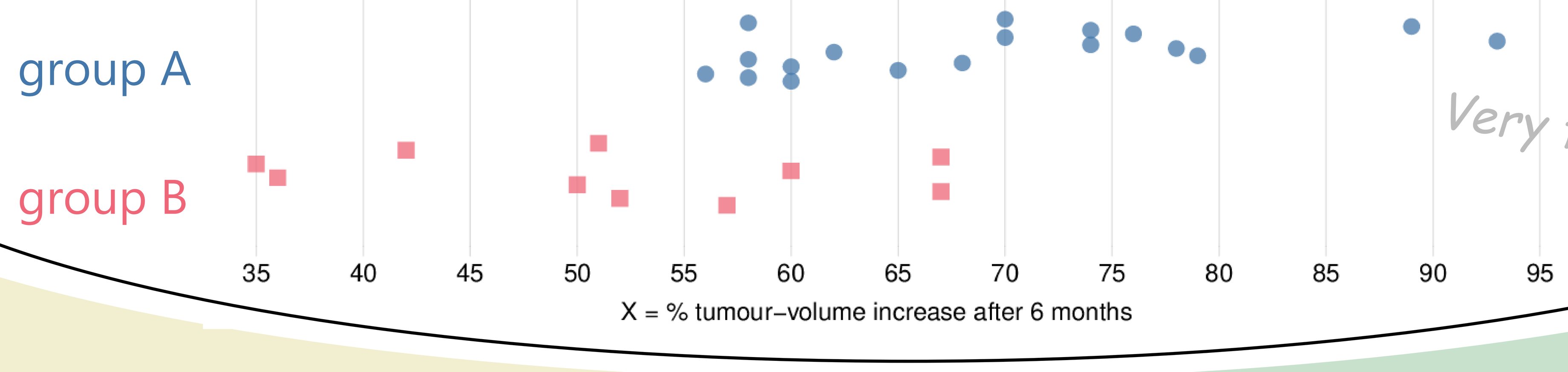
USER-FRIENDLY SOFTWARE FOR BAYESIAN ANALYSIS OF MEDICAL DATA

PierGianLuca Porta Mana, Kjetil Dyrland, Alexander Selvikvåg Lundervold
Dept of Computer Science, Electrical Engineering, and Mathematical Sciences, HVL; MMIV, HUS

Sampling theory

Simple example question:
do treatment A and treatment B have different effects on tumour increase X?



Very few data!

Bayesian theory

Typical conclusions from sampling theory:

" Assuming that the two full populations:

- are gaussian and independent
- have identical variances (F-test, $p = 0.44$)

*It's actually slightly more probable that the variances are **different***

and that the sample sizes where decided before running the experiment, then:

The hypothesis that the population means are equal has a p-value 0.00043 (two-tail t-test: +4.0)

What does the number "0.00043" really mean?

The sample-mean difference of X is 17.6
The 95% confidence interval is [8.6, 26.7] "

*This p-value is wrong if the sample sizes 18 & 10 were **decided not in advance** but by some other rule!*

*This does **not** mean that 8.6 < X < 26.7 with 95% probability!*
It means that this technique to construct the interval contains the true value in 95% of all imaginary datasets.
*But what's the best interval that contains X for **our** dataset?*

American Statistical Association's official statement

THE AMERICAN STATISTICIAN
2019, VOL. 73, NO. S1, 1–19: Editorial
https://doi.org/10.1080/00031305.2019.1583913

Moving to a World Beyond "$p < 0.05$"

- Don't base your conclusions solely on whether an association or effect was found to be "statistically significant" (i.e., the p-value passed some arbitrary threshold such as $p < 0.05$).
- Don't believe that an association or effect exists just because it was statistically significant.
- Don't believe that an association or effect is absent just because it was not statistically significant.
- Don't believe that your p-value gives the probability that chance alone produced the observed association or effect or the probability that your test hypothesis is true.
- Don't conclude anything about scientific or practical importance based on statistical significance (or lack thereof).

