fMRI in context: Paradigm to practice

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OR: The perish of “Publish or Perish”

A short overview about

- What’s the problem?
  - the problems of p-values
  - the reproducibility crisis
  - questionable research practices

- Possible Solutions
  - Understanding the consequences of claiming $p < 0.05$
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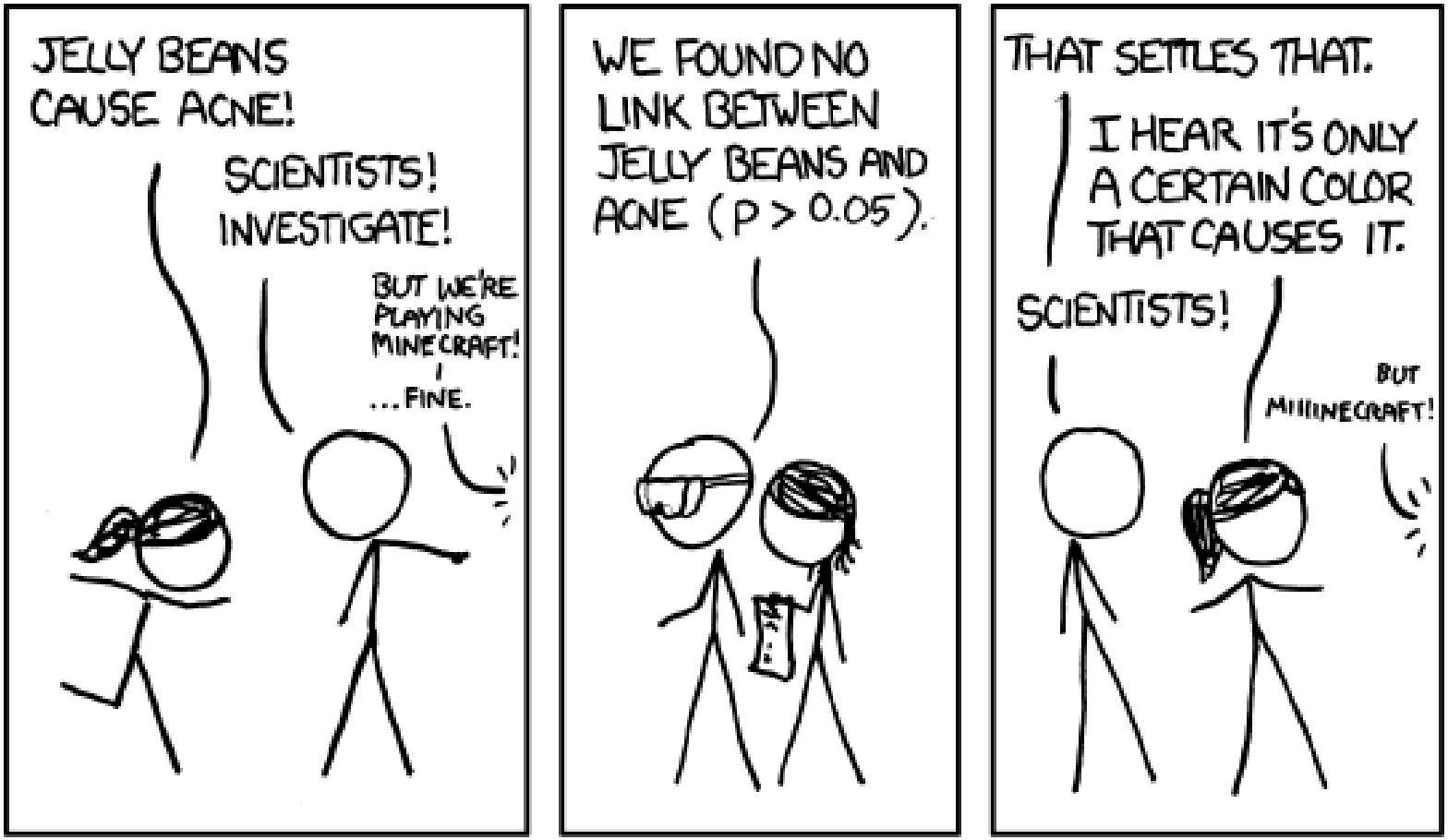
Significant ($p < 0.05$)



https://xkcd.com/882/

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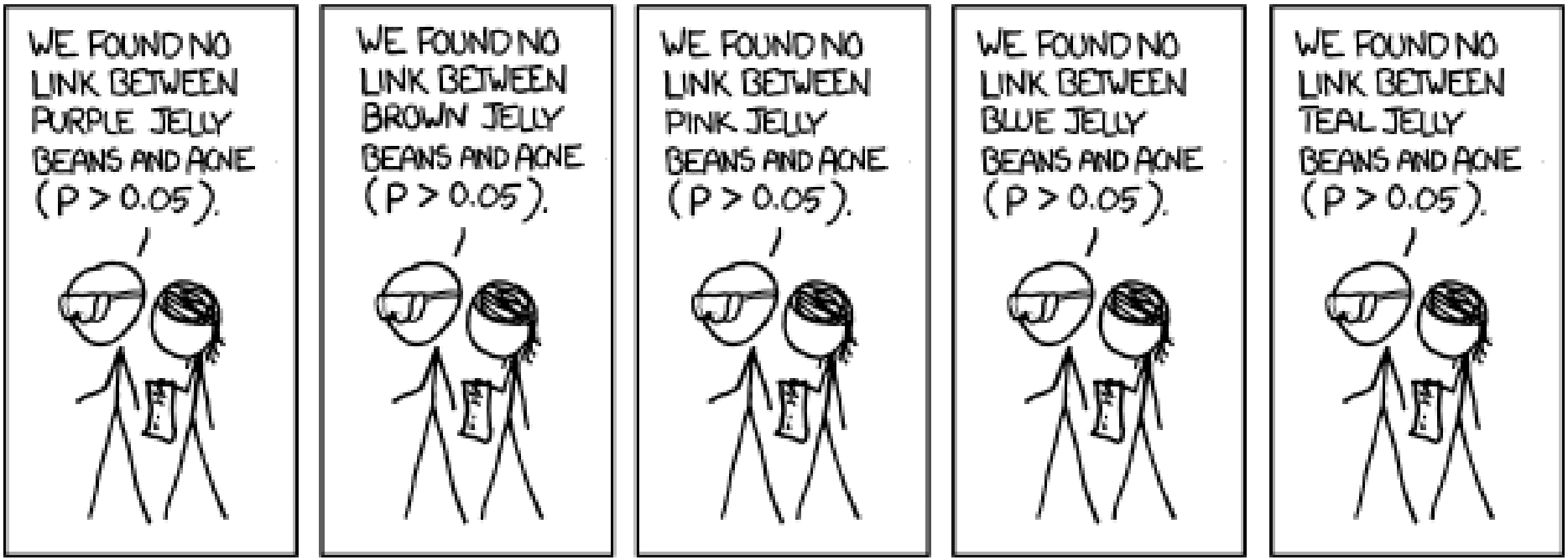

