Avoiding Conflict of Interest
Recognize and Manage COI

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Disclosures

NIH
- R01HL080053
- R01HL098305
- U01HL092040
- NC-002502
- K24 HL113128 03
- T32 HL076136 10

Industry Research Support
- Siemens Medical Systems
- GE Healthcare
- Genentech
- Medis
- BMS
- HeartFlow, Inc
Talk Outline

- Definition and Principles
- Journals and NIH
- Outside Activities - Management and Implications
- Clinical
A conflict of interest is a set of circumstances that creates a risk that professional judgement or actions regarding a primary interest will be unduly influenced by a secondary interest.

Primary interest refers to the principal goals of the profession or activity, such as the protection of clients, the health of patients, the integrity of research, and the duties of public officer.
Secondary interest includes personal benefit and is not limited to only financial gain but also such motives as the desire for professional advancement, or the wish to do favors for family and friends (nepotism).

These secondary interests are not treated as wrong in and of themselves, but become objectionable when they are believed to interfere with the primary interests.

Conflict of interest rules in the public sphere mainly focus on financial relationships since they are relatively more objective, and quantifiable, and usually involve the political, legal, and medical fields.
These folks managed to have no conflict of interest
Conflict of Interest in Medicine

- **Primary interest** – clinical work, research, administration
- **Secondary interest** – financial interests through work with outside entities (industry), personal – promotion

• A determination that an individual has a “conflict of interest” is not a judgment that he or she has done anything wrong – it is simply a statement of fact about existing interests or relationships.

• Most penalties are not due to a COI but due failure of disclosure
Principles of COI Disclosure

COI is about managing relationships, expectations, perception and reputation if there is no interest - there is no conflict.

**Purpose:** transparency, allow others, including your peers, to make their judgement on potential sources of intellectual bias and pressure (reputation, promotion, financial).

Typical places requesting disclose of COI: Partners, MGPO, Societies, Journals, CME.
Notables for COI

• Lack of *empirical evidence* to describe the impact of conflict of interest in the health care industry.

• Business interests influence the direction of cancer research and the adoption of new practices in therapy.

• University projects which receive industry funding are more likely to produce research outcomes which favor their funders.

• A 2017 *systematic review* by the Cochrane Collaboration found that pharmaceutical and medical device industry sponsored studies are more often favorable to the sponsor's product compared with studies with other sources of sponsorship.
Notables for COI

• The trend toward treating clinical research as a business has coincided with a range of problems which are likely the result of business connections.

• Funders seek and court scientists to author papers and lend their person reputations to add credibility to research findings.

• The Physician Payments Sunshine Act of 2010 requires that financial relationships of physicians and teaching hospitals with manufacturers be reported and made publicly available via the Open Payments Program website.
What do you need to disclose?

• Research supported by grants received by the PI on behalf of the institution (federal, non-profit organizations, industry)

• Activities outside of the MGH/Partners Employment
  • Nature of the relationship
    • travel
    • consultant
    • stakeholder
    • owner of patents under investigation
    • employee

• hard to keep track, most individuals may not be adequately disclosing their conflicts (often required for the last 3 years)
Where and when to disclose?

- **Public Health Service (NIH) regulations**
  - Disclosure by investigators
  - Review and assessment by institution

- **Investigator disclosure obligations**
  - Annual process
  - Transaction-based
  - PHS-funded investigators – **must disclose a new significant financial interest within 30 days of acquiring it!**

- Investigator training requirement (PHS-funded researchers)
- At Partners, disclosures done electronically – on Insight
How do the Journal Editors of 52 influential (high impact factor for their specialty) do? - BMJ 2017

- Financial payments from industry of 713 editors at the associate level and above

- Comparison of disclosure by pharmaceutical and medical device manufacturers for general and research related payments in 2014 with disclosure on journal websites

- 361/713 (50.6%) - general payments; 139 (19.5%) - research payments

- COI readily accessible on the journal websites for 17/52 (32.7%) of journals
Declare your COI for Journal submissions

ICMJE Form for Disclosure of Potential Conflicts of Interest

Instructions

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form is designed to be completed electronically and stored electronically. It contains programming that allows appropriate data display. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in six parts.
1. **Identifying information.**

2. **The work under consideration for publication.**

   This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking "No" means that you did the work without receiving any financial support from any third party -- that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check "Yes".