2. Don't Say "Statistically Significant"

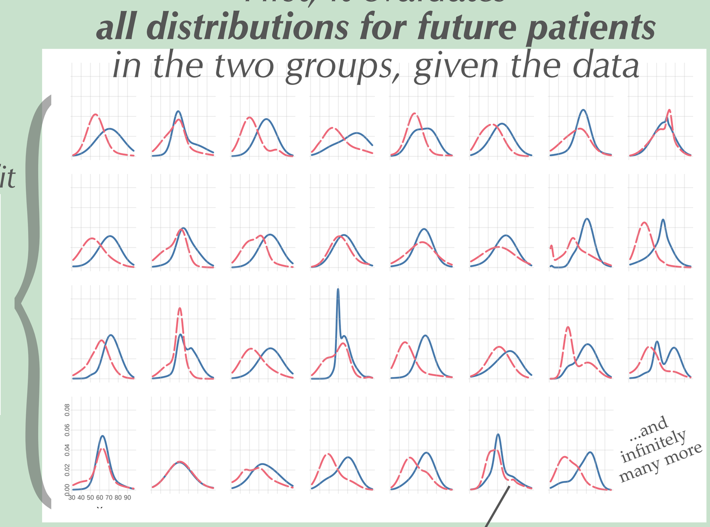
We conclude, based on our review of the articles in this special issue and the broader literature, that it is time to stop using the term "statistically significant" entirely. Nor should variants such as "significantly different," "$p < 0.05$," and "nonsignificant" survive, whether expressed in words, by asterisks in a table, or in some other way.

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; alterna-

An intuitive understanding of how Bayesian probability theory works:

*First, it evaluates **all distributions for future patients** in the two groups, given the data*

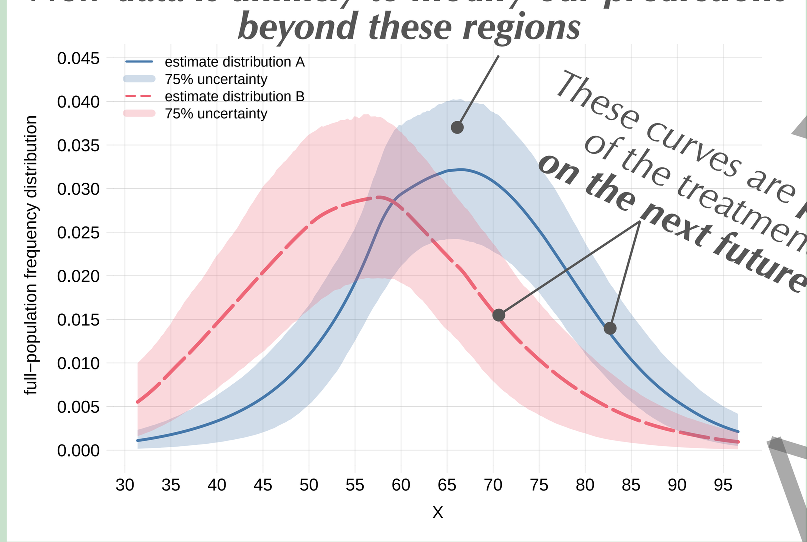


No assumptions of gaussianity anywhere

these distributions are all weighted according to their data fit and combined

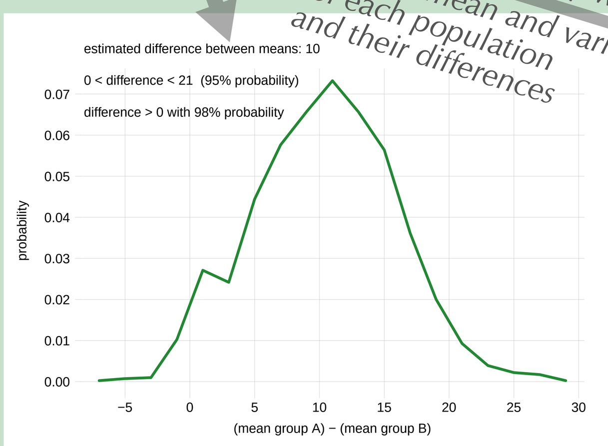
Main result: estimates of full distributions and uncertainty of estimates.

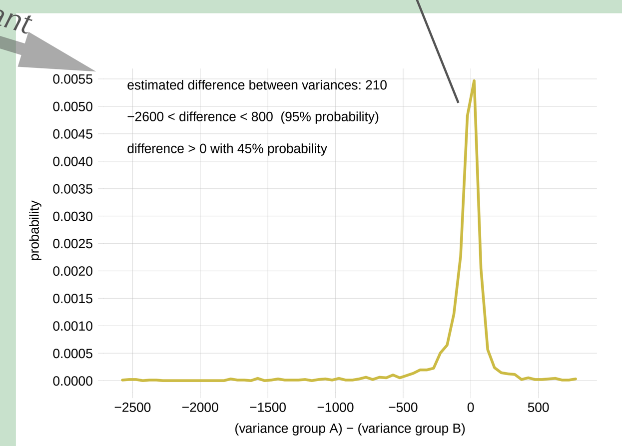
New data is unlikely to modify our predictions beyond these regions



*These curves are **predictions** of the treatment effect **on the next future patient***

We can estimate any quantity we want
For example the mean and variance of each population and their differences





*These detailed probabilities can be used in a **cost/benefit analysis** (decision theory)*

"Treatment A costs \$, gives a% benefit.
Treatment B costs \$\$, gives b% benefit.
Which treatment should we choose?"

