Challenges to Epidemiology

in a world of imperfect evidence, polarisation, misinterpretation, and conflicts of interest

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Evidence-based decision making

Evidence-based Medicine
Best available research evidence
Clinical expertise
Patient's values

Evidence-based Public Health
Best available research evidence
Resources, including practitioner expertise
Population characteristics, needs & values

Evidence-Based Medicine Working Group, 1992
Sackett et al., 1996
Jacobs et al., 2012
Greenhalgh et al., 2014
Smith, Rennie, 2014
Ioannidis, 2016
A representation of the scientific method

- Generate and specify hypothesis
- Design study
- Conduct study and collect data
- Analyse data and test hypothesis
- Interpret results
- Publish and/or conduct next experiment

Adapted from Munafo et al., 2017
A representation of the scientific method

Generate and specify hypothesis

Design study

Conduct study and collect data

Analyse data and test hypothesis

Interpret results

Publish and/or conduct next experiment

Adapted from Munafo et al., 2017
Generating and specifying hypotheses

Altman (1994): “We need less research, better research, and research done for the right reasons”

What matters?

What is known?

Studies are designed and discussed in isolation

- Fewer than 25% preceding RCTs cited in RCTs published 1963-2004
  (Robinson, Goodman, 2011)

- Less than half of trial investigators were aware of relevant systematic reviews when they designed their studies
  (Cooper et al, 2005)

Adapted from Chalmers et al., 2014
A representation of the scientific method

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5. Interpret results
6. Publish and/or conduct next experiment

Adapted from Munafo et al., 2017
Design and conducting studies

Effect estimate = effect + bias + error

E.g.:
High risk groups
Intermediate outcomes
Control group

Source: Ioannidis et al., 2014
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Adapted from Munafo et al., 2017
Analysing data

Retracted

Source: http://knowyourmeme.com/photos/912144-anti-vaccination-movement
Analysing data

- More than 1 in 10 of the $p$-values were incorrect in a sample of over 250 psychology papers found.

- More than 90% of the mistakes were in favour of the researchers’ expectations (when mistakes changed the conclusion).

Source: Bakker, Wicherts, 2011
Analysing data

Data-dredging or P-hacking

“Post hoc analysis”
(e.g. “post hoc” removal of outliers, data transformation, inclusion/exclusion of covariables)

Cherry picking results

Source: http://www.thelastamericanvagabond.com/anthony-tyler/p-hacking-institutionalized-science-can-fabricated/

Source: Nuzzo, 2015
Analysing data

P-hacking

Abstract

Background: Although the focus of scientific studies on the beneficial properties of chocolate with a high cocoa content has increased in recent years, studies determining its importance for weight regulation, in particular within the context of a controlled dietary measure, have rarely been conducted.

Methodology: In a study consisting of several weeks, we divided men and women between the ages of 19-67 into three groups. One group was instructed to keep a low-carb diet and to consume an additional daily serving of 42 grams of chocolate with 81% cocoa content (chocolate group). Another group was instructed to follow the same low-carb diet as the chocolate group, but without the chocolate intervention (low-carb group). In addition, we asked a third group to eat at their own discretion, with unrestricted choice of food. At the beginning of the study, all participants received extensive medical advice and were thoroughly briefed on their respective diet. At the beginning and the end of the study, each participant was weighed and measured for height. Dietary intake was assessed using a 7-day food diary.
Analysing data

P-hacking

**Economics**
Brodeur et al (*AEJ:A, in press*)
“Star Wars: The empirics strike back”

**Psychology**
Masicampo Lalande (*QJEP, 2012*)
“A peculiar prevalence of p values just below .05”

**Biology**
Head et al (*PLOS Biology 2015*)
“Extent and Consequences of P-Hacking in Science”

Source: [http://datacolada.org/41](http://datacolada.org/41)
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Interpretation of results

“Creative ways” of interpreting P-values:

- a little significant (p<0.1)
- flirting with conventional levels of significance (p > 0.1)
- on the very fringes of significance (p = 0.099)
- not absolutely significant but very probably so (p > 0.05)
- a robust trend toward significance (p=0.0503)
- approached but did not quite achieve significance (p>0.05)
- at the brink of significance (p=0.06)
- just escaped significance (p=0.07)
- just shy of significance (p=0.053)
- loosely significant (p=0.10)
  ...
Interpretation of results

Gormally, Nuzzo, 2015

Source: https://caragormally.wordpress.com/portfolio/eureka/
Interpretation of results

**Cognitive Fallacies in Research**

- **Hypothesis Myopia**: Collecting evidence to support a hypothesis, not looking for evidence against it, and ignoring other explanations.
- **Texas Sharpshooter**: Seizing on random patterns in the data and mistaking them for interesting findings.
- **Asymmetric Attention**: Rigorously checking unexpected results, but giving expected ones a free pass.
- **Just-So Storytelling**: Finding stories after the fact to rationalize whatever the results turn out to be.

*Nuzzo, 2015*
A representation of the scientific method

Publish and/or conduct next experiment

Interpret results

Generate and specify hypothesis

Design study

Conduct study and collect data

Analyse data and test hypothesis

Adapted from Munafo et al., 2017
Published literature

Publication bias

...and this is where we put the non-significant results.

Less chance of publication

“Non-significant” results

Published later

Lower impact journals

Someecards user card

University of Bristol

MRC Integrative Epidemiology Unit
Published literature

Financial conflicts of interest

- Overestimated benefits
- Underestimated side effects
  - No independent trials
  
  *Jefferson et al., 2014*

- Industry sponsored systematic reviews more likely to report no association between soft drinks and obesity

  *Bes-Rastrollo et al., 2013*

- Industry tried to undermine and distort the emerging science

  *Brandt et al., 2012*
Published literature

Non-financial conflicts of interest

Imagine that you’re…

- Peer reviewing a study using cell lines from an aborted fetus and morally oppose fetal cell research

- An editor and receive a paper from a former supervisor

- One of the top malarial researchers and are asked to review a paper of a direct competitor
So what?
Why Most Published Research Findings Are False

John P.A. Ioannidis

- Small studies
- Small effect sizes
- Low prior probability of a relationship being true
- High flexibility in study designs and analysis
- High commercial and other conflicts of interest
- Testing by several independent teams
Reproducibility crisis

IS THERE A REPRODUCIBILITY CRISIS?

- 7% Don't know
- 52% Yes, a significant crisis
- 38% Yes, a slight crisis
- 3% No, there is no crisis

1,576 researchers surveyed

Baker et al., 2016
What now?
Transparency

PROSPERO

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

GitHub

GitLab

Data Sharing Statements (ICMJE)
Open trials

- Collaborative and open database for all available structured data and documents on all clinical trials
Open Science Framework
A scholarly commons to connect the entire research cycle
Publication

Pre-publication
- Peer review system:
  - Unanonymised peer review
  - Criteria for acceptance

Publication

Post-publication

bioRxiv - THE PREPRINT SERVER FOR BIOLOGY

open access

Commons

PubMed
Way forward

- Involve multiple stakeholders
- Team work
- Constant assessment
- Shift incentives
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References

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- Deer B. How the case against the MMR vaccine was fixed. BMJ. 2011;342:c5347.
Problems in study design, conduction and analysis:

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Publication bias & conflicts of interest:

- Godlee F, Clarke M. Why don't we have all the evidence on oseltamivir? BMJ. 2009;339:b5351.
Reproducibility crisis and transparency:


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- International Clinical Trials Registry Platform (ICTRP) (WHO): http://www.who.int/ictrp/en/
- International prospective register of systematic reviews (PROSPERO): https://www.crd.york.ac.uk/PROSPERO/
- GitHub: https://github.com/
- GitLab: https://about.gitlab.com/
- ICMJE Conflict of Interest Disclosure Forms: http://www.icmje.org/about icmje/faqs/conflict-of-interest-disclosure-forms/
- OpenTrials: https://opentrials.net/
- Open Science Framework: https://osf.io/
- Equator network: Source: http://www.equator-network.org/
- bioRxiv: www.biorxiv.org