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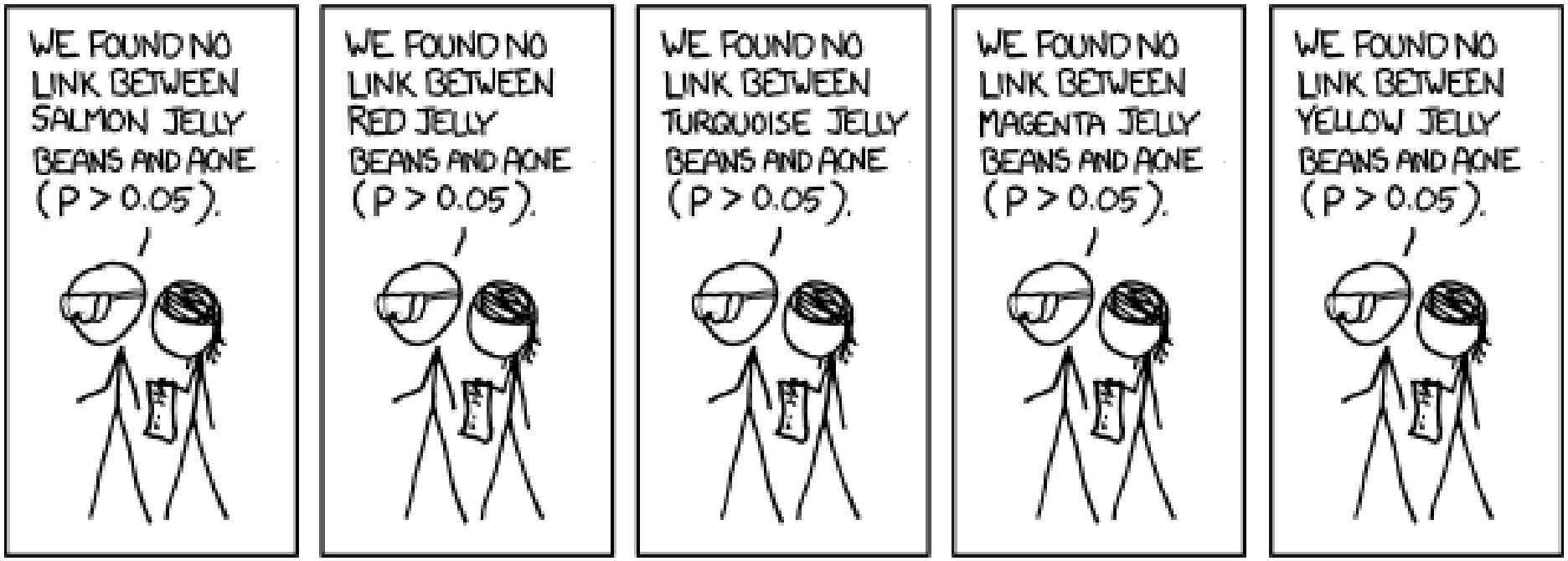

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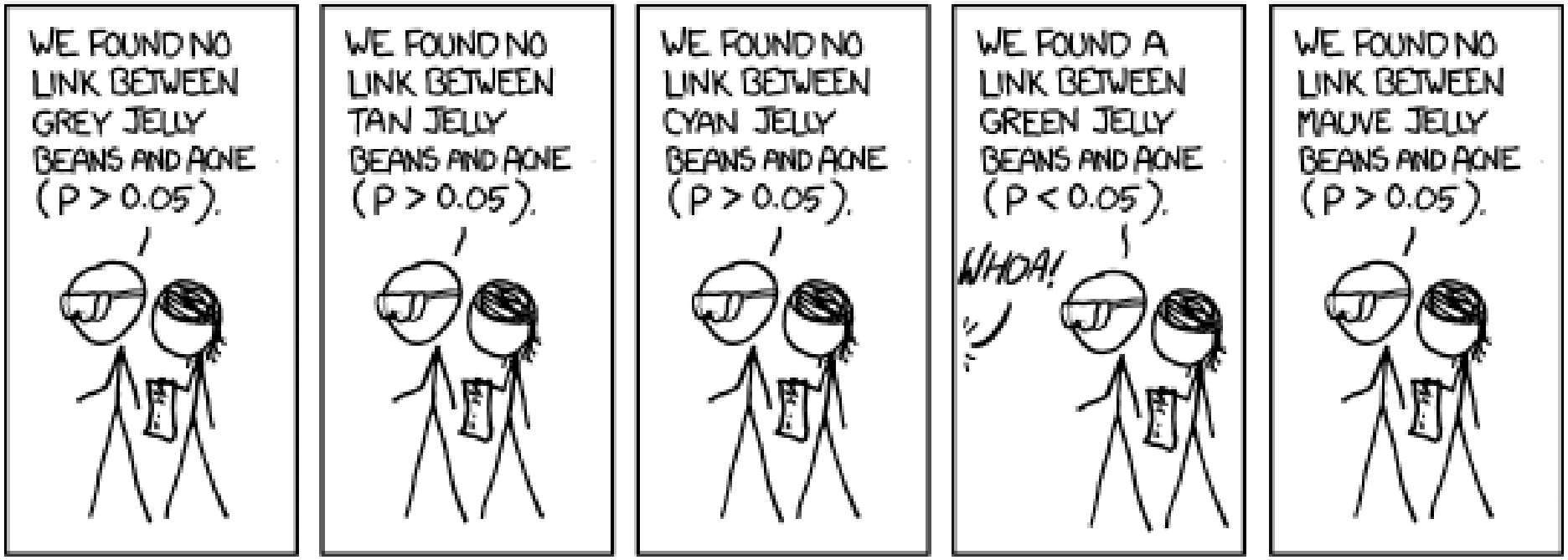

