Ethical Issues in Scientific Publication

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Topics

- Scope
  - Math stat & methodological publications
  - Applied collaborative publications in other disciplines
- Issues
  - Plagiarism
  - Multiple submissions
  - Splitting
  - Refereeing
  - Citation
  - Multiple authorship and responsibility
  - Conflict of interest and disclosure
  - Ghost and guest authorships
  - Science and advocacy

Credentials?

- ASA Committee on Professional Ethics (2008-10)
  - Monday 8:30, CC206: Real-Life Ethical Dilemmas Encountered in the Practice of Statistics: Resolution Leading to Policy Change
- Considerable editorial experience
- But no special moral authority.
- You will hear
  - Widely accepted standards in science
  - Common sense, with some opinion
  - Personal experience underlying my sense of common sense
- Statistical education does not routinely train to this. So, in case something was missed…

Plagiarism

- Publication of another's ideas and/or text without attribution or permission.
  - Violates the originator's intellectual property rights
  - Damages the presumption of integrity underpinning scientific work
- Examples
  - Wholesale expropriation
  - Modest excerpting without labeling
- Conveying common knowledge in your words
  - Expression mirrors thought
  - Establishes credibility

Multiple submissions

- Sending your paper, or multiple versions of it, to more than one journal at once
  - Obtains varied feedback more quickly
  - Allows exploration of journal fit
  - Shortens publication time
- A victimless crime?
  - Squanders a limited, stressed resource: journal editors and reviewers
  - Degrades quality of reviews
  - Delays/preempts publications by others
  - Increases journal costs, costs of access, decreases publisher incentive

Split reports

- Multiple niche papers for different outcome variables to increase publication count, when one comprehensive report would do.
- Same issues as multiple submissions.
- Also, resulting extra publications may replicate reporting of core study methods, wasting more journal pages and reducing access by others.
- However
  - Journals and reviewers may resist comprehensive publications
    - Paper length restriction
    - Narrow perspective
  - Alternative: core methods publication + targeted results papers

Refereeing

- Submitted papers are privileged communications between authors and journal editor(s). Referees are agents of the journal editor(s).
- Hence, submitted papers are confidential. It is
  - ethical to seek advice on a manuscript from a colleague, or to ask a good student or colleague to a portion of your review.
  - unethical to redistribute the manuscript or its content otherwise, for you, or any colleague or student who sees the manuscript. These become your agent in conducting the review, and assume your obligations.
- If you can't do a reasonably careful review, return the manuscript to the editor so someone else can.
  - Slipshod reviews damage and even kill careers.

Refereeing

- Notify editors if your review will be substantially delayed.
- Don’t reuse ideas from the manuscript, or hold your review of the manuscript so someone else can. This is plagiarism.
- Do not delay submitting your review so someone else in the research area can publish first. This is also scientific misconduct.
- Disclose potential conflict of interest to the editor when you become aware of it. Better yet, decline to review when a neutral party might perceive a conflict of interest concern.

Refereeing

- Your responsibility is to the journal, not the author, Give the journal editor your dispassionate advice.
- But…
  - Be honest with the author, but be at least polite and encouraging when you can. Discouraging referees reports can end research and demoralize researchers.
  - Don't just say what's wrong. Guide the author to improve the paper.
- Caveat
  - Give the author benefit of the doubt, but don't waste a lot of effort if you strongly feel the author can't be helped, or the manuscript has not been carefully prepared.

Citations

- Citation counts, because people are obsessively counting citations. Citations are a primitive but widely used guide to scientific influence.
  - Science Citation Index
  - Journal impact scores
  - Highly-cited articles
- Cite what you use.
- Cite the most relevant, useful papers.
- Don’t just cite yourself and friends!
- Cite even your rivals.

Authorship criteria -- one approach: International Committee of Medical Journal Editors

"Authorship credit should be based on

1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data;

2) drafting the article or revising it critically for important intellectual content; and

3) final approval of the version to be published.

