AAMC
Tomorrow's Doctors, Tomorrow's Cures

Learn
Serve
Lead

Unconscious Bias and Reproducible Science

Ross McKinney, Jr, MD

Association of
American Medical Colleges

Conflict of interest notices

- Relevant conflicts of interest in this talk:
  - I am employed by the AAMC
  - Over many years I consulted or spoke for pharmaceutical companies (speaking ended before 2002)
  - I spent 14 years at Duke responsible for Conflict of Interest management in the School of Medicine

AAMC

The Challenge of Doubt

There seems to be a rising cultural skepticism about science

- A belief that scientists reconfigure their findings to support a cultural-political-economic agenda

- Skepticism about even well-established facts like “Vaccines save lives”
- If you aren’t going to believe what scientists are discovering, why fund them?
  - Reproducibility issues just add fuel to the fire

Bias

- A systematic distortion of a statistical result due to a factor not allowed for in its derivation. (Oxford)
- Systematic error introduced into sampling or testing by selecting or encouraging one outcome or answer over others (Merriam-Webster)
- Derived from a French word “biais” that means “an oblique line” (first appears in English mid-16th Century)

AAMC

Bias in Science - McKinney

- Bias: a tendency to skew research results as a consequence of held beliefs or practical motivations on the part of the investigator
  - These held beliefs may be based on principles, previous evidence and interpretation, or relationships
  - These held beliefs are generally unconscious
  - The practical motivations may be financial, including employment

Bias in science

- Bias can be reflected in study design, conduct, or reporting
  - Study design may be established to favor a desired outcome
  - Data may be filtered or sampled in such a way to obtain a desired result
  - Reporting may be selective
- Any of these biasing steps might be due to unconscious beliefs

AAMC

Turner NEJM Study - 2008

- **74** Studies of 12 anti-depressants; 12,564 patients
- **38** studies with positive results submitted to the FDA, of which 37 were published, 1 not
- **36** with negative FDA results
  - 3 published, 22 not published
  - 11 published with data selection to appear positive
- In literature, **94%** of publications were positive

Turner: NEJM 2008;258:252-260

AAMC

Validating Science

- Some degree of bias is inevitable in all science – the goal is to minimize it
  - We all have hypotheses & beliefs
  - Scientists are rewarded for establishing new ideas and positive results
    - More publications, grants, higher pay, personal satisfaction
    - There is, thus, a strong bias toward novel findings

Validating Basic Science

In basic science, we have means to limit the effects of bias, if we choose to use them:

- Controls – often blinded
- Randomization
- Statistical tests
  - Adequately powered sample sizes
  - Pre-specified analytic plan
- Consistency with a logical hypothesis
  - Mixed blessing: confirmation bias

Validating Basic Science

- Reproduction
  - Often done by others
  - Requires publication of methods, provision of reagents
  - Note – may be a challenge in proprietary research
- Peer review

AAMC

Validating Clinical Research

Reproducibility is the key test for validation, but…

In clinical research, trials are often too expensive to reproduce

Don’t want to put people at risk unnecessarily

- Clinical equipoise in therapeutic trials
- If one therapy is already established as better, how do we randomize? Would you volunteer?

Concerns in Clinical Research

Primary means of validation is audit (specifically, monitoring)

Audit is not generally effective as a means to identify bias evidenced through:

- Problems in study design
- Subjectivity in endpoint and AE assessments
- Inappropriate statistical criteria

Articles as written may not reflect the initial study design (rarely checked against the protocol)

Two overall strategies

1) Prospective management of subjectivity to prevent problems related to bias
2) Management of issues when the source of bias (often conflict of interest) is apparent and known

McKinney & Pierce – JAMA 2017;317:1727

AAMC

The Bias/Reproducibility issue

Requires both a broad cultural shift and an institutional response

Culture first: return to traditional scientific methods

- Pre-specified experiments and analytic plans
- Good controls
- Well validated reagents (esp. cell lines and monoclonal antibodies)

AAMC

Bias and culture

Publish accurate methods, complete data

- Encourage & facilitate replication
- Encourage sharing of data

Lab directors/PIs need to be engaged

- Mentoring
- Internal peer review
- Regular lab meetings and presentations of work in progress (facilitates ideas and finds unrecognized systematic errors)

AAMC

Institutions and bias

What are some ideas that institutions could try?

- Investigators should have access to adequate biostatistical support
- Consider sampling labs – audit
- Require adequate power calculations before any animal or human subjects experiment
- Consider the effects of promotion criteria

Granting agencies and bias

Grant reviews should emphasize planned controls and validity checks, not just preliminary data

Increased emphasis on subsequent validation by others rather than self-reference, in grant applications as well as the promotion process

AAMC

Summary

- Unconscious bias can affect the validity of research
- Institutions and granting agencies can play a role
  - In creating a healthier culture
  - In providing tools like biostatistical support that can improve the science

AAMC

AAMC

Tomorrow's Doctors, Tomorrow's Cures

Learn

Serve

Lead

Thank you for listening!

Association of
American Medical Colleges