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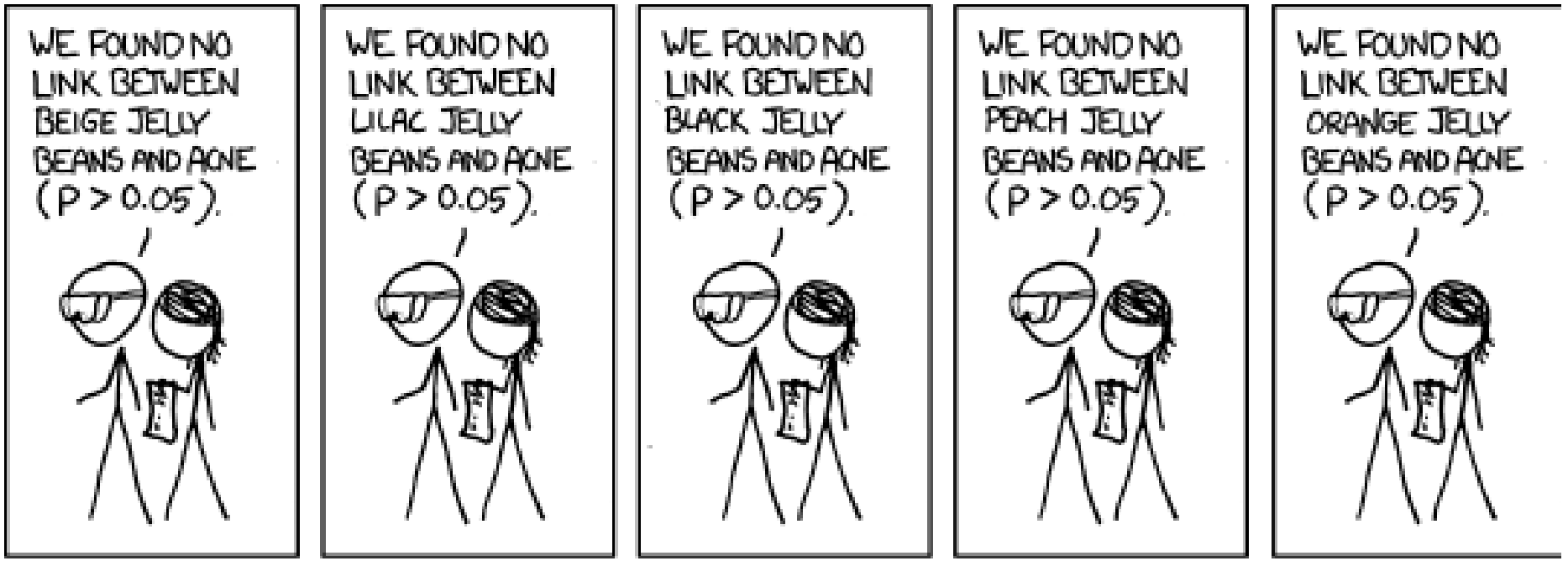

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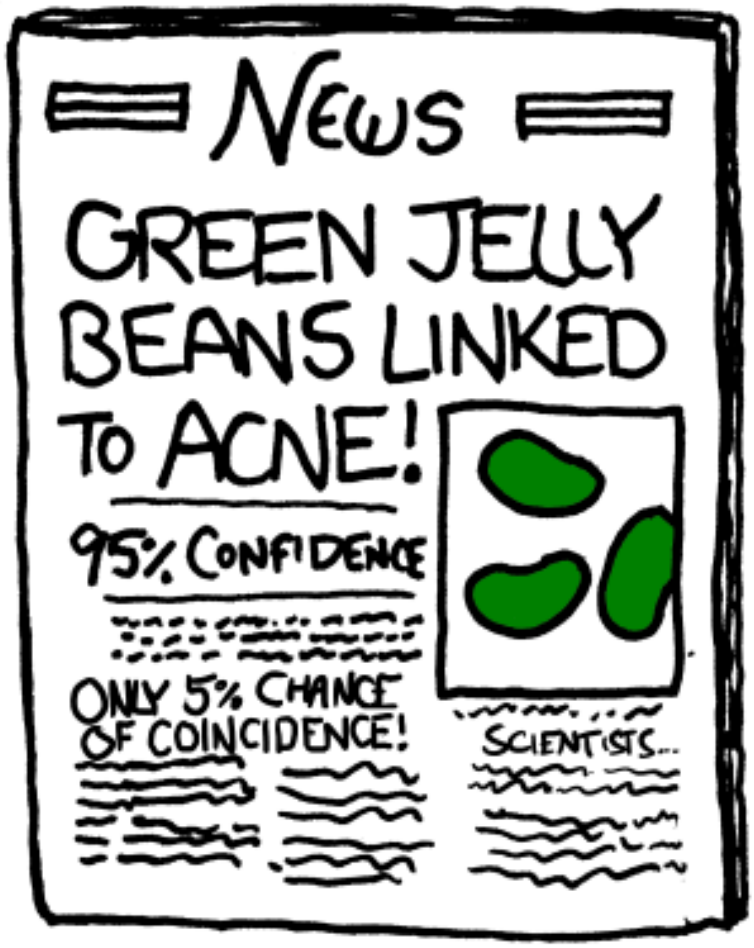

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Significant ($p < 0.05$)

P-value-hacking, data dredging, torturing the data until it confesses, data massaging, not conducting proper multiple comparison correction, researcher degrees of freedom …. It has many names … and leads to real world problems

- Are we really p-hacking?
- How are we p-hacking (most of us unintentionally)?
- Why is it a problem?
- How can we solve the problem?

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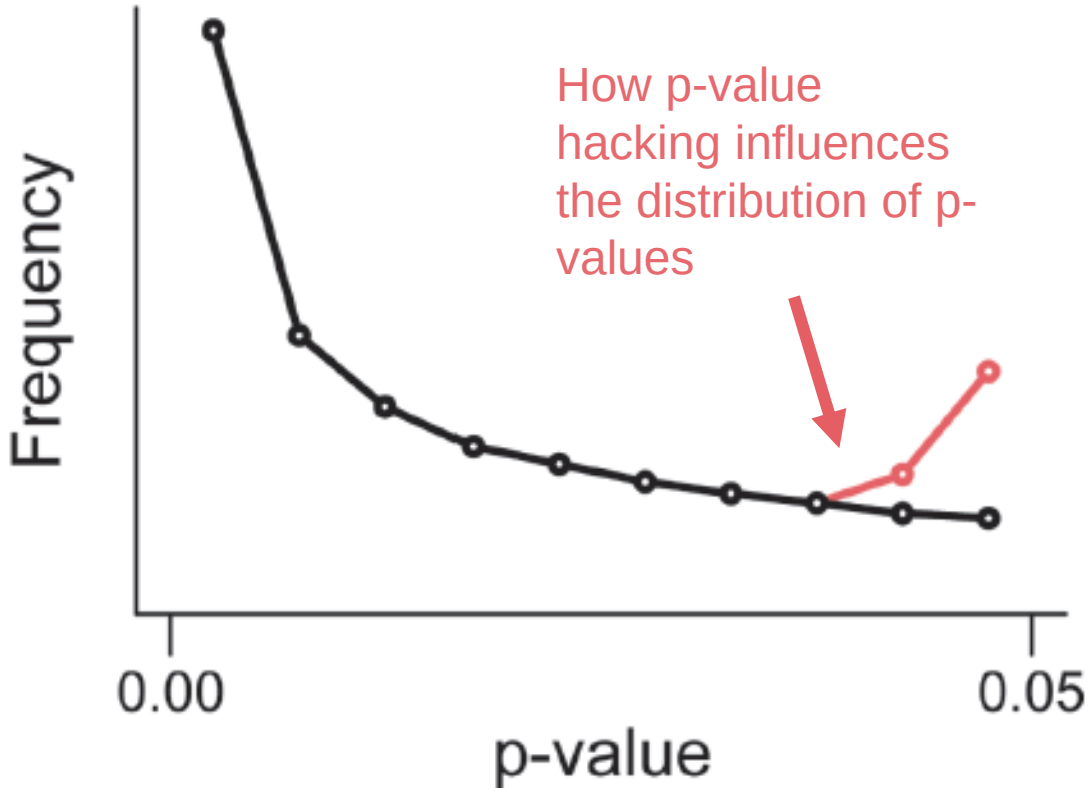
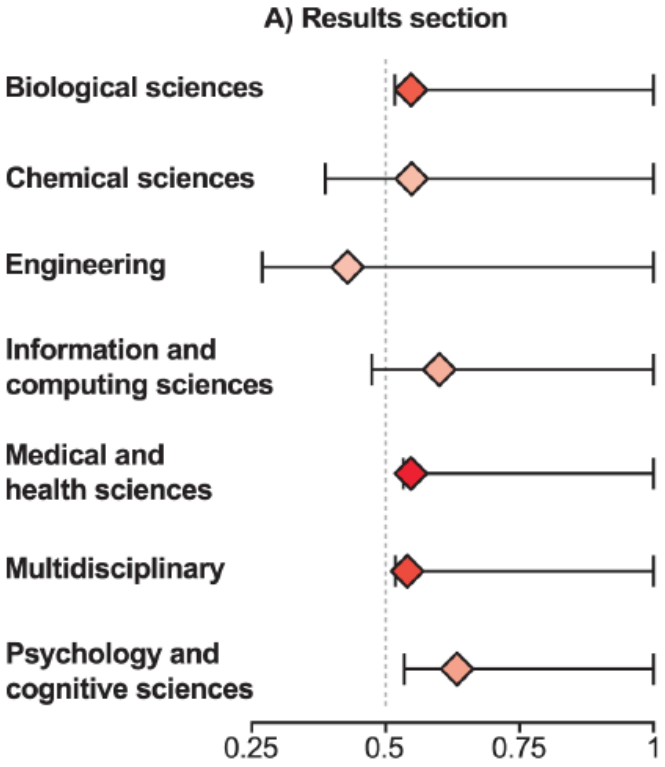
Are we really p-hacking?