Authors should meet conditions 1, 2, and 3.

When a large, multi-center group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript (3)."

Authorship criteria

- Aren't uniform across disciplines.
- Interpretation of "substantial contributions to…." varies across disciplines.
- Each discipline perceives contributions within the discipline as more substantial than those from without: a ubiquitous problem for statisticians.
- Authorship allocation may appear unfair and sometimes is.
  - If any doubt, discuss in advance.
  - Not any doubt, confirm in advance.
  - Above easier said than done.

Dimensions for assessing your own contributions

- Innovation in statistical method
- Statistical advance within the substantive field
- Impact on design
- Impact on analysis and interpretation
- Depth and duration of hard work
- Potential impact of the publication: need for attributing responsibility

Ghost and guest authorships

- Late involvement of academics as primary ("guest") authors for studies conceived, executed, and interpreted by sponsor.
- Papers largely written by sponsor or retained medical writing/ communications/public relations firm ("ghost") authors.
- Research programs may export serial publications this way. Responsibility for data analyses in ghost authored manuscripts is implicitly accepted by and attributed to the guest authors, though really attributable to ghost authors employed by sponsor or medical writing/marketing firm.

Ghost and guest authorships

Lisse JR, Perlman M, Johansson G, Shoemaker JR, Schechtman J, Skalky CS, et al. ADVANTAGE Study Group. Gastrointestinal tolerability and effectiveness of rofecoxib versus naproxen in the treatment of osteoarthritis: a randomized, controlled trial. Ann Intern Med. 2003;139:539-46.

"[The sponsor] designed the trial, paid for the trial, ran the trial… [The sponsor] came to me after the study was completed and said, 'We want your help to work on the paper.' The initial paper was written at [the sponsor], and then it was sent to me for editing… Basically, I went with the cardiovascular data that was presented to me."

Jeffrey Lisse, M.D.

This paper has been attacked for omitting some drug-associated deaths in the ADVANTAGE Trial from the report.

Ghost and guest authorships

OPEN ACCESS Freely available online

PLoS MEDICINE

Ghost Authorship in Industry-Initiated Randomised Trials

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Competing Interests: The authors have declared that no competing interests exist.

ABSTRACT

Background

Ghost authorship, the failure to name, as an author, an individual who has made substantial contributions to an article, may result in lack of accountability. The prevalence and nature of ghost authorship in industry-initiated randomised trials is not known.

Ghost and guest authorships

"We found evidence of ghost authorship for 33 trials (75%; 95% confidence interval 60%–87%). The prevalence of ghost authorship was increased to 91% (40 of 44 articles; 95% confidence interval 78%–98%) when we included cases where a person qualifying for authorship was acknowledged rather than appearing as an author. **In 31 trials, the ghost authors we identified were statisticians.** It is likely that we have overlooked some ghost authors…."

Ghost and guest authorships: April 2008

SPECIAL COMMUNICATION

Guest Authorship and Ghostwriting in Publications Related to Rofecoxib

A Case Study of Industry Documents From Rofecoxib Litigation

Joseph S. Ross, MD, MHS
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Harlan M. Krumholz, MD, SM

Context Authorship in biomedical publication provides recognition and establishes accountability and responsibility. Recent litigation related to rofecoxib provided a unique opportunity to examine guest authorship and ghostwriting, practices that have been suspected in biomedical publication but for which there is little documentation.

Objective To characterize different types and the extent of guest authorship and ghostwriting in 1 case study.

AUTHORSHIP IN BIOMEDICAL

Ghost and guest authorships: April 2008

Abstract Conclusions

"This case-study review of industry documents demonstrates that clinical trial manuscripts related to rofecoxib were authored by sponsor employees but often attributed first authorship to academically affiliated investigators who did not always disclose industry financial support. Review manuscripts were often prepared by unacknowledged authors and subsequently attributed authorship to academically affiliated investigators who often did not disclose industry financial support."

