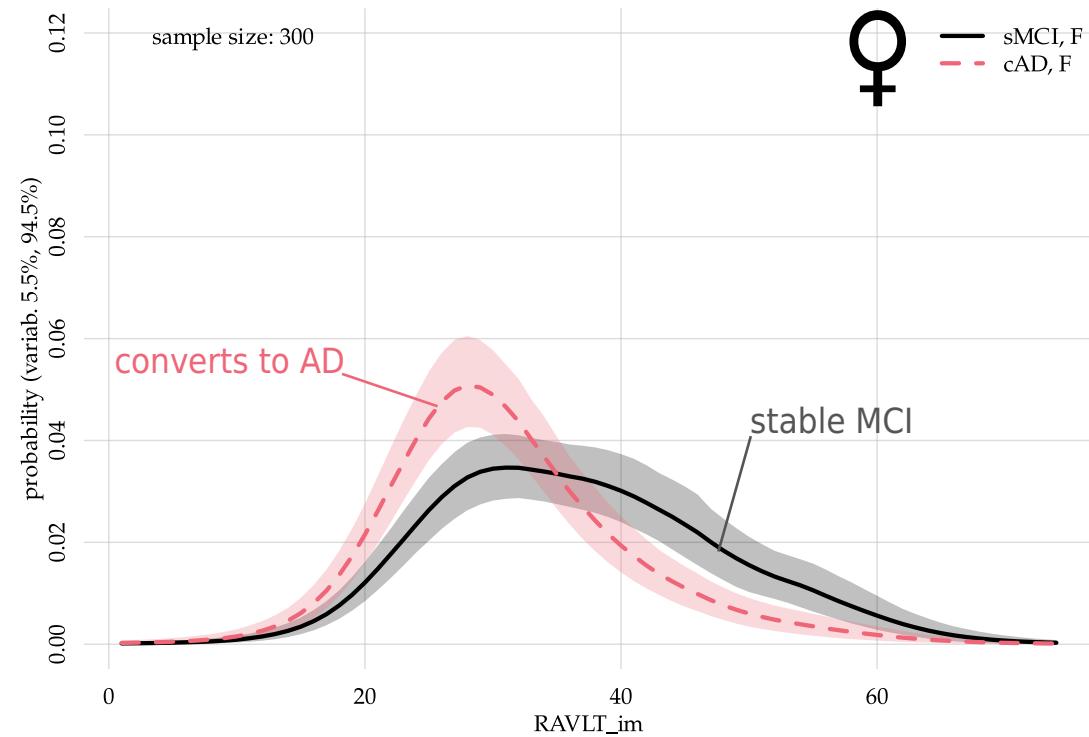
female



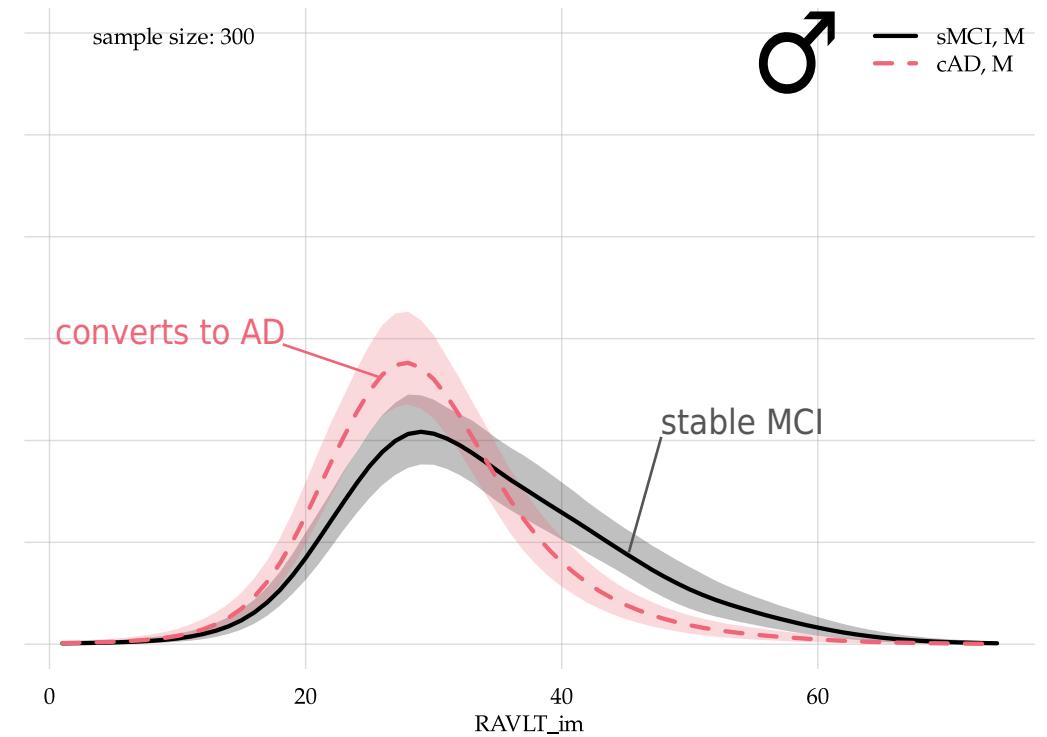
male



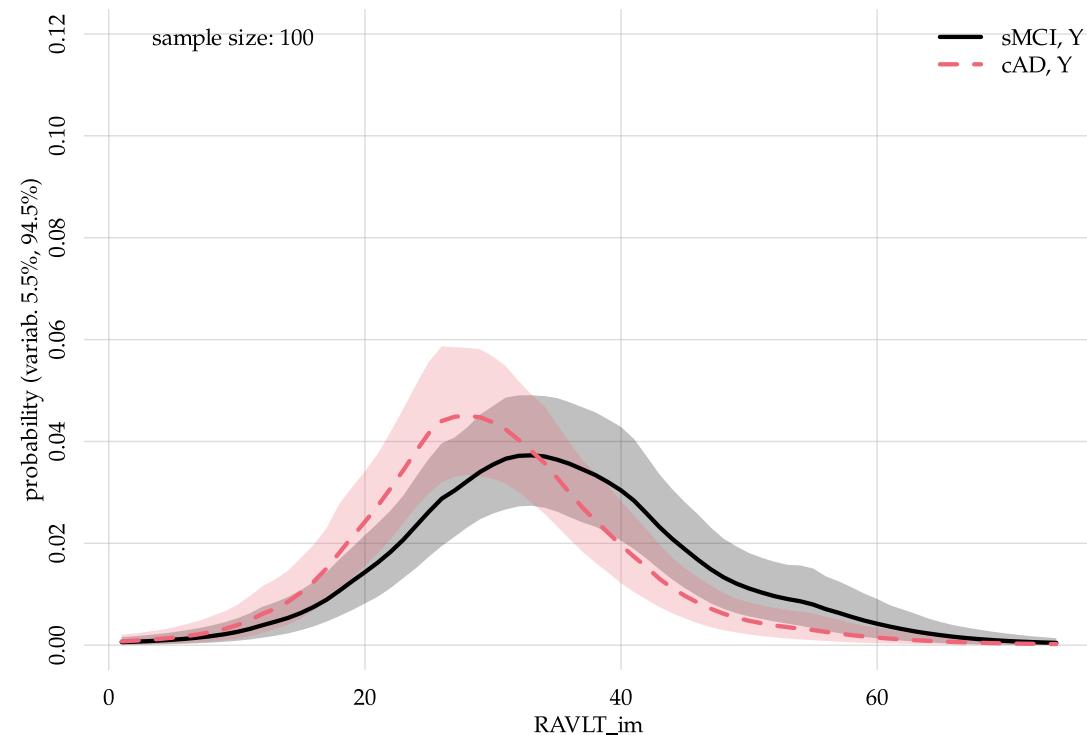
female



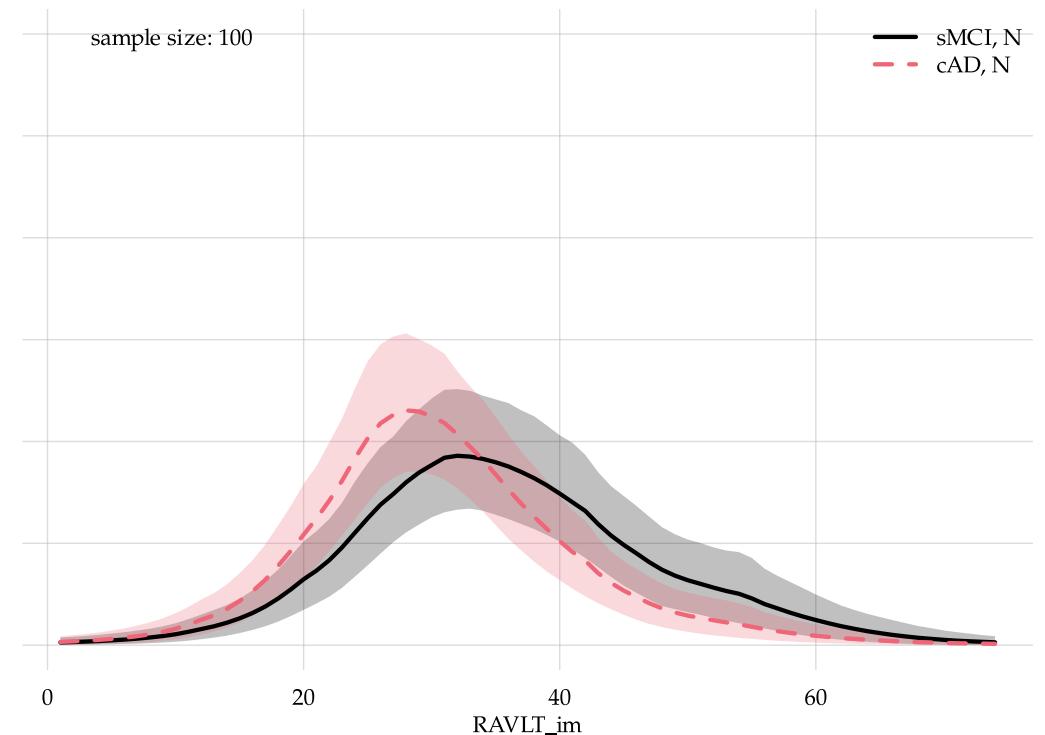