Head et al. 'The Extent and Consequences of P-Hacking in Science'. *PLoS Biol* 2015.

- strong evidence for p-hacking in the literature





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Are we really p-hacking?

Head et al. 'The Extent and Consequences of P-Hacking in Science'. *PLoS Biol* 2015.

- Conclusion: evidence of p-hacking, but effect weak in relation to real effect sizes, not likely to cause distortions in the literature

Head et al. study criticized by Dorothy V Bishop et al: https://peerj.com/preprints/1266/

- no control over the type of p-values entered into the analysis
- lack of 'bump' is not indicative of lack of p-hacking
- study by Head et al. provides evidence of p-hacking, but cannot be used to estimate extent and consequences of p-hacking!
- **-> Bishop's simulation shows instead: potential for systematic bias is substantial!**

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How are we p-hacking?

Analytic flexibility

- We can analyse our data in multiple justifiable ways, but only report the way “that worked” (i.e.: $p < 0.05$)
- How to p-hack by neuroskeptic: https://youtu.be/A0vEGuOMTyA

Selection/publication bias

- we (and journals) prefer the lowest p-value given a choice and often do not report higher p-values (or do not publish non-significant results)

Selective debugging

- We are more likely to look for mistakes in an analysis which created non-significant results -> we are selecting in favour of mistakes that produce false positives

[http://blogs.discovermagazine.com/neuroskeptic/2015/05/18/p-hacking-a-talk-and-further-thoughts/]

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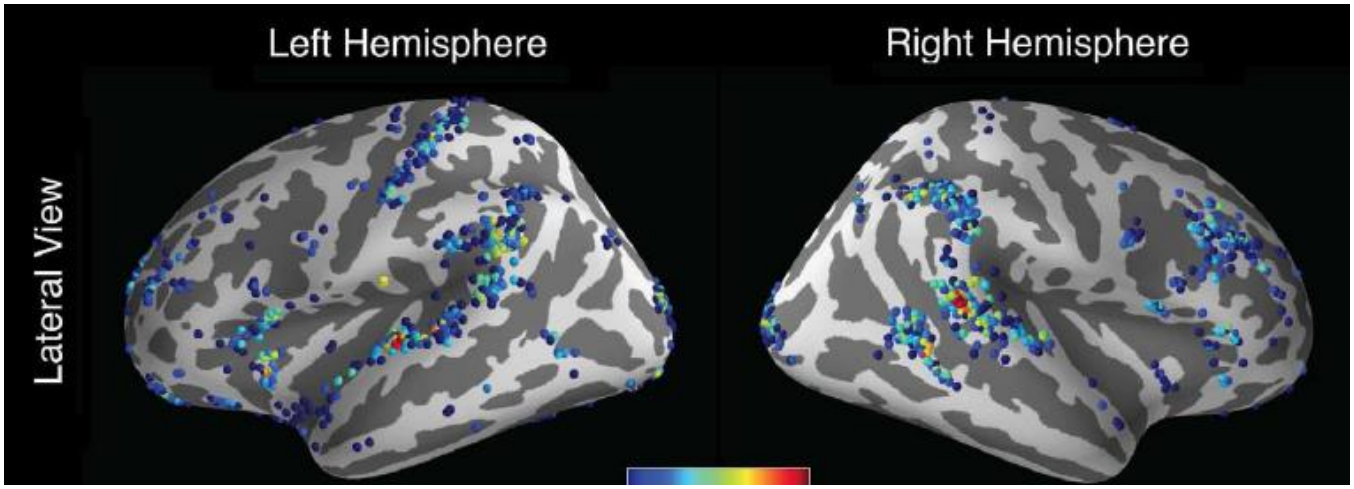
Analytic flexibility in fMRI

Carp, Joshua. 'On the Plurality of (Methodological) Worlds: Estimating the Analytic Flexibility of fMRI Experiments'. *Frontiers in Neuroscience* 2012:

- Potential for false positives increases with analysis flexibility
- This study tested 34560 different ways of analysing one fMRI dataset
- Some outcomes were consistent across pipelines, others showed methods-related variability in activation strength, location, and extent