3. **Relevant financial activities outside the submitted work.**

   This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

   Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work's sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

   For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.
4. **Intellectual Property.**

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

5. **Relationships not covered above.**

Use this section to report other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work.

**Definitions.**

- **Entity:** government agency, foundation, commercial sponsor, academic institution, etc.
- **Grant:** A grant from an entity, generally (but not always) paid to your organization
- **Personal Fees:** Monies paid to you for services rendered, generally honoraria, royalties, or fees for consulting, lectures, speakers bureaus, expert testimony, employment, or other affiliations
- **Non-Financial Support:** Examples include drugs/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc.
- **Other:** Anything not covered under the previous three boxes
- **Pending:** The patent has been filed but not issued
- **Issued:** The patent has been issued by the agency
- **Licensed:** The patent has been licensed to an entity, whether earning royalties or not
- **Royalties:** Funds are coming in to you or your institution due to your patent

- until recently, journals did not even have the option of receiving a grant "on behalf of the institution"
Disclosure of COI - NIH Grants

"The public trust in what we do is just essential, and we cannot afford to take any chances with the integrity of the research process."

— Dr. Francis Collins, Director, NIH

- Similar to Journals
- If you receive federal funding for your research, you must report new significant financial interests within 30 days of acquiring them.
- Significant interest: >5k annually
Managing COI from Outside Activities
Environmental hazards and human health: 176 studies of the potential impact of Bisphenol A on human health

<table>
<thead>
<tr>
<th>Funding</th>
<th>Harm</th>
<th>No Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Industry</td>
<td>0</td>
<td>13 (100%)</td>
</tr>
<tr>
<td>Independent</td>
<td>152 (86%)</td>
<td>11 (14%)</td>
</tr>
</tbody>
</table>

Baker et al.
Industry Relationships – Guiding Principles

- Interactions with industry, properly managed, are fundamentally important for successfully fulfilling our academic mission.... Partners policies and practices governing industry interaction should encourage and facilitate interactions where there are clear and strong benefits ....

(Report of the Partners Commission on Interactions with Industry, 2009)
If we like relationships with industry, why are we worried about conflicts of interest?

• Financial interests create the risk of **actual bias** – actually affecting our decisions

• But even the perception of biased decision-making is bad:
  - Undermines the integrity of research and protection of interests and safety of human research subjects
  - Damages the individual’s and institution’s reputation
  - Erodes public trust
  - Undermines our hospitals’ charitable activities

• We want to allow and encourage principled relationships with industry to take place, but do it so that we address the **concerns, avoid bias** and the **perception of bias**, and thereby protect academic integrity and our institutional reputation.

• We are institutions of public trust and protecting that trust is critical.
Partners approach to managing industry relationships for research

- The focus is on recognizing the concern and managing it.
- Generally, management means management – proceed with disclosure and other steps.
  - A few – but important – exceptions involve prohibitions or presumptive prohibitions.
If we like relationships with industry, why are we worried about conflicts of interest?

• And it’s not just bias and academic integrity – there are laws involved here!
  ➢ Federal regulations on PHS-funded research
  ➢ Anti-kickback laws and False Claims Act (jail time!)
  ➢ Common Rule
  ➢ FDA laws
  ➢ State and federal laws governing charitable tax-exempt corporations
  ➢ State and federal public access laws
Outside Activities - Basics

• Partners policies apply to certain types of your outside activities - specifically, any activity that is beyond the scope of your Partners duties and that either:
  • requires the expertise you use in your Partners position, or
  • involves a company that does or could do business with Partners, even a non-medical one (i.e., any vendor or potential vendor)

• Examples:
  • Personal consulting, non-promotional talks or trainings, CME faculty
  • Scientific advisory boards, Board of Directors, expert witness
  • Founder of a start-up company

• You as an individual, not the institution, are the contracting party with the outside entity and you sign the agreement in your personal capacity, not in an institutional capacity

• Outside activities that are covered by the policy must be performed on your own time, without substantial use of Partners resources and without using the institution’s name (except in very limited fashion)
Outside Activities Basics

• Partners supports our staff having Outside Activities, within appropriate parameters – considered to contribute to our ability to best carry out our charitable mission

• Most Outside Activities are allowable - OII helps between 1500 and 2000 investigators per year enter into such agreements

• Some exceptions – promotional activities, speakers bureaus, “Executive Positions” for full-time HMS faculty

