



Conflicts of Interest

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What is Conflict of Interest?

A set of conditions in which professional judgment concerning a primary interest *(patient's welfare or the validity of research)* tends to be or appears to be unduly influenced by a secondary interest *(financial gain)*.



What is Conflict of Interest?

Some fact known to a participant that if revealed later, would make a reasonable person feel misled or deceived (or a physician, researcher, teacher or editor feel defensive)



COI: Asymmetry between interests

- Other ethical dilemmas (termination of care, confidentiality, or the use of human subjects in research): **both competing interests** have a presumptive claim to priority, and the problem is in deciding which to choose.
- In conflicts of interest: only one of the interests has a claim to priority, and the problem is to ensure that the other interest does not dominate



Whom does it involve?



Physicians: treating patients




Institution

Researchers: conducting research

Teachers: teaching students




Areas of Concern

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- Self-referral by physicians
 - Physicians' risk sharing in HMOs and hospitals,
 - Gifts from drug companies to physicians: Pharma. industry spends \$12 billion annually on gifts and payments to physicians
 - Hospital purchasing and bonding practices,
 - Industry-sponsored research
 - Research on patients




Institutional COI

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- When an institution has equity in a company, or holds a patent on a compound, process, or therapy and investigators employed by the institution conduct research that could affect the value of the equity interest or the future of the compound



Conflict of Interest

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- The primary interest
 - ✓ health of patients
 - ✓ integrity of research
 - ✓ education of students




Conflict of Interest

- The secondary interest
 - Not necessarily illegitimate in itself, may be a necessary part of professional practice.
 - Its relative weight in professional decisions may pose problems



Conflict of Interest

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- The secondary interest
 - Personal: preference for family and friends; desire to alleviate human pain and suffering
 - Commercial: industry influence, patents
 - Political: Institutional COI
 - Academic: Desire for prestige, power and faculty advancement, interest in obtaining positive results, pressure to publish
 - Financial: Financial gain



How to assess/grade COI?



Severity of a COI depends on

- the likelihood that professional judgment will be influenced, or appear to be influenced, by the secondary interest, and
- the seriousness of the harm or wrong that is likely to result from such influence or its appearance.



Impacts of COI



Patient Care

- Violation of right to informed consent of participant if not told about the financial interest of investigator/institution
- Investigators may ignore AEs which can harm health of patients in the trial
- These results (where AEs are under-reported) can be responsible for licensing – thereby endangering the health of public