Colour indicates number of pipelines yielding activation for that location

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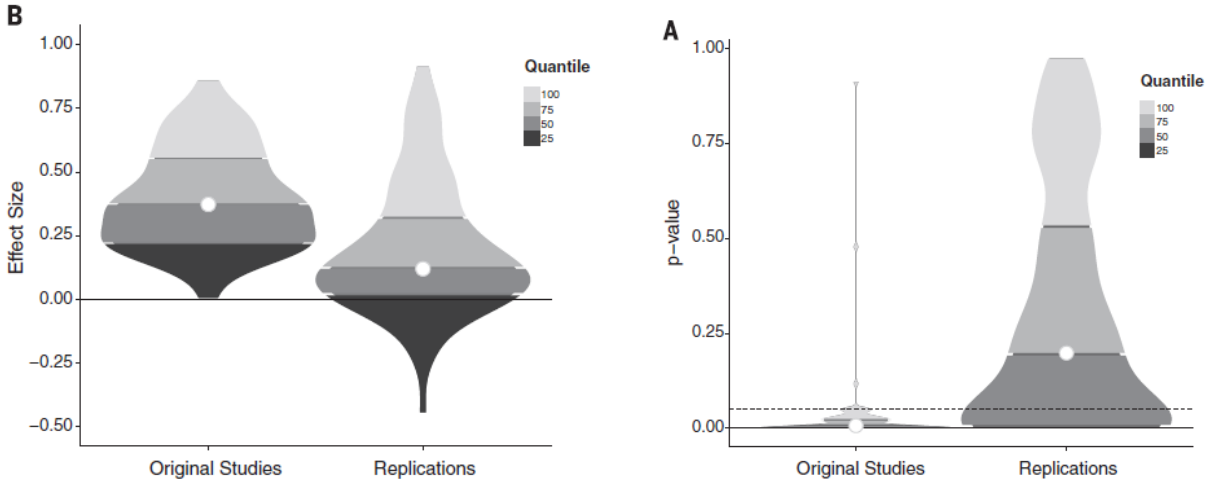
Why is it a problem?

The replication/reproducibility "crisis"

- a large-scale (**100 studies**), collaborative effort to reproduce psychological science studies published in 3 journals was conducted
- The mean effect size of the replicated effects was **half the effect size** of the original effects
- **97%** of original studies had significant results ($p < .05$), but only **36%** of the replications had significant results



[Open Science Collaboration. 'Estimating the Reproducibility of Psychological Science'. *Science* 2015]

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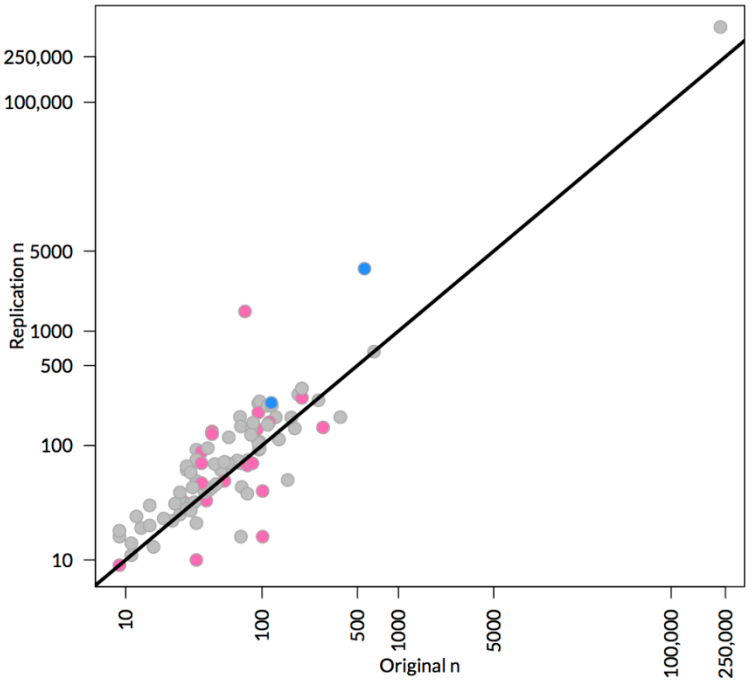
Why is it a problem?

The replication/reproducibility "crisis"

- only 36% of the studies were reproduced – this sounds very bad ...
- but: many of the studies being replicated had a small sample size, which is already a problem:
  - small sample size studies are almost impossible to replicate in the first place!
  - **The smaller the sample and effect size, the less likely the research findings are to be true.**



http://simplystatistics.org/?p=4336

Ioannidis, John P. A. 'Why Most Published Research Findings Are False'. *PLoS Med* 2005

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Questionable Research Practices

- include p-hacking, HARKing (hypothesizing after results are known), lack of replication, publication bias (file drawer problem), low statistical power, lack of data sharing, selective reporting (cherry picking), selective stopping, …

why are we doing that?

- incentives in academia conflict with what is good for science
  - the need to produce many novel and striking results
    - Frequent publication is one of the few methods to demonstrate academic talent – 'publish or perish'
  - we compete for a limited number of prestigious publication slots
  - we have to protect knowledge from competitors

http://figshare.com/articles/The_Resistable_Rise_of_Questionable_Research_Practices/1540908

http://orca.cf.ac.uk/59475/1/AN2.pdf

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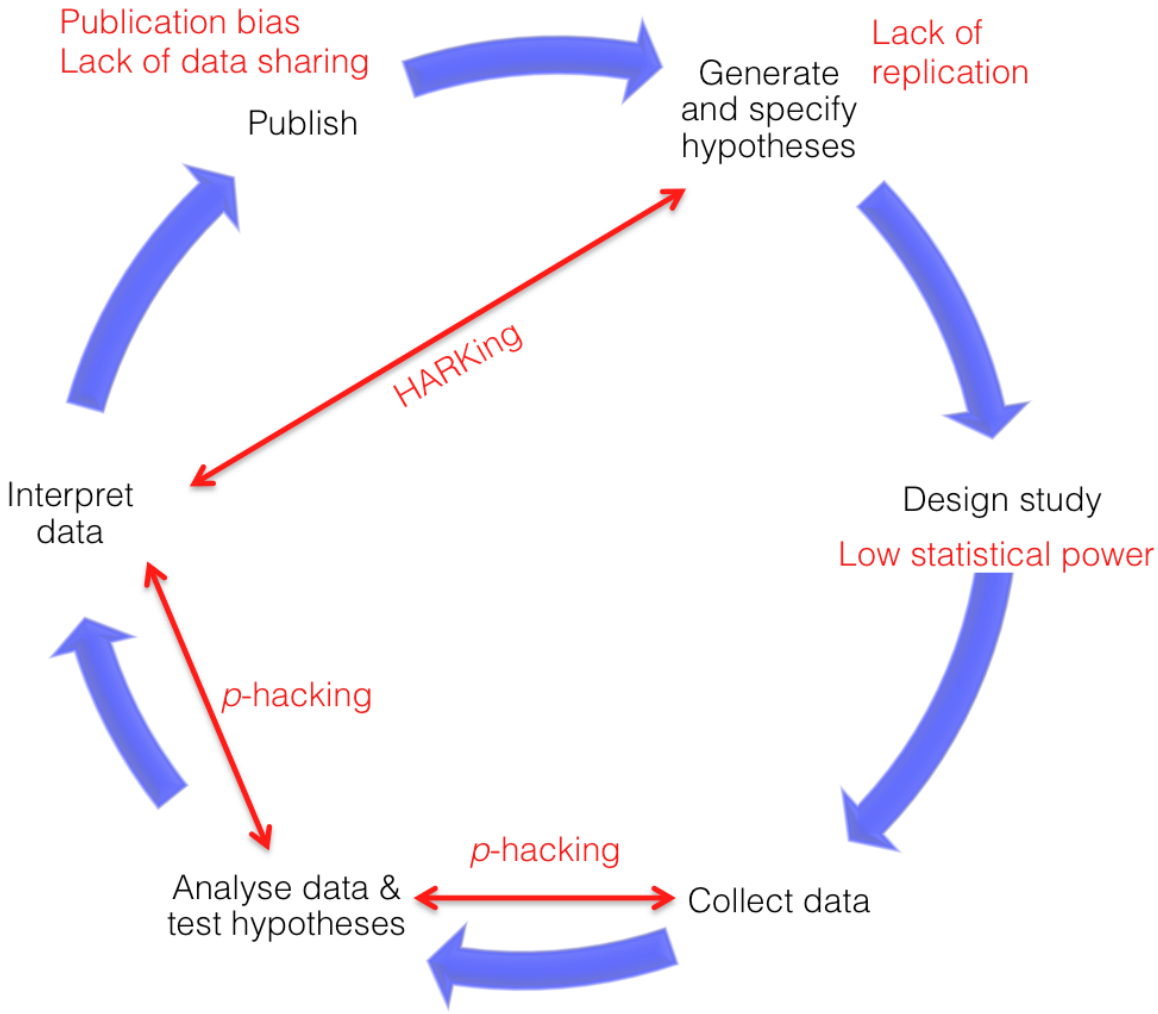
Questionable Research Practices