" Assuming that the two full-population distributions are probably smooth, we predict:

- The distributions of **future treatment outcomes** will be as in the plots, within uncertainties shown
- Future patients under treatment A will have on average $X \approx 67$, and $61 < X < 72$ with 95% probability
- Future patients under treatment B will have on average $X \approx 56$, and $49 < X < 65$ with 95% probability
- The difference between the treatment means will be within [0, 21] with 95% probability
- Variance of X under treatment B will be **larger** than under treatment A with 55% probability
- Average X under treatment B will be **smaller** than under treatment A with **98%** probability

These results say that treatment B is very probably better than A at slowing down tumour growth.
However, there is still a ~2% probability that A could be better than B.
If we want to reduce this uncertainty to less than 1%, then we need more data. "

Compare the two analyses

The statements of sampling theory are:

- vague
- obscure or misleading ("significant"?)
- heavily dependent on tacit assumptions
  gaussianity, stopping rules, ...
- subject to doubts and corrections
  "should I use this test or that test?" "Bonferroni correction?"

The predictions of Bayesian theory are:

- detailed
- quantitative
- easy to interpret and understand
  eg: "fraction x% of population will have effect y"
- calculated always in the same way
  for any sample size, stopping rule, number of hypotheses

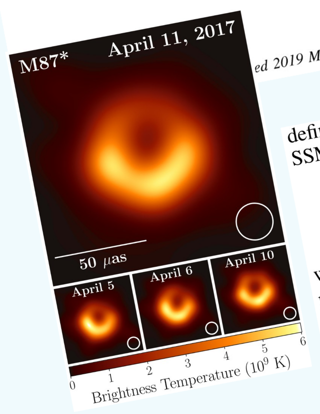
This was just a simple example. Bayesian theory deals in the same way with multiple hypotheses, variates, and correlation questions

Bayesian theory is used, for example, for all inferences about the black hole observed in the galaxy M87

The Astrophysical Journal Letters, 875:L1 (17pp), 2019 April 10
https://doi.org/10.3847/2041-8213/ab0ec7

First M87 Event Horizon Telescope Results. I. The Shadow of the Supermassive Black Hole

The Event Horizon Telescope Collaboration
(See the end matter for the full list of authors.)
...ed 2019 March 1; revised 2019 March 12; accepted 2019 March 12; published 2019 Ap...



define the joint model-parameter posterior distributions for the SSM model, following Bayes' theorem, by

$$P(\Theta, \mathcal{M}|D) = \sum_{\mathcal{I}} \frac{P(D|\Theta, \mathcal{I})P(\mathcal{I}|\mathcal{M})\pi(\Theta)\pi(\mathcal{M})}{P(D)}, \quad (62)$$

where $P(D|\Theta, \mathcal{I})$ is formally the likelihood, $\mathcal{I}$ refers to a particular snapshot image from $\mathcal{M}$ obtained with probability $P(\mathcal{I}|\mathcal{M})$, and $\pi(\Theta)$ and $\pi(\mathcal{M})$ are the priors on parameters Θ and the model $\mathcal{M}$, respectively. We now discuss each of these

True! That's why we are developing a user-friendly app to do Bayesian analysis on (non-imaging) medical data

Machine Learning

The maths are taken care of under the hood
The app suggests meaningful questions to be asked (in line with ASA's statement)
examples: future statistics, correlations, relevance, and more
It works with combinations of continuous and discrete variables:
Automatic imputation of missing data
No assumptions of gaussianity, linearity, or other (ie: it's nonparametric)
No need to wonder which test or formula to use, no corrections of any kind

We're already using a prototype version for drug-discovery and Alzheimer research

Please get in touch if you want to test it and help us making a great app!

Bibliography
American Statistical Association 2016: *Statement on Statistical Significance and p-values*
American Statistical Association 2019: *Moving to a World Beyond "p < 0.05"*
Jaynes 2003: *Probability Theory: The Logic of Science*
MacKay 1994: *Information Theory, Inference, and Learning Algorithms*
Hjort, Holmes, Müller, Walker 2003: *Bayesian Nonparametrics*
Müller, Rodríguez 2013: *Nonparametric Bayesian Inference*
Dunson, Bhattacharya 2011: *Nonparametric Bayes regression and classification through mixtures of product kernels*
Sox, Higgins, Owens 2013: *Medical Decision Making*
The Event Horizon Telescope Collaboration 2019: *First M87 Event Horizon Telescope results. I–VI*

Acknowledgements
Trond Mohn Research Foundation, grant number BFS2018TMT07
Research Council of Norway, grant number 294594