Conflicts of Interest in Research:

Exploration and Case Studies of Managing CoI in Research and Development

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Disclosure

I am currently employed as an independent consultant for several small Medical Device companies, primarily in strategic advisory roles and customer education.

- Palette Life Sciences,
- AirXpanders,
- Imatrex

I'm paid at an hourly rate consistent with AAPM guidelines with no stock or performance bonuses.

I'm also a voting member of the AAPM Ethics Committee, and helped craft portions of the Code of Ethics as a member of TG-611.

The Problem

With Conflicts of Interest (CoI)
A paper published in The New England Journal of Medicine in 2009—29 percent of payments from prosthesis manufacturers went unreported—by physicians who presented or served on a board or committee at a large orthopedic conference. Most claimed the conflict was not relevant to their presentation or position, or that they had misunderstood the disclosure requirements.

Misusing your trusted position in society to enrich yourself "on the side" is wrong. Full Stop.

Medical Professional
Professor
Author of Scientific Paper
Grant recipient
AAPM member
AAPM Code of Ethics
Employer Contract
Local Laws
... Professional Reputation Erodes Personal Integrity

Make your stock (options) more valuable
Be given a "free" trip
Increase your odds of being funded
Make your paper seem more important

Code of Ethics – under AAPM reports
Money and Power (appear to) create Bias

Interests with financial incentives appear especially problematic:
- Developing a product when you will benefit from its success
- Advising a company how to handle a problem or create a solution – or serving on the board
- Being employed by a company (full-time, or part-time consulting)
- Accepting research grants, travel reimbursements, honoraria or other in-kind perks

Interests stemming from Authority, Power or Influence are also problematic:
- Leadership in multiple committees or organizations
- Access to confidential or privileged information create a conflict
- Contributing to papers, presentations = “gift of opportunity” and inclusion

Gifts make the receiver feel obliged to give something in return

See the System Imperfections That Drive Bias

Medical Physicists are some of the hardest working people I know. That drive comes from a combination of:
- needing your creative work to be recognized
- feeling you must live up to the investment society has placed on you
- competition, between individuals, institutions and companies

This can power creativity. It makes our field better!
But, it can also create a wish to please funders and your university, sometimes at the expense of objectivity.

Repeated Nudges drive direction, consciously or unconsciously.
Solutions
for Managing
Conflicts of Interest (COI)

Inventory your Interests

What do you "want" to succeed? Which entities support you?
- employment, funding, income, prestige, esteem, professional alignment

Who do you feel flattered by, or indebted to?

Not all interests are "in conflict" with primary duties, but be aware of how they bias your behavior
- Unbiased research, and unbiased leadership is a worthy goal in itself

Identify which interests may conflict with AAPM’s interests, or may appear to
- Unintentionally or otherwise

By declaring them, you acknowledge them, and imply you can be trusted to manage them

Having interests that conflict usually stems from completely legitimate duties and activities
- unless you engineer to profit from them, or appear to do so

Dealing with Conflicts: Identify, Prevent, Manage

- Identify: Inventory of vested interests
- Prevent: If you see that paths are going to intersect, don’t go there.
  - Be if you’re on the Editorial Board of a journal, reconsider joining a University library committee that recommends journal subscriptions.
- Manage: handle the situation once it manifests
  - Always: Declare – be transparent.
  - Occasionally: Recuse – excuse yourself from a decision where you cannot be impartial.
  - Sometimes: Resolve or Eliminate by staying active in only one or the other positions.
    - Resign position
    - Refuse gifts or offers to pay for expenses (increasingly often)
How to Construct CoI Disclosures

Goal: Be proactive and transparent about the ideas/things you are vested in. Straightforward, simple and precise wording, covering:

1. Past and Present funding and/or other resources related to the project
2. Role
3. Future Incentives. Future incentives are stock, options, or other bonuses related to the performance of the product/company in the marketplace.

*Jane Doe has been the recipient of research [travel] grants from Company A, while participating in the [design/development/evaluation] of Product B. She receives no other financial bonus or incentives.*

Or

*She holds stock in Company A and receives a portion of profits from Product B.*

Ask: What would you be embarrassed of, or need to defend, if it were discovered later? The specific amounts and degree of detail that is appropriate will be context-sensitive. Expect more rigor when more influence is at stake. Seek or ask for guidance if specific direction is not given.

Example Case Studies

For Managing Conflicts of Interest (CoI)

Example 1: Company X has provided you with a free version of their product to do an evaluation of it. Do you declare this “gift” in the subsequent manuscript?

Example 2: Your retirement portfolio includes an index fund, and after researching what the fund invests in, you determine that some large Diagnostic Imaging Companies are held. Do you need to declare this in your AAPM presentation?

Example 3: Your spouse works for Company A in your field. Your assets are joint. As you are submitting your ASTRO abstract, do you declare the interest in their employer?
Case Study: CHEERS study

A highly regarded institution proposed a 10-year, $100 M study to NIH.

- **Hypothesis:** 1 drink per day can reduce heart disease and diabetes risk.
- Funded: mostly by Anheuser-Busch, InBev, Heineken and other alcohol companies through donations to a private foundation that raises money for the NIH.
- Design: PI and NIH were in close contact with funders regarding design of the study, but the protocol was "rigorously vetted" and reviewed. Trial was approved with full funding.

What issues might be present? Or appear to be present?