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How can we solve the problem?

Acknowledge that p-values are a very unreliable measure for significance and often misinterpreted

- p-values are often equated with strength of relationship, but small effects can have low p-values and vice versa
  - use of effect size measures can help to judge importance
- p-values are highly unstable and variable with small changes in the sampling (see the dance of the p-values: https://www.youtube.com/watch?v=u5uN3drVSkE) !
- "If you use *p*=0.05 to suggest that you have made a discovery, you will be wrong at least 30% of the time. If experiments are underpowered, you will be wrong most of the time." (David Colquhoun)

Colquhoun, David. 'An Investigation of the False Discovery Rate and the Misinterpretation of P-Values'. *Royal Society Open Science* 2014

[Head, et a. 'The Extent and Consequences of P-Hacking in Science'. *PLoS Biol* 2015]

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Is the following statement true, or false?

We investigate an effect which is real in 30 % of the cases with a test which has a power of 35 % and

set our significance threshold to a p-value to 0.05

If we claim that we have found a significant effect,

the probability that we are wrong is 5 %

TRUE OR FALSE?

http://www.nicebread.de/whats-the-probability-that-a-significant-p-value-indicates-a-true-effect/

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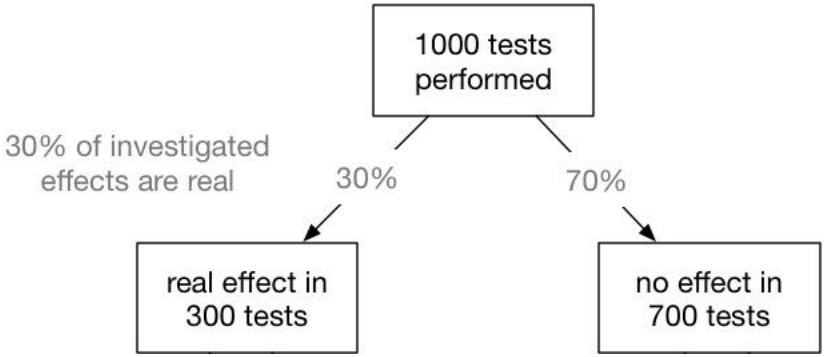

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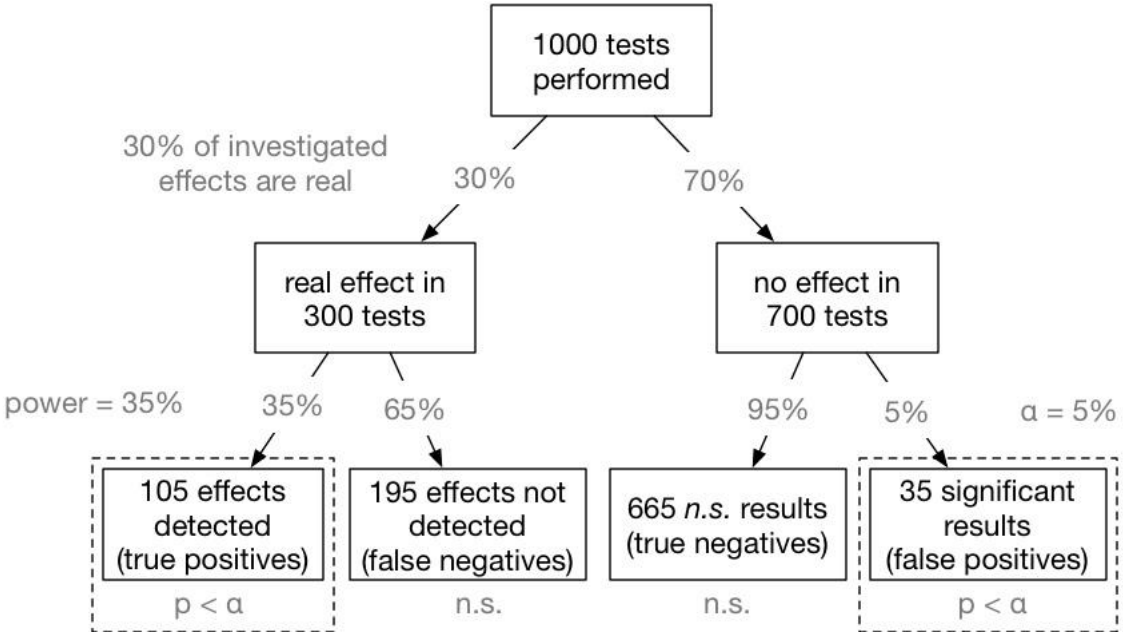