The nature of “Conflict of Interest” (COI)

- Multidimensional, including financial conflicts and desires
  - prestige, and to feel useful.
  - protect job or please superior.
  - support a scientific group, grant application, or student.
  - help friends and colleagues succeed.

- American Association of Medical Colleges (AAMC) definition equates actual conflict and appearance of conflict.
  - ***COI can be inherent in an environment***.
  - ***Potential present in all work environments.***
  - ***Academia not privileged in this respect!***

- *But,scrutiny/enforcement inevitably tends to focus* on the measurable, hence financial issues, in high stakes situations. These are less frequent in purely academic publications.

The Clinical Research COI Problem

- Perceived selective data suppression
  - Medical journal editors "found themselves playing a game of research hide-and-seek…."

    Jeffrey Drazen, Editor-in-Chief

    New England Journal of Medicine (NEJM)
  - "In one sense, all journals are bought—or at least cleverly used—by the pharmaceutical industry."

    Richard Smith, Former Editor

    British Medical Journal (BMJ)
  - "We were burned very badly."

    Catherine D'Angelis, Editor-in-Chief

    Journal of the American Medical Association (JAMA)
  - "The reporting of trial outcomes is not only frequently incomplete but also biased and inconsistent with protocols...."

    Chan, Hrobjartsson, Haahr, Gøtzsche, Altman, *JAMA* 2004;291.

Professional context and societal expectations of marketing and clinical scientific research

	Marketing and medical communications		Clinical scientific research
Product benefit is	Presumed		Desired
Predisposition to	Advocacy		Neutrality or skepticism
Reward for	Dissemination, acceptance of advocacy	COI?	Confirmation, acceptance of innovation
Primary responsibility to	Client business arm	COI?	Patients and scientific community

Worthy enterprises, but potentially a toxic mix.

Selective Reporting? January 2008

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Selective Publication of Antidepressant Trials and Its Influence on Apparent Efficacy

Erick H. Turner, M.D., Annette M. Matthews, M.D., Eftihia Linardatos, B.S., Robert A. Tell, L.C.S.W., and Robert Rosenthal, Ph.D.

ABSTRACT

Selective reporting? January 2008

- Abstract: "Studies viewed by the FDA as having negative or questionable results were, with 3 exceptions, either not published (22 studies) or published in a way that, in our opinion, conveyed a positive outcome (11 studies)."

- For the "FDA-negative or questionable" publication-positive studies:

  "Although for each … the finding with respect to the primary outcome was nonsignificant, each publication highlighted a positive result as if it were the primary outcome. The nonsignificant results for the prespecified primary outcomes were either subordinated to nonprimary positive outcomes (in two reports) or omitted (in nine)."

Selective reporting? April 2008

SPECIAL COMMUNICATION

Reporting Mortality Findings in Trials of Rofecoxib for Alzheimer Disease or Cognitive Impairment

A Case Study Based on Documents From Rofecoxib Litigation

Bruce M. Psaty, MD, PhD
Richard A. Kronmal, PhD

CLINICAL TRIALS REGISTRATION IS

Sponsors have a marketing interest to represent their products in the best light. This approach conflicts with scientific standards that require the symmetric and comparable reporting of safety and efficacy data. Selective reporting of the results of clinical trials can misrepresent the risk-benefit profile of drugs. We summarize how the sponsor represented

Selective reporting? April 2008

- Company did not inform FDA of 2001 ITT pooled analysis of total mortality in two large trials suggesting triple mortality risk with Vioxx, with significant elevation in both studies.
- Publication of alternative per-protocol and on-treatment follow-up analyses, with less unfavorable safety results.