male



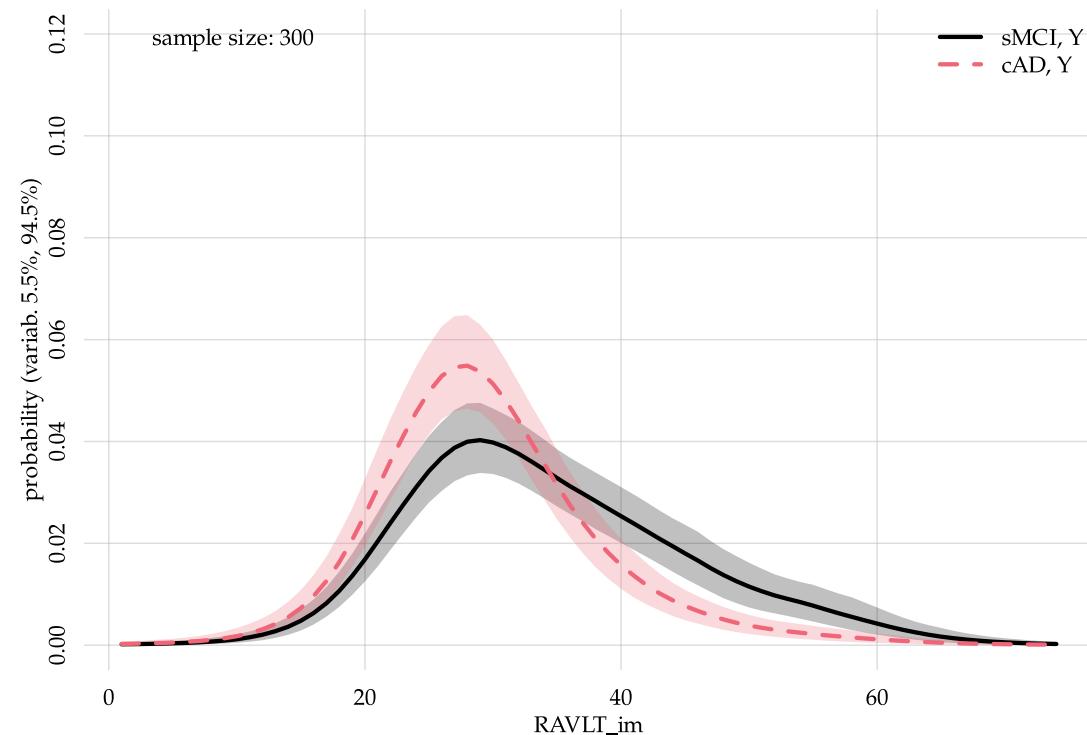
has APOE-4 allele



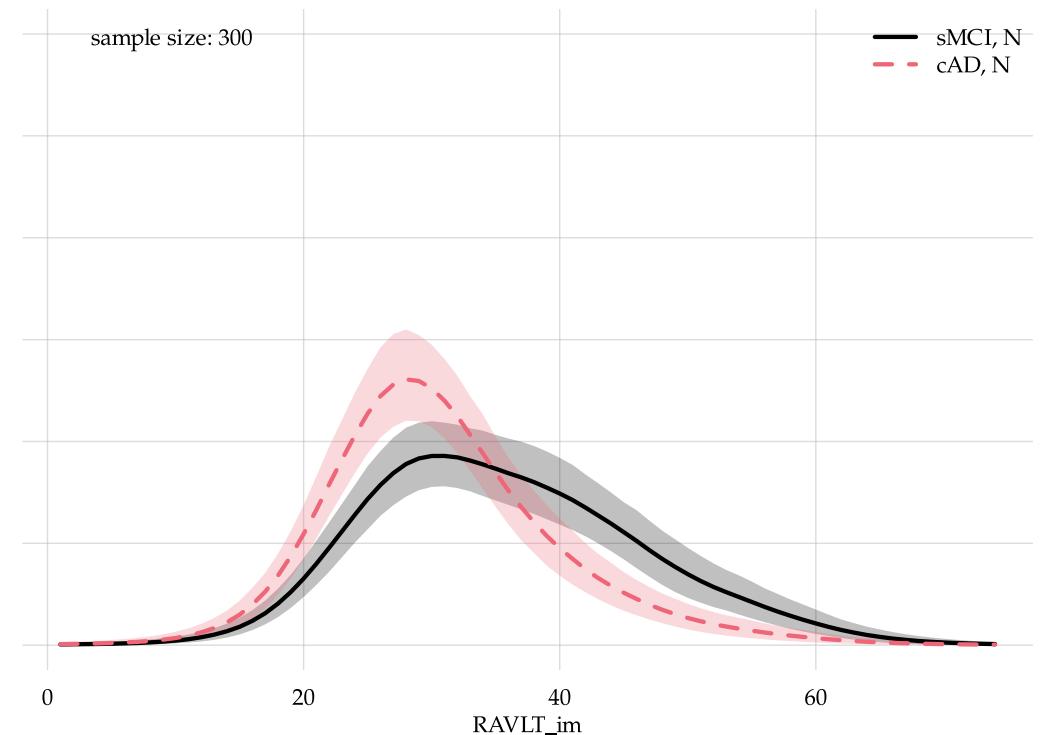
does not have APOE-4 allele