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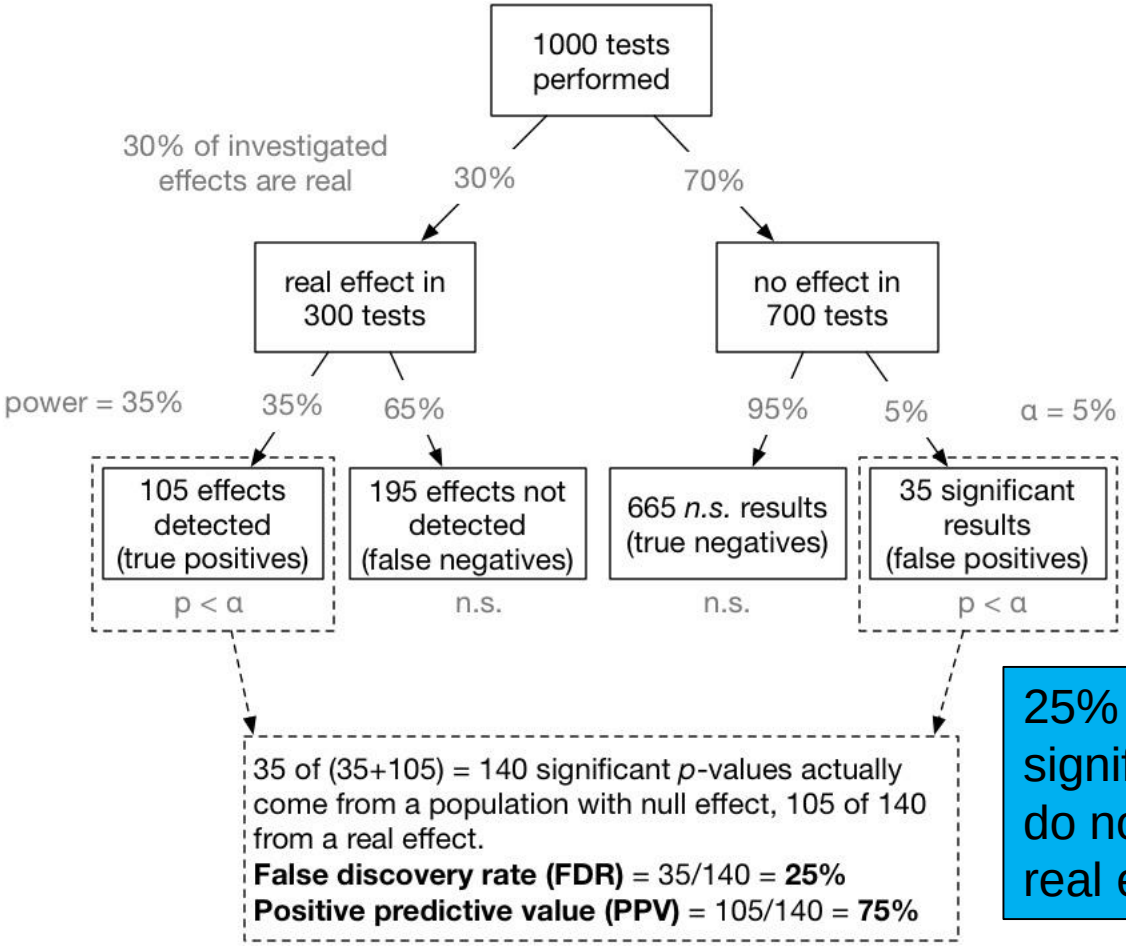

25% of all significant *p*-values do not indicate a real effect!

http://www.nicebread.de/whats-the-probability-that-a-significant-p-value-indicates-a-true-effect/

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How can we solve the problem?

Acknowledge that p-values are a very unreliable measure for significance and often misinterpreted!

- non-parametric randomisation tests and Bayesian statistics can help

- **However:**
  - Banning p-values (1) will not solve the problem, as publication bias will happen also with the alternatives (confidence intervals, Bayesian credible intervals, …)
  - Effect size measures only partly help as they are often inflated in small sample size studies!

(1) http://www.nature.com/news/psychology-journal-bans-p-values-1.17001

[Head, et a. 'The Extent and Consequences of P-Hacking in Science'. *PLoS Biol* 2015]

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How can we solve the problem?

Incentivise replication of effects instead of novelty

- Perform your own replication studies in-house in independent samples and publish failed replications
  - E.g.: Lane et al. ‘Failed Replication of Oxytocin Effects on Trust: The Envelope Task Case’. *PLoS ONE* 2015
- Publish failed experiments to reduce the publication bias (e.g. in a self publishing manner if journals do not accept the work)

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How can we solve the problem?

Preregistration of studies

- Define analysis pipeline before analysing the data
- Peer review before study is conducted based on hypotheses & methods
- studies will be published regardless of the results they show
- Circumvents post-hoc hypothesis generation / cherry-picking

- Dan Simons: “It keeps us from convincing ourselves that an exploratory analysis was a planned one.”

http://www.dansimons.com/index.html

http://www.nature.com/news/how-to-make-biomedical-research-more-reproducible-1.18684?WT.mc_id=TWT_NatureNews

http://www.stat.columbia.edu/~gelman/research/unpublished/p_hacking.pdf

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How can we solve the problem?

Preregistration of studies

- Journals already offering registered reports:
  - Cortex
  - AIMS Neuroscience
  - Attention, Perception & Psychophysics
  - Perspectives on Psychological Science
  - Experimental Psychology
  - Drug and Alcohol Dependence
  - Social Psychology

http://www.theguardian.com/science/head-quarters/2014/may/20/psychology-registration-revolution

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“Hide results to seek the truth”

Since the early 2000s physicists actively fight bias and error

- After realizing that new estimates of physical constants were closer to already published values (“confirmation bias”)
- By: blinding analysis, removing data labels, altering data values
- Consequence of blinding: Analytical decisions have been completed and debugged before the final result is visible to the researcher

Easy transfer to fMRI analysis possible:

- data acquired from controls and patients and we are interested in the differences between the two groups
- Why not hiding the group membership and treating all the same until analysis pipeline refined?
- If pipeline is done: reveal the group membership and look at results, but do not change pipeline

http://www.nature.com/news/blind-analysis-hide-results-to-seek-the-truth-1.18510

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How can we solve the problem?

Reduce the influence of impact factors on science careers

- Impact factors are calculated annually as the mean number of citations to articles published in any given journal in the two preceding years
  - Problem: distribution is highly skewed (85% of the articles have *fewer* citations than the average) -> **mean is inappropriate**

- It has become one of the most determinant factor in the award of grants and promotions (ARC Australia: “H-index and number of publications are discussed in the panel, with nature, science and PNAS papers holding most weight (1)”)

- Most scientists play the impact ladder game: start in high impact journals and go down, instead of aiming for a journal based on the readership and trying to publish fast
  - time-wasting and demoralising rounds of rejection and delay of information distribution

https://www.science.org.au/emcr-pathways-issue-5/behind-closed-doors-observing-arc-selection-meeting

http://occamstypewriter.org/scurry/2012/08/13/sick-of-impact-factors/

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How can we solve the problem?