• But even allowable activities have implications, especially in terms of future research activities. Important to understand the implications up-front

• Lindsay – consulting, relationships w companies

• Gretchen – impact on reseaech work
Outside Activities - Work with OII

- General outside activity process requirements:
  - There must be a written agreement that is reviewed in advance by OII
    - Some limited exceptions to written agreement and OII review requirements (for example expert witness engagements)
    - OII is reviewing for institutional issues only!!
  - In some cases, review and approval by supervisor and/or review by Partners-level committees required

- Outline of process
  1. Send agreement and completed Consulting Questionnaire to PHSOII@partners.org
  2. OII reviews CQ and agreement, “issue spots” with investigator
  3. OII communicates next steps to investigator about agreement, need for supervisor review/committee review (usually sends “addendum” for agreement)
     - Committee review or relationships with start-ups to which we license technology require more intensive review
Start-up Considerations

- Standard OII review and outside activities policies apply
  - Written agreement; no inappropriate overlap with Partners or use of Partners resources; no executive position or company promotional activity
  - Technically OII review not required until you have something more than stock - but recommend that you come to us early - we can help you understand choices

- Can research on the technology continue to be done at Partners?
  - If Partners takes equity in the company via license or otherwise, the presumption is no clinical research on the technology at Partners

- Can the investigator conduct research on the technology?
  - HMS COI rules can come into play if an investigator acquires cash or equity financial interests in the company from any source: directly from company, indirectly through license agreement, via IP policy

- Public Health Service (“PHS”) Researchers
  - If an investigator’s Partners research is funded by PHS, a financial interest must be must be reported in Insight within 30 days if it is a “new” Significant Financial Interest—and forming a start-up is acquiring a reportable SFI!
Key HMS & Partners Clinical Research Policy

• **HMS 1(a): Clinical Research Rule**
  - **Presumption against**, but not an absolute prohibition against, engaging in such clinical research when you have such a financial interest (above the minimal levels), but exceptions can be granted under limited circumstances.
  - Not a green light – blinking red. Must show compelling circumstances and that COI is manageable.
  - Petition process for exception – OII can help you with this.
HMS 1(b): Sponsored Research Rule

- Formerly, you were prohibited from receiving sponsored research support (clinical or non-clinical) from a company in which you owned equity (above de minimis).
- This rule also recently (November 2015) changed to be a rebuttable presumption.

HMS 1(c): Executive Positions

- Full-time HMS faculty may not hold executive positions in biomedical companies.

HMS 1(d): Membership on Board of Directors

- No clinical research and no sponsored research from company if you are on its Board of Directors even if unpaid.
Other key policies

- **Conflict of Commitment**: 20%/1 day per week.
- Most new outside activities **need to be reviewed** by the Office for Interactions with Industry.
- **Most relationships allowed** – only a few prohibited
  - Some company-paid speaking engagements are OK, some not – “Speakers Bureau” prohibited
  - Ghostwriting prohibited
- Policy **prohibiting gifts** from vendors.
- Other policies that directly pertain to our clinical care and educational activities.
Managing COI with OII

A Principal Investigator (PI) has equity interests in a company (stock options >30k)

Limitations to research: xxxxx

A PI is a consultant to a company (<10k)

– limitations to research in this area
Who manages COI at MGH/BWH/HMS/Partners?

- **The Office of Industry Interactions (OII)** - relationships with industry
  - **Christopher Clark** - Director
  - **Kim Lincoln and Sharon Wilson** - Program Managers for Research
  - **Erin Stewart** - Program Manager for Outside Activities

- **Partners COI Policies:**
  - [https://pulse.partners.org/hub/departments/oii/policies](https://pulse.partners.org/hub/departments/oii/policies)
Pharmaceutical Industry-Sponsored Meals and Physician Prescribing Patterns for Medicare Beneficiaries

Carolina Duong, BA; Thomas Aguilar, MD; Chen Wei Xiang, MD; MPH; Grace A. Lin, MD, MA; W. John Bavry, PhD; R. Adams Dickey, MD, MBA

**IMPORTANCE** The association between industry payments to physicians and prescribing rates of the brand-name medications that are being promoted is controversial. In the United States, industry payment data and Medicare prescribing records recently became publicly available.

**OBJECTIVE** To study the association between physicians’ receipt of industry-sponsored meals, which account for roughly 40% of the total number of industry payments, and rates of prescribing the promoted drug to Medicare beneficiaries.