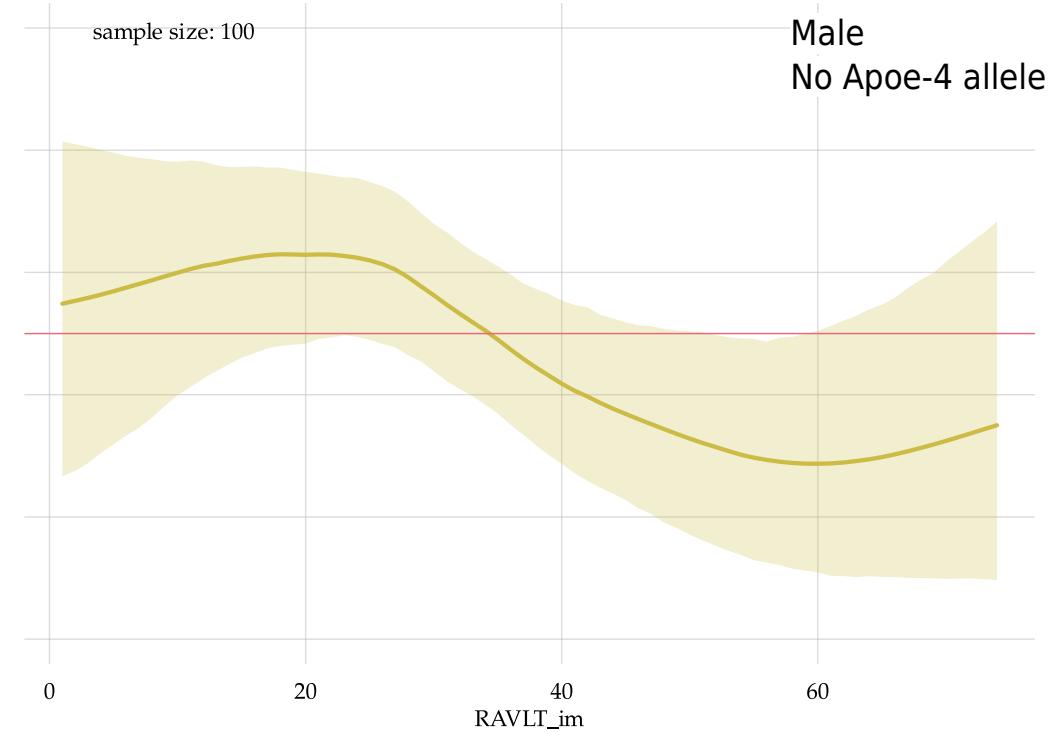
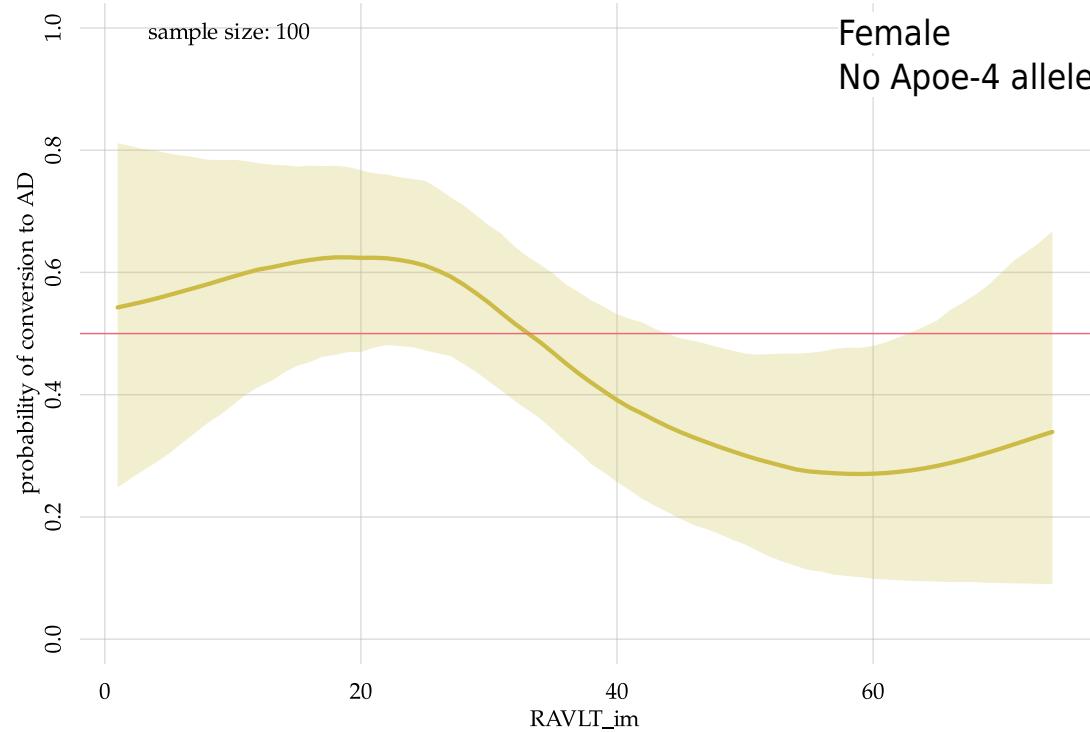
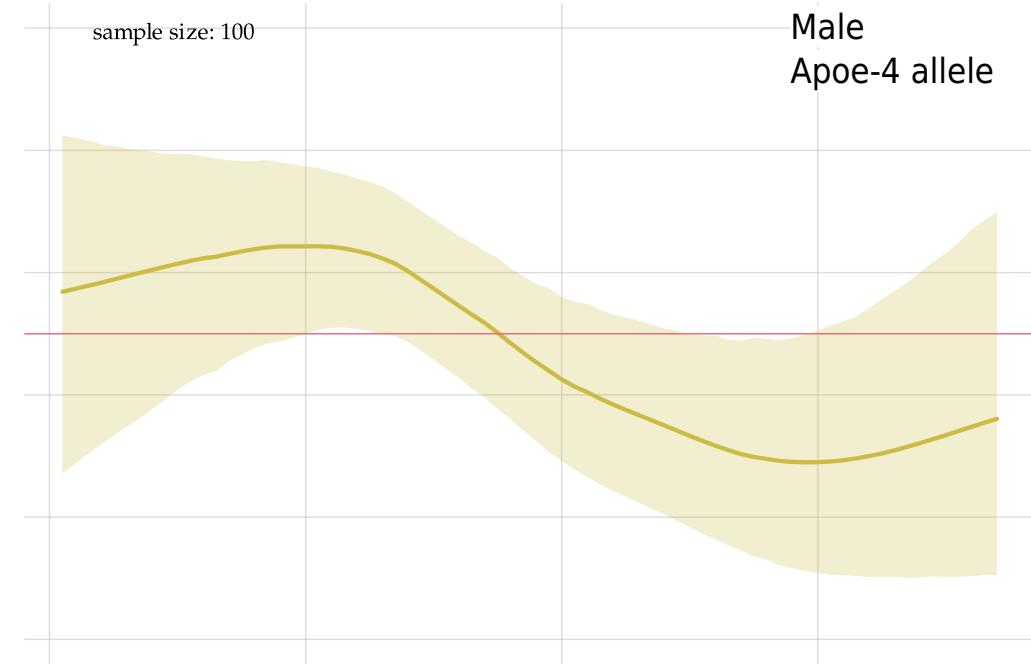
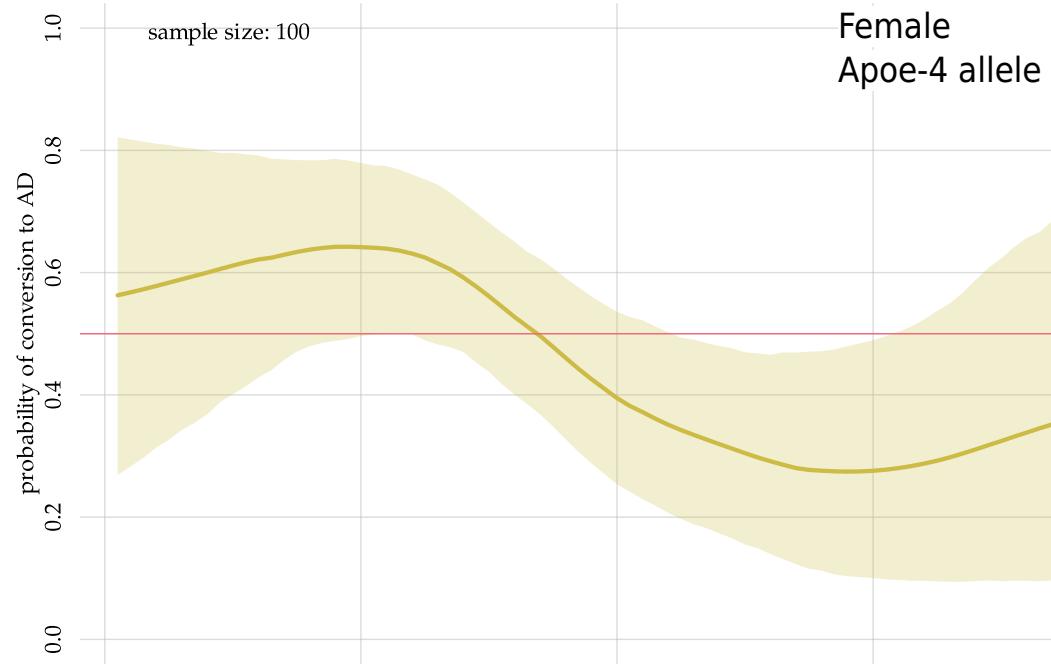
has APOE-4 allele