Reduce the influence of impact factors on science careers

- Right now scientists' success is measured mainly based on the amount of high-impact articles
- To increase the impact factor of journals: results that are positive, novel, eye-catching, surprising, and simple to understand are favoured
- Therefore: negative results, complicated results, or replication studies are difficult to publish and it is often not worth the effort (especially for early career scientists)
- journals fear that pre-registration reduces their impact factor and are therefore opposing it?
- impact factors positively correlate with retractions due to fraud or error (Fang et al. 2012)

Fang, et al. 'Misconduct Accounts for the Majority of Retracted Scientific Publications'. *PNAS* 2012

http://www.theguardian.com/science/blog/2013/jun/05/trust-in-science-study-pre-registration

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Peer review

Peer review is crucial for science:

- identifies weaknesses
- encourages authors to provide more evidence (and do more work)
- Ensures that details for others to understand and replicate experiments are presented
- leads to greater reproducibility and fewer retractions

But:

- publication is heavily incentivized -> publication rates grow dramatically -> more work for reviewers, but no incentives to do good peer review
- Some scientists do not review at all or delay review for months
- Often, no discussion between authors and reviewers happens, as the journals reject quickly if there is some negative feedback
- Reviewer comments are mostly not published

[https://academickarma.wordpress.com/]

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Peer review 2.0

One solution proposed by http://academickarma.org:

- Academic Karma is a journal independent peer-review network by Lachlan Coin and Louis Stowasser from Brisbane
- to get your paper reviewed you need to review other papers

- The review is open and transparent and the reviewing work can now be used to evaluate academics
  - Right now publishing papers with high impact counts in grants a lot, but delivering high quality reviews does not count at all …
- Reviews can be send to different journals avoiding unnecessary reviewer work

[https://academickarma.wordpress.com/]

Peer review 2.0

Another solution proposed by https://publons.com/

- allows to record, verify, and showcase peer review contributions in a format you can include in job and funding applications (without breaking reviewer anonymity)

Others:

- http://www.rubriq.com/
  - independent peer review service attempting to improve the publishing process, pay 100$ per review
- https://www.peerageofscience.org/

http://www.nature.com/news/the-scientists-who-get-credit-for-peer-review-1.16102

Gasparyan et al. 'Rewarding Peer Reviewers: Maintaining the Integrity of Science Communication'. Journal of Korean Medical Science 2015

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Post-Publication Peer-Review

- Could offer a better debate about scientific work
- Getting credit for reviews

examples:

- http://www.ncbi.nlm.nih.gov/pubmedcommons/
- https://pubpeer.com/
- https://publons.com/
- http://www.ploslabs.org/openevaluation/
- https://www.researchgate.net/publicliterature.OpenReviewInfo.html
- http://f1000research.com/about

https://www.researchgate.net/post/What_are_your_thoughts_on_and_experiences_with_open_post-publication_peer-review#view=561e67326307d94eba8b45a1

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New forms of publishing

publication portals / megajournals for fast publication (e.g. for null-results):

- http://f1000research.com/
  - author-led process, publishing all scientific research within a few days
  - Open, invited peer review of articles is conducted after publication, focusing on scientific soundness rather than novelty or impact
- https://peerj.com/
  - 26 days until published including peer-review
  - offers publication of pre prints: draft of an article to get feedback

- Others: sciencematters.io, thewinnower.com, *PLOS ONE, BMJ Open, SAGE Open, Scientific Reports, Open Biology, SpringerPlus, …*

http://blog.impactstory.org/the-3-dangers-of-publishing-in-megajournals-and-how-you-can-avoid-them/

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New forms of publishing

publication portals / megajournals for fast publication (e.g. for null-results):

- Advantages
  - Excellent research has been published in these journals
  - Boost citation and readership
  - They publish fast (PLOS ONE: 6months, PeerJ: 51 days, F1000: few days)
  - They are cheap (PeerJ: from 99 $)

- Disadvantages
  - They do not always have a good reputation (‘article dumping’ …)
  - Low impact factors (which shouldn’t be a disadvantage, as articles should be judged by their own merits …)

http://blog.impactstory.org/the-3-dangers-of-publishing-in-megajournals-and-how-you-can-avoid-them/

Self-Archiving of Articles

Should we pay additional money to make our articles open-access?

- Maybe not.

- there are existing repositories and maybe we should use them instead of paying additional fees for open access publishing in the established journals
- transparent feedback on our work from the whole community “post” publication adds additional value
- The output of publicly funded work has to be accessible for everyone and this should not cost additional money for society!

https://pandelisperakakis.wordpress.com/2015/09/09/how-to-negotiate-with-publishers-an-example-of-immediate-self-archiving-despite-publishers-embargo-policy/

Self-Archiving of Articles

Your are allowed to self-archive your paper after the last review step (i.e. not yet layouted by the journal)

- However, some publishers request an embargo time of 6 or 12 months (e.g. Springer)
  - This embargo time can be negotiated to 0 with the publisher: https://pandelisperakakis.wordpress.com/2015/09/09/how-to-negotiate-with-publishers-an-example-of-immediate-self-archiving-despite-publishers-embargo-policy/

To find information about the journals' policies:
http://www.sherpa.ac.uk/romeo/

https://pandelisperakakis.wordpress.com/2015/09/09/how-to-negotiate-with-publishers-an-example-of-immediate-self-archiving-despite-publishers-embargo-policy/

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Self-Archiving of Articles

Your are allowed to publish your work as pre-print and then later submit it to normal Journals

- This would allow that your article is read, even before peer-review and you can get feedback from the community
  - E.g. 10% of the articles on bioRxiv have comments

- http://www.theguardian.com/science/occams-corner/2015/sep/07/peer-review-preprints-speed-science-journals
- https://peerj.com/blog/post/115284878302/dorothy-bishop-on-her-preprint-experiences-at-peerj/
- https://en.wikipedia.org/wiki/List_of_academic_journals_by_preprint_policy

Self-Archiving of Articles

- http://www.zenodo.org/
  - Developed by CERN and funded by EU project FP7
- http://arxiv.org/
  - document server operated by Cornell University for pre-prints in physics, maths, engineering
- http://biorxiv.org/
  - document server operated by Cold Spring Harbor Laboratory for pre-prints in biology, neuroscience …
- http://riojournal.com/
  - publish project proposals, data, methods, workflows, software, project reports and research articles
- http://figshare.com/
  - repository where users can make all of their research outputs available in a citable, shareable and discoverable manner

How could academic publishing look like in the future?

1. replicate a study to see whether an effect from an exploratory analysis is reliable and publish as '**replication study**' regardless of result
2. improve experiment and submit the methods to a journal independent peer-review (e.g. Academic Karma) where the **reviewers get credit** for the important reviewing work they do
3. the manuscript and experiment is peer-reviewed based on the methods and the methods can be improved further and accepted in a journal as a '**pre-registered study**'
4. then the study is conducted and analysed as planned and published regardless of the results as a '**pre-registered study**'
5. then the data should be shared publicly and explored further, but the results from these analyses are published as '**exploratory studies**'
6. GOTO 1

during 1 to 5 all published work and reviewing comments should be made publically accessible independent of journals in a self-archiving fashion

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Thank you for your attention.

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