- The New York Times completed an investigation and ran story in March 2018. The story accused NIH employees of courting the alcohol industry, including giving talks strongly suggesting that the study's results would endorse moderate drinking as healthy.
- The study had attracted 105 participants and spent $4 million before it was suspended.
- Trial was closed a few months after the NYT story.
- Personnel actions were taken against employees that violated policies.

Appearances Matter: An Apparent CoI, real or not, can destroy public trust.

Case Study: P-Hacking the Data

Data analysis is the primary significance variable. A p-value of 0.05 or less is the long-accepted common standard for publication. In the era of Big Data, it can be tempting for hackers to support your desired hypothesis!

Let's pick an example from a social science that leads to strong "nudge" feelings for a desired outcome.

Hypothesis: "The U.S. economy is affected by whether Democrats or Republicans are in office.

Before data is collected, variables need to be well-defined... because the nuances can change the answer.

Interest #1: Find data to support your hypothesis
Interest #2: Make it into a publishable manuscript

Try it! [https://fivethirtyeight.com/features/science-isnt-broken/#part1](https://fivethirtyeight.com/features/science-isnt-broken/#part1)

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Algorithm Red vs Algorithm Blue

[https://fivethirtyeight.com/features/science-isnt-broken/#part1](https://fivethirtyeight.com/features/science-isnt-broken/#part1)
Case Study: Licensing IP

A researcher has an exceptional treatment planning algorithm and creates intellectual property (IP). A patent is issued, and the University is negotiating the license rights to a hot new start-up company for product development.

- Can the researcher invest in the company?
- What if the researcher is also the founder of that start-up company?

Ideas:
- Elimination of conflict by not investing during negotiations.
- If researcher is a founder, recusal from terms of negotiations.

What if you don’t manage your CoI?

- Risk undeclared bias → irreproducible or misleading research results
- Risk of setting back the progress of science and patient care

Conflict measures:
- Violation of HIPAA code of ethics, as well as any employer requirements.
- If a complaint is lodged, would result in revocation of AAPM/ASTRO membership.

The failure to effectively manage such conflicts results in:
- Greater risk of personal and public mistrust
- Reduced confidence in research results
- Diminished public and patient support for medical research.

The Research Community System

Research Process Regulation

- Identify
- Prevent
- Manage:
  - Declare
  - Recuse
  - Resolve/Eliminate

Research Product – Manuscript, Tool, Recommendation, etc.

Peer review works not because your colleagues are unbiased, but rather because they have different biases...
diversity of experience!

Critical assessment:
- Peer review of paper
- Reproducibility
- Outcome comparison

Blinded Peer review, Scoring of grant

Working with IRB

Transparent funding process

Well-formed hypothesis

Robust data analysis methods

Critical assessment:
- Peer review of paper
- Critical assessment:
- Research Product – Manuscript, Tool, Recommendation, etc.
Summary
Conflicts of interest are pervasive in medical research; they are not inherently unethical. Conflicts are not only financial; they can also be related to career advancement or power. If you aren’t actively keeping inventory and managing your conflicts, you are vulnerable to bias. Bias often operates on an unconscious level, impairing judgment.
No one is free of bias or conflicts. However, working together as a system where everyone has different biases, the research forefront can advance effectively. This area is rapidly evolving further methods for managing conflicts and bias. Expect it to be context-specific. Stay current on disclosure recommendations and research practices.

Thank You

Why are there so few Studies with Null Results?
It has long been argued that null studies are less publishable. A more objective view comes from a 2015 study published in PLOS ONE.
Followed how many null results were found in trials funded by the National Heart, Lung and Blood Institute.
- Rule introduced in 2000 in part because of a general sense that researchers were subtly altering their work — after it was begun — to achieve positive results.
- In the 30 years before 2000, 57 percent of trials published showed a “significant benefit.”
- Afterward, only 8 percent did.
- Conclusion: Researchers themselves suppress null results.
Lack of Reproducibility in Science

“In There a Reproducibility Crisis?”, Monya Baker, NATURE VOL 533 26 MAY 2016

Solutions – Pro Moves to work with Bias

No longer publish p-values? Basic and Applied Social Psychology will not publish p-values. Report other statistical values such as confidence interval. Detail all methods.

Report can evaluated/rejected data

Label research as Pre-Specified or Exploratory

- Report on any steps of hypothesis formulation in introduction – don’t skimp!

- Thorough: Publish hypothesis specifics and data analysis procedure in advance of data collection, with date stamp

- Make full data sets available for publications, open source code when possible. Some journals require it

- Note: complicated by HIPAA in some cases

- OpenScience Framework (www.osf.io): free project management tools!

- Moves toward open science, and for a change in the academic environment that currently incentivizes secrecy and the hoarding of data, are perhaps our best chance to improve research reproducibility
Solutions — Pro Moves for Data Analysis

Create a Validation Process for your lab:

- In house — split data into 2 independent groups,
  - Split your hypothesis randomly
  - Use separate data for second analysis (for hypothesis formulation)
  - Get a collaborating group to independently validate your hypothesis with their own data
  - Write this into grant as a last step, provide another group funding to independently validate

- Recommended practice for Varian Research funding
- Highly recommended practice for Varian Research funding

Be aware of & follow AAPM guidelines for research

- Code of Ethics, Disclosure
- University for Core Technology Management, non-profit
- Guidelines for emerging research topics