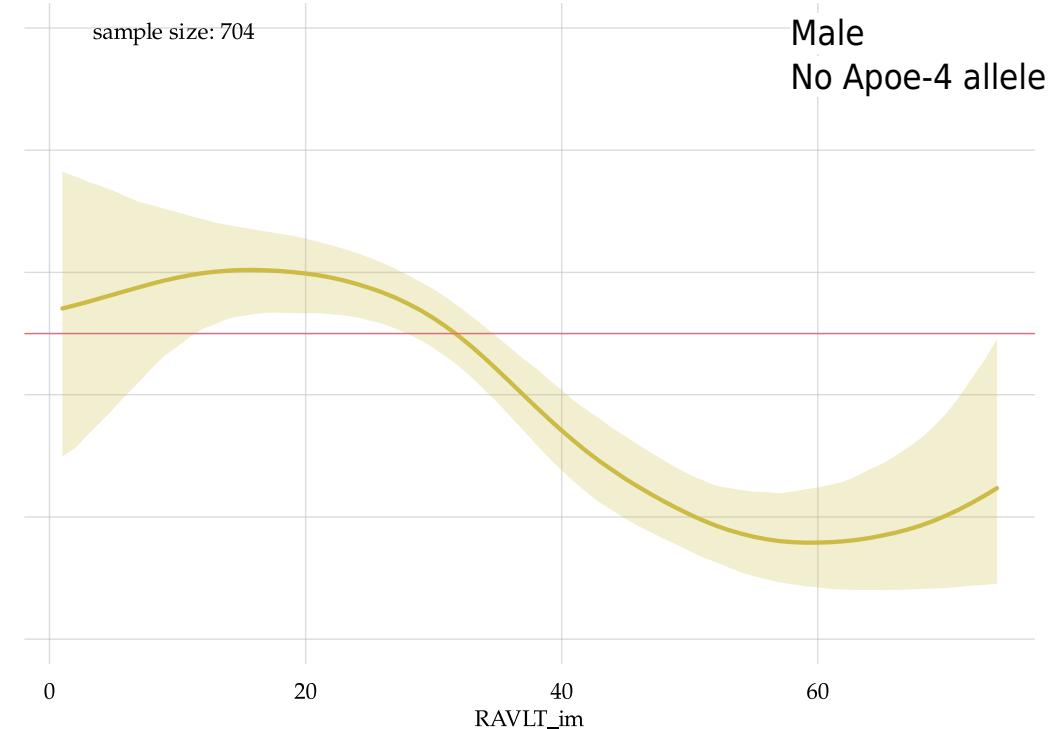
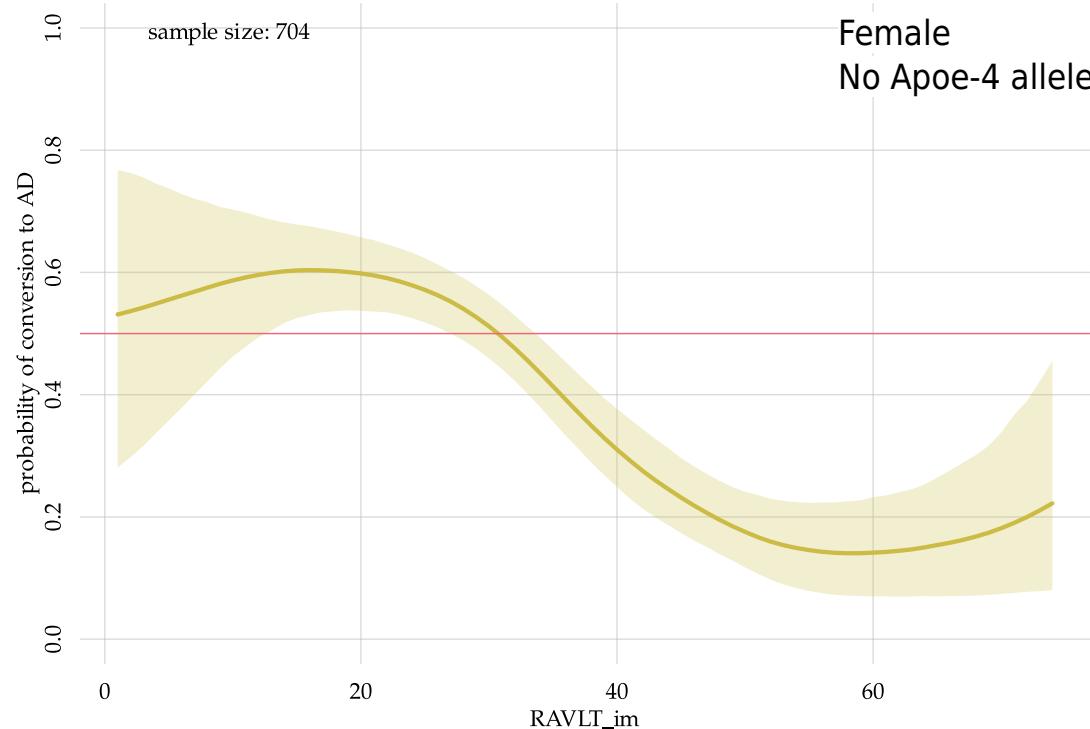