Discrepancy between Results and Abstract Conclusions in Industry- vs Nonindustry-funded Studies Comparing Topical Prostaglandins

TARIQ ALASBALI, MICHAEL SMITH, NOA GEFFEN, GRAHAM E. TROPE, JOHN G. FLANAGAN, YAPING JIN, AND YVONNE M. BUYS

• PURPOSE: To investigate the relationship between industry- vs nonindustry-funded publications comparing the efficacy of topical prostaglandin analogs by evaluating the correspondence between the statistical significance of the publication's main outcome measure and its abstract conclusions.

studies had proindustry abstract conclusions. Both readers and reviewers should scrutinize publications carefully to ensure that data support the authors' conclusions.

Discrepancy between Results and Abstract Conclusions in Industry- vs Nonindustry-funded Studies Comparing Topical Prostaglandins

Statistically significant main outcome measures were reported in 7 (24%) industry-funded publications and in 2 (20%) nonindustry-funded publications ($P = 1.00$, Fisher exact test). Correspondence between the results of the main outcome measure and the abstract conclusions was found in 11 (38%) of the industry-funded publications vs 10 (100%) of the nonindustry-funded publications ($P = .0006$, Fisher exact test). Twenty-six (90%) of the industry-funded studies had proindustry conclusions.

Annals of Internal Medicine | ARTICLE

The ADVANTAGE Seeding Trial: A Review of Internal Documents

Kevin P. Hill, MD, MHS; Joseph S. Ross, MD, MHS; David S. Egilman, MD, MPH; and Harlan M. Krumholz, MD, SM

Background: Seeding trials, clinical studies conducted by pharmaceutical companies that are designed to seem as if they answer a scientific question but primarily fulfill marketing objectives, have not been described in detail.

Purpose: To describe a known seeding trial, ADVANTAGE (Assessment of Differences between Vioxx and Naproxen To Ascertain Gastrointestinal Tolerability and Effectiveness), through documents of the trial sponsor, Merck & Co. (Whitehouse Station, New Jersey).

Data Sources: Merck internal and external correspondence, reports, and presentations elicited to inform legal proceedings of *Cona v Merck and Co., Inc.*, and *McDarby v Merck and Co., Inc.* The documents were created between 1998 and 2006.

Data Extraction: An iterative case-study process of review, discussion, and re-review of documents to identify themes relevant to the design and conduct of ADVANTAGE. To supplement the case-study review, the authors did a systematic review of the literature to identify published manuscripts focused on seeding trials and their conduct.

Data Synthesis: Review of the documents revealed 3 key themes: The trial was designed by Merck's marketing division to fulfill a marketing objective; Merck's marketing division handled both the scientific and the marketing data, including collection, analysis, and dissemination; and Merck hid the marketing nature of the trial from participants, physician investigators, and institutional review board members. Although the systematic review of the literature identified 6 articles that focused on the practice of seeding trials, none provided documentary evidence of their existence or conduct.

Limitations: The legal documents in these cases provide useful, but limited, information about the practices of the pharmaceutical industry. This description of 1 company's actions is incomplete and may have limited generalizability.

Conclusion: Documentary evidence shows that ADVANTAGE is an example of marketing framed as science. The documents indicate that ADVANTAGE was a seeding trial developed by Merck's marketing division to promote prescription of Vioxx (rofecoxib) when it became available on the market in 1999.

Ann Intern Med. 2008;149:251-258. www.annals.org

For author affiliations, see end of text.

Seeding trials, August 2008

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Avoid intermingling science with advocacy

- Statisticians are legitimately involved in both.
  - OK to do dispassionate science, OK to advocate.
- For any project, your role should be one or the other, not both, and clear to the reader from context or explicit labeling and/or disclosure.
- The integrity of scientific communication is compromised when the role of the statistician in scientific reporting is blurred.
- We come under suspicion easily, because all the data come through us.
  - A few highly-publicized cases can have major impacts, even if unfairly perceived. (See JAMA editorial policy of statistical review.)

THANKS FOR YOUR ATTENTION.

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