**DESIGN, SETTING, AND PARTICIPANTS** Cross-sectional analysis of industry payment data from the Federal Open Payments Program for August 1 through December 31, 2013, and prescribing data for individual physicians from Medicare Part D, for all of 2013. Participants were physicians who wrote Medicare prescriptions in any of 4 drug classes: statins, cardioselective β-blockers, angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers (ACE Inhibitors and ARBs), and selective serotonin and serotonin-norepinephrine reuptake inhibitors (SSRIs and SNRIs). We identified physicians who received industry-sponsored meals promoting the most-prescribed brand-name drug in each class (pravastatin, metoprolol, olmesartan, and desvenlafaxine, respectively). Data analysis was performed from August 20, 2015, to December 15, 2015.

**EXPOSURES** Receipt of an industry-sponsored meal promoting the drug of interest.

**MAIN OUTCOMES AND MEASURES** Prescribing rates of promoted drugs compared with alternatives in the same class, after adjustment for physician prescribing volume, demographic characteristics, specialty, and practice setting.

**RESULT** A total of 279,689 physicians received 63,524 payments associated with the 4 target drugs. Ninety-five percent of payments were meals, with a mean value of less than $10. Pravastatin represented 8.8% (SD, 9.9%) of statin prescriptions, olmesartan represented 3.3% (7.4%) of cardioselective β-blocker prescriptions; olmesartan represented 1.6% (9.5%) of ACE inhibitor and ARB prescriptions; and desvenlafaxine represented 0.6% (0.8%) of SSRIs and SNRIs prescriptions. Physicians who received a single meal promoting the drug of interest had higher rates of prescribing pravastatin over other statins (odds ratio [OR], 1.18; 95% CI, 1.17-1.19), metoprolol over other β-blockers (OR, 1.70; 95% CI, 1.68-1.72), olmesartan over other ACE inhibitors and ARBs (OR, 1.52; 95% CI, 1.51-1.53), and desvenlafaxine over other SSRIs and SNRIs (OR, 2.18; 95% CI, 2.13-2.23). Receipt of additional meals and receipt of meals costing more than $20 were associated with higher relative prescribing rates.

**CONCLUSIONS AND RELEVANCE** Receipt of industry-sponsored meals was associated with an increased rate of prescribing the brand-name medication that was being promoted. The findings represent an association, not a cause-and-effect relationship.
Physicians who received a single meal (<$20$ value) promoting the drug of interest had higher rates of prescribing

- rosuvastatin over other statins (odds ratio [OR], 1.18; 95%CI, 1.17-1.18)
- nebivolol over other $\beta$-blockers (OR, 1.70; 95%CI, 1.69-1.72)
- olmesartan over other ACE inhibitors and ARBs (OR, 1.52; 95%CI, 1.51-1.53)
- desvenlafaxine over other SSRIs and SNRIs (OR, 2.18; 95%CI, 2.13-2.23)
COI for Clinicians* - Sunshine act

*No general disclosure requirements
Take home points to remember

• There is no avoidance but there is disclosure and management of COI
• Where there is a “conflict of interest,” that should not be viewed as a “bad” thing – think IOM definition – and most can be managed.
• Most research can be undertaken and carried out fully consistent with your academic responsibilities.
• Our primary interests as academic researchers must remain intact.
• Partners and OII support and encourage relationships with industry, and are there to help.

• **Two specific things to remember:**
  - If you receive federal funding for your research, **you must report new significant financial interests within 30 days** of acquiring them.
  - **Most outside activities need to be reviewed by OII** beforehand.
If we like relationships with industry, why are we worried about conflicts of interest?

- Decisions and judgments relating to our charitable activities should be based on the best interests of, and should be conducted in furtherance of, our charitable patient care, research and educational missions.

- Financial interests created by relationships with industry create the risk that our decisions in carrying out our charitable activities (primary interest) may be biased, or be perceived as being biased, by those financial interests (secondary interest).
  - Research – the design, conduct, and reporting must be objective and based on academic criteria.
  - Clinical Care – decisions must be based on patients’ interests.
  - Education – information presented must be unbiased and based on scientific merit.

- The focus is not on “research misconduct” but subtle bias

- Ultimately this is about the integrity of our charitable institutional activities and our institutions.