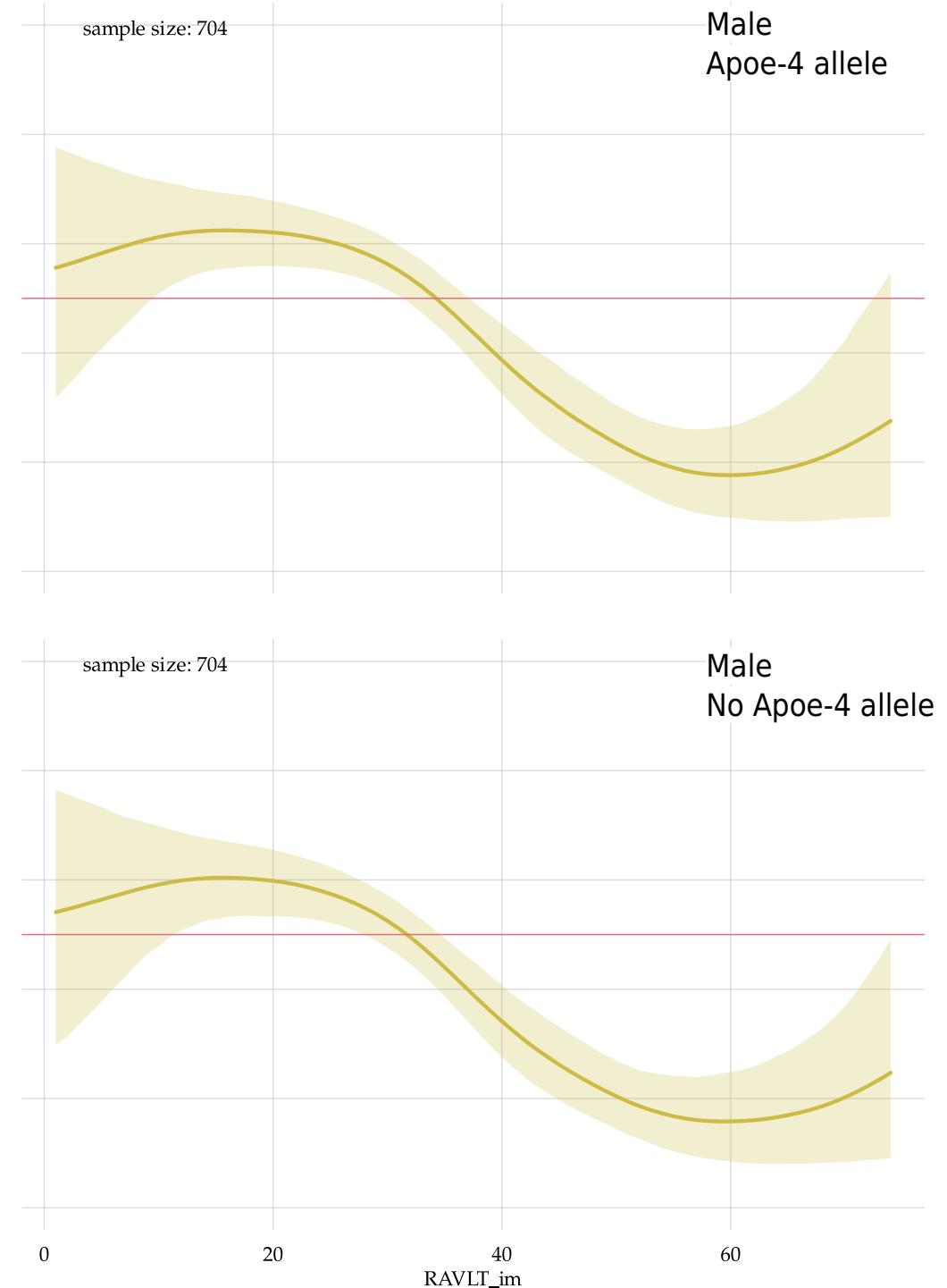
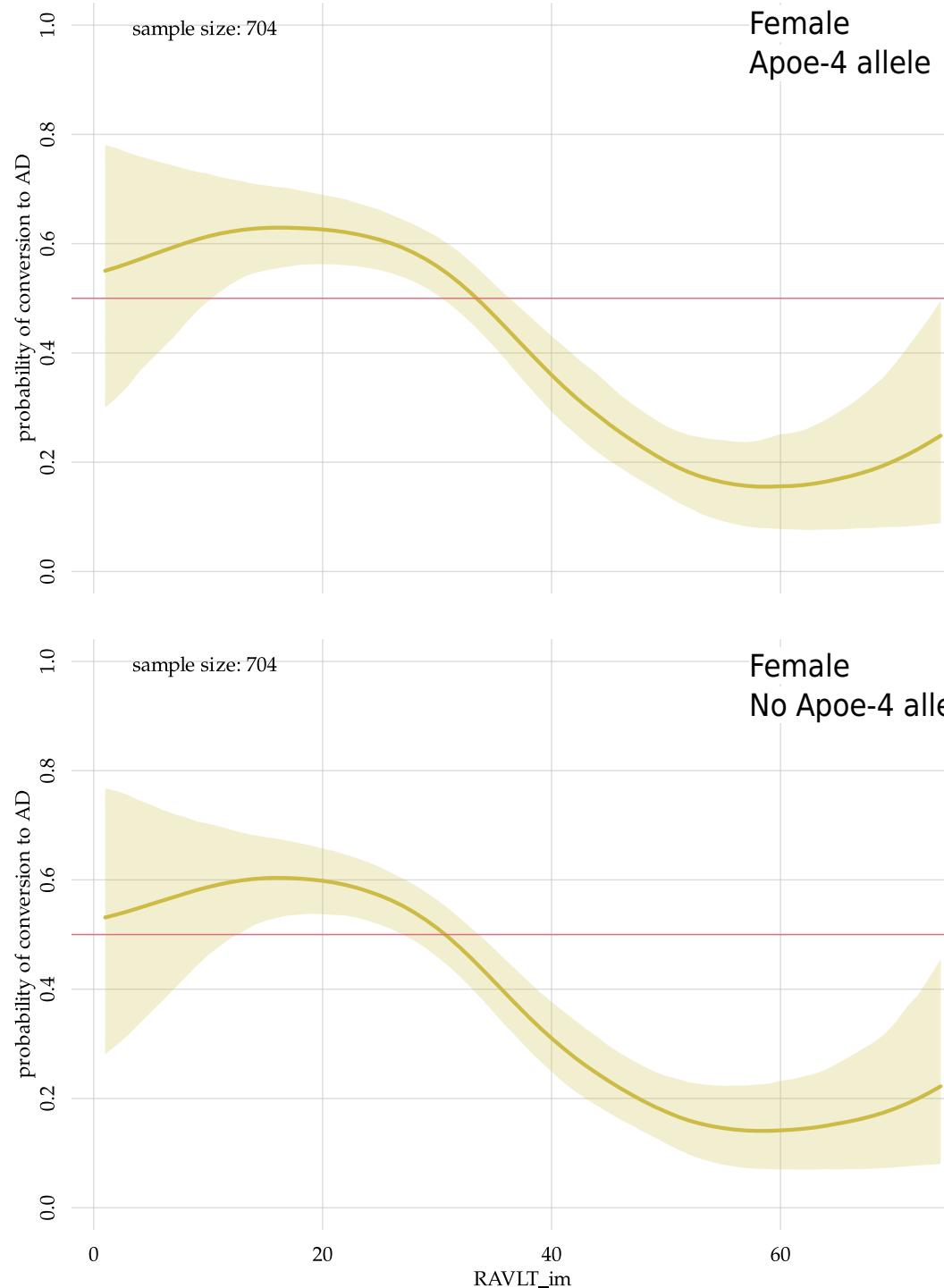
does not have APOE-4 allele



# Probability of conversion to AD (sample size: 100)



# Probability of conversion to AD (sample size: 704)



Why isn't this method more widely taught and used?

# Why isn't this method more widely taught and used?

**A✓** Idea simple, but underlying maths challenging

$$f(y|x, \pi, \Theta) = \sum_{h=1}^k \left\{ \frac{\pi_h \prod_{j=1}^p \mathcal{K}^{(x_j)}(x_j; \Theta_h^{(x_j)})}{\sum_{l=1}^k \pi_l \prod_{j=1}^p \mathcal{K}^{(x_j)}(x_j; \Theta_l^{(x_j)})} \right\} \mathcal{K}^{(y)}(y; \Theta_h^{(y)})$$

$$f(y, x) = \int \left\{ \mathcal{K}^{(y)}(y; \theta^{(y)}) \prod_{j=1}^p \mathcal{K}^{(x_j)}(x_j; \theta^{(x_j)}) \right\} dP(\theta), \quad \theta = \{\theta^{(y)}, \theta^{(x_1)}, \dots, \theta^{(x_p)}\}$$
$$P = \sum_{h=1}^k \pi_h \delta_{\Theta_h}, \quad \Theta_h = \{\Theta_h^{(y)}, \Theta_h^{(x_1)}, \dots, \Theta_h^{(x_p)}\} \sim P_0 = P_0^{(y)} \prod_{j=1}^p P_{0j}^{(x)}$$

# Why isn't this method more widely taught and used?

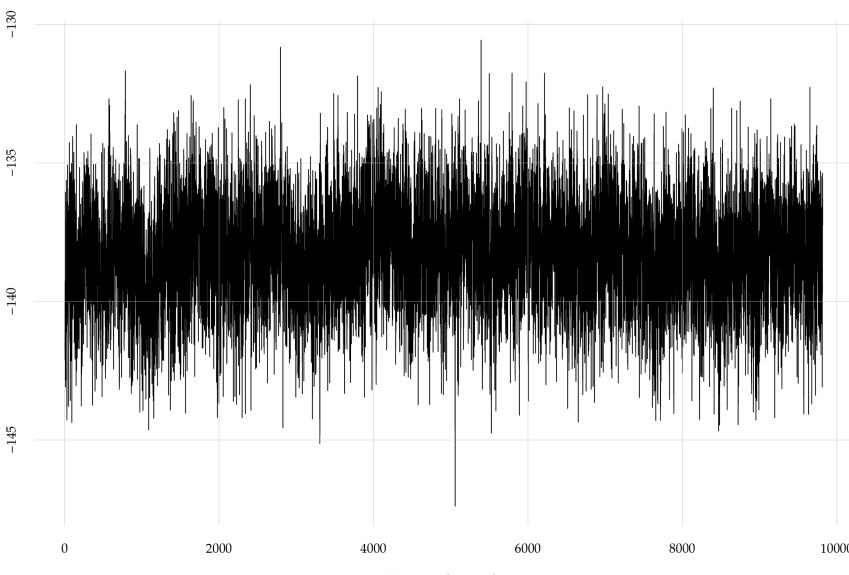
⚠️ Idea simple, but underlying maths challenging

$$f(y|x, \pi, \Theta) = \sum_{h=1}^k \left\{ \frac{\pi_h \prod_{j=1}^p \mathcal{K}^{(x_j)}(x_j; \Theta_h^{(x_j)})}{\sum_{l=1}^k \pi_l \prod_{j=1}^p \mathcal{K}^{(x_j)}(x_j; \Theta_l^{(x_j)})} \right\} \mathcal{K}^{(y)}(y; \Theta_h^{(y)})$$

$$f(y, x) = \int \left\{ \mathcal{K}^{(y)}(y; \theta^{(y)}) \prod_{j=1}^p \mathcal{K}^{(x_j)}(x_j; \theta^{(x_j)}) \right\} dP(\theta), \quad \theta = \{\theta^{(y)}, \theta^{(x_1)}, \dots, \theta^{(x_p)}\}$$

$$P = \sum_{h=1}^k \pi_h \delta_{\Theta_h}, \quad \Theta_h = \{\Theta_h^{(y)}, \Theta_h^{(x_1)}, \dots, \Theta_h^{(x_p)}\} \sim P_0 = P_0^{(y)} \prod_{j=1}^p P_{0j}^{(x)}$$

#112: rel. MC standard error: 0.023 | eff. sample size: 1890 | needed thinning: 8



⚡⌚ Computationally expensive



# Why isn't this method more widely taught and used?

## 🔧💻 DIY-coding: there is no user-friendly software

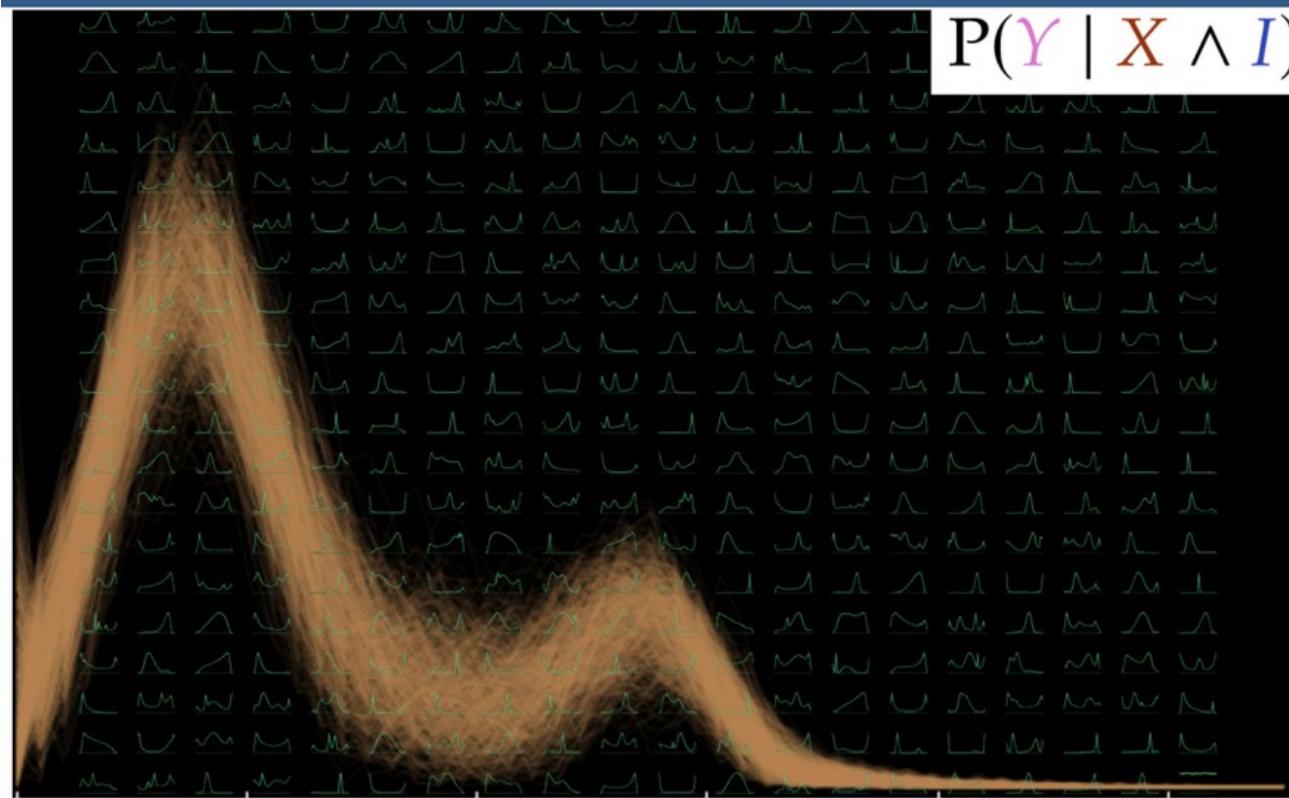
```
992         }
993     }
994     ## Probability of data
995     for (d in 1:npoints) {
996       K[d] ~ dcat(prob = W[1:ncomponents])
997       ##
998       if (vn$R > 0) { # continuous open domain
999         for (v in 1:Rn) {
1000           Rdata[d, v] ~ dnorm(mean = Rmean[v, K[d]], var = Rvar[v, K[d]])
1001         }
1002       }
1003       if (vn$C > 0) { # continuous closed domain
1004         for (v in 1:Cn) {
1005           Caux[d, v] ~ dconstraint(Clat[d, v] >= Cleft[d, v] &
1006                                     Cleft[d, v] <= Cright[d, v])
1007           Clat[d, v] ~ dnorm(mean = Cmean[v, K[d]], var = Cvar[v, K[d]])
1008         }
1009       }
1010       if (vn$D > 0) { # continuous rounded
1011         for (v in 1:Dn) {
1012           Daux[d, v] ~ dconstraint(Dlat[d, v] >= Dleft[d, v] &
1013                                     Dleft[d, v] < Dright[d, v])
1014           Dlat[d, v] ~ dnorm(mean = Dmean[v, K[d]], var = Dvar[v, K[d]])
1015         }
1016       }
1017       ## if (vn$L > 0) { # latent
1018       ##   for (v in 1:Ln) {
1019       ##     Laux[d, v] ~ dconstraint(Llat[d, v] >= Lleft[d, v] &
1020       ##                               Lleft[d, v] < Lright[d, v])
1021       ##     Llat[d, v] ~ dnorm(mean = Lmean[v, K[d]], var = Lvar[v, K[d]])
1022       ##   }
1023       ## }
1024       if (vn$O > 0) { # nominal
1025         for (v in 1:On) {
1026           Odata[d, v] ~ dcat(prob = Oprob[v, K[d], 1:Omaxn])
1027         }
1028       }
1029       if (vn$N > 0) { # nominal
1030         for (v in 1:Nn) {
1031           Ndata[d, v] ~ dcat(prob = Nprob[v, K[d], 1:Nmaxn])
1032         }
1033       }
1034       if (vn$B > 0) { # binary
1035         for (v in 1:Bn) { # Bprob is the probability that Bdata=1
1036           Bdata[d, v] ~ dbern(prob = Bprob[v, K[d]])
1037         }
1038       }
```

# Why isn't this method more widely taught and used?



## DIY-coding: there is no user-friendly software

```
992 }
993 }
994 ## Probability of data
995 for (d in 1:npoints) {
996   K[d] ~ dcat(prob = W[1:ncomponents])
997   ##
998   if (vn$R > 0) { # continuous open domain
999     for (v in 1:Rn) {
1000       Rdata[d, v] ~ dnorm(mean = Rmean[v, K[d]], var = Rvar[v, K[d]])
1001     }
1002   }
1003   if (vn$C > 0) { # continuous closed domain
1004     for (v in 1:Cn) {
1005       Caux[d, v] ~ dconstraint(Clat[d, v] >= Cleft[d, v] &
1006                                 Clat[d, v] <= Cright[d, v])
1007       Clat[d, v] ~ dnorm(mean = Cmean[v, K[d]], var = Cvar[v, K[d]])
1008     }
1009   }
1010   if (vn$D > 0) { # continuous rounded
1011     for (v in 1:Dn) {
1012       Daux[d, v] ~ dconstraint(Dlat[d, v] >= Dleft[d, v] &
1013                                 Dlat[d, v] < Dright[d, v])
1014       Dlat[d, v] ~ dnorm(mean = Dmean[v, K[d]], var = Dvar[v, K[d]])
1015     }
1016   }
1017   ## if (vn$L > 0) { # latent
1018   ##   for (v in 1:Ln) {
1019   ##     Laux[d, v] ~ dconstraint(Llat[d, v] >= Lleft[d, v] &
1020   ##                               Llat[d, v] < Lright[d, v])
1021   ##     Llat[d, v] ~ dnorm(mean = Lmean[v, K[d]], var = Lvar[v, K[d]])
1022   ##   }
1023   ## }
1024   if (vn$O > 0) { # nominal
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1026       Odata[d, v] ~ dcat(prob = Oprob[v, K[d], 1:Omaxn])
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1028   }
1029   if (vn$N > 0) { # nominal
1030     for (v in 1:Nn) {
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1034   if (vn$B > 0) { # binary
1035     for (v in 1:Bn) { # Bprob is the probability that Bdata=1
1036       Bdata[d, v] ~ dbern(prob = Bprob[v, K[d]])
1037     }
1038 }
```



$$P(Y | X \wedge I)$$

# Bayesian nonparametric inference

---

[Documentation](#)

This repository provides an [R package](#) and some theoretical background for Bayesian nonparametric inference under exchangeability, or “inference about populations”. The package is under rapid development and has not reached a stable phase. This means that function names and arguments may still change. The package name is also still under consideration. However, the core functionalities and probability calculations work. While the code is still in its ‘0.X’ phase, we recommend contacting the developers if you want to start using the package for a research project. We would love more “beta-testers”!

## Links

[Browse source code](#)

## License

[Full license](#)

GPL (>= 3)

## Citation

[Citing inferno](#)

## Developers

PierGianLuca Porta Mana

Author, maintainer

Aurora Grefsrud

Author

Håkon Mydland

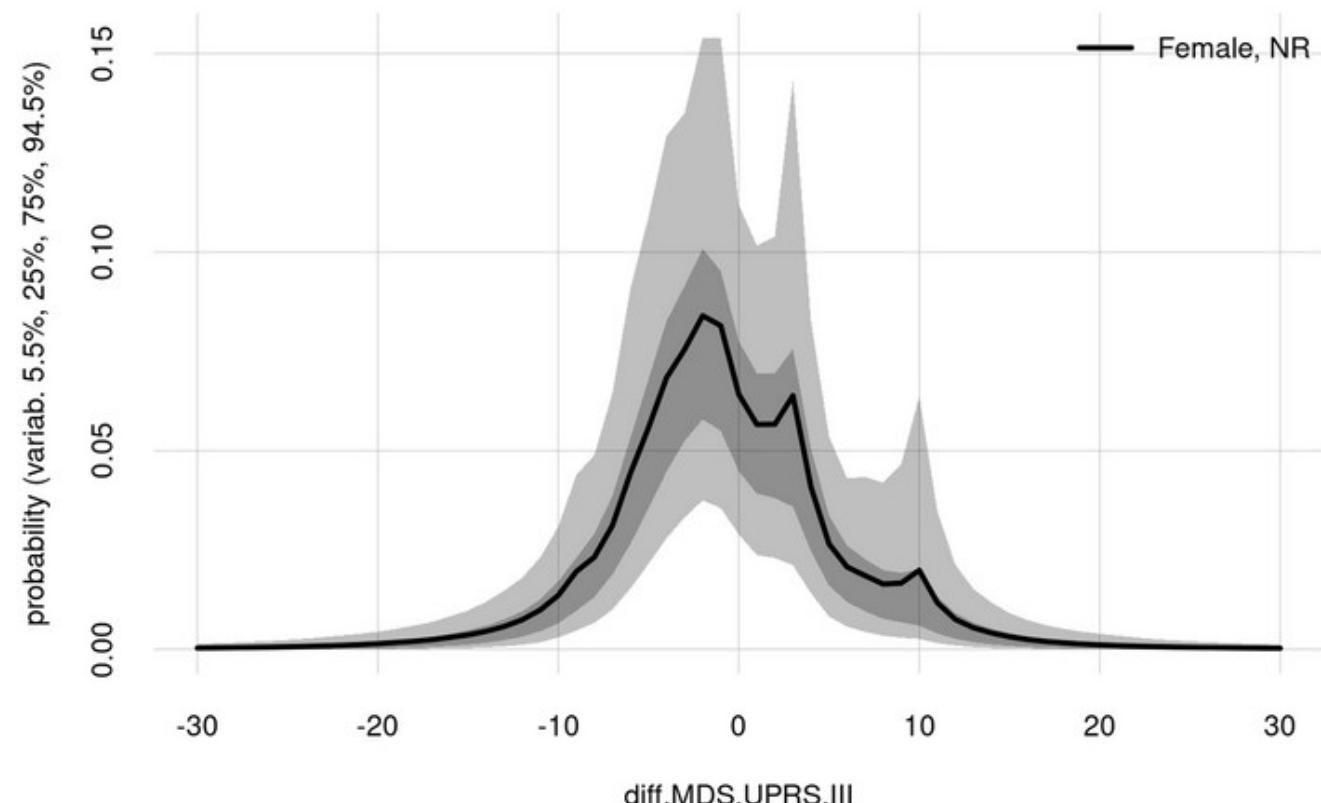
Author

)

Each probability thus obtained has two accompanying quantiles and related uncertainty. Both can be visualized with the `plot()` function:

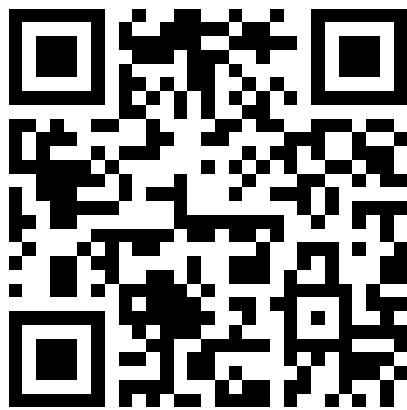
```
plot(probabilities)
```

## On this page

[Purpose](#)[Metadata](#)[Learning](#)[Drawing inferences](#)

If you want to see more examples with discussion:

Open Science Framework DOI:10.31219/osf.io/8nr56



# Personalized prognosis & treatment using an optimal predictor machine An example study on conversion from Mild Cognitive Impairment to Alzheimer's Disease

P.G.L. Porta Mana 

Western Norway University of Applied Sciences <[pgl@portamana.org](mailto:pgl@portamana.org)>

I. Rye 

University of Oslo

A. Vik 

Haukeland University Hospital,  
Bergen

M. Kociński 

University of Bergen

A. Lundervold 

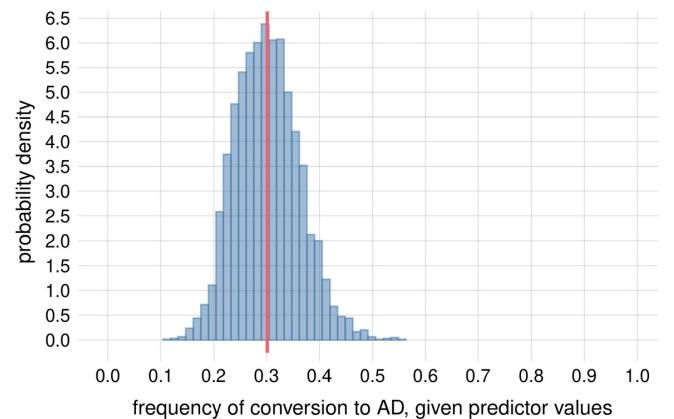
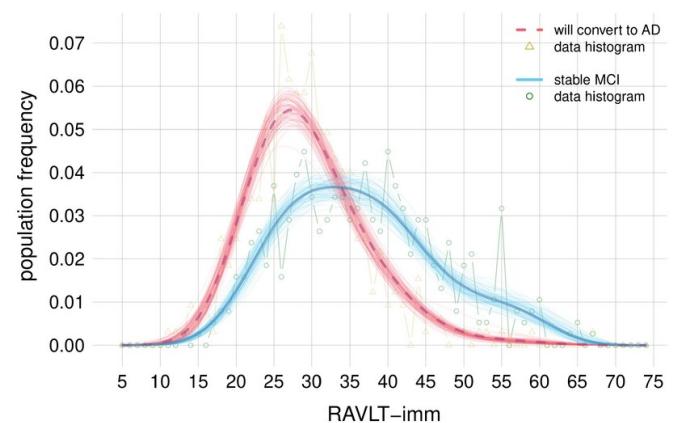
Mohn Medical Imaging and Visualization Centre (MMIV), Department of Radiology,  
Haukeland University Hospital, Bergen  
University of Bergen

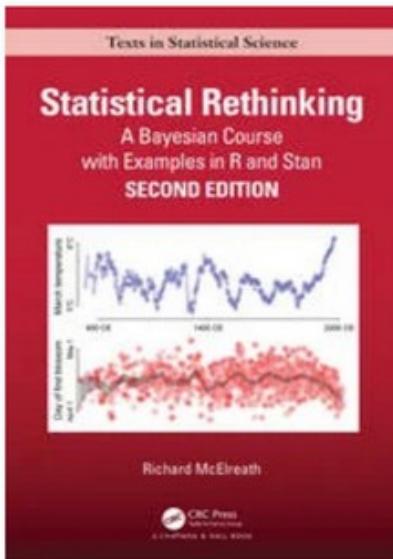
A. J. Lundervold 

Department of Biological and Medical Psychology, University of Bergen

A. S. Lundervold 

Mohn Medical Imaging and Visualization Centre (MMIV), Department of Radiology,  
Haukeland University Hospital, Bergen  
Western Norway University of Applied Sciences





Book



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By *Richard McElreath*

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eBook Published	16 March 2020
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Imprint	Chapman and Hall/CRC
DOI	<a href="https://doi.org/10.1201/9780429029608">https://doi.org/10.1201/9780429029608</a>

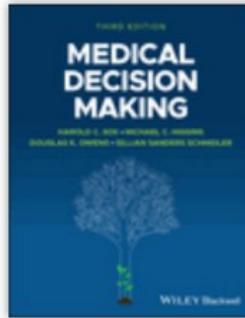
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Author(s): Harold C. Sox, Michael C. Higgins, Douglas K. Owens, Gillian Sanders Schmidler

First published: 2 February 2024

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Editorial

# The ASA Statement on *p*-Values: Context, Process, and Purpose

Ronald L. Wasserstein & Nicole A. Lazar

Pages 129-133 | Published online: 09 Jun 2016

Cite this article

<https://doi.org/10.1080/00031305.2016.1154108>



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Figures & data

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## The ASA's Statement on *p*-Values: Context, Process, and Purpose

Ronald L. Wasserstein & Nicole A. Lazar

Pages 129-133

In February 2014, George Cobb, Professor Emeritus of Mathematics and Statistics at Mount Holyoke College, posed these questions to an ASA discussion forum:

Q: Why do so many colleges and grad schools teach  $p = 0.05$ ?

A: Because that's still what the scientific community and journal editors use.

Q: Why do so many people still use  $p = 0.05$ ?

A: Because that's what they were taught in college or grad school.

Cobb's concern was a long-worrisome circularity in the sociology of science based on the use of bright lines such as  $p < 0.05$ : "We teach it because it's what we do; we do it because it's what we teach." This concern was brought to the attention of the ASA Board.

## 4. Other Approaches

In view of the prevalent misuses of and misconceptions concerning *p*-values, some statisticians prefer to supplement or even replace *p*-values with other approaches. These include methods that emphasize estimation over testing, such as confidence, credibility, or prediction intervals; Bayesian methods; alternative measures of evidence, such as likelihood ratios or Bayes Factors; and other approaches such as decision-theoretic modeling and false discovery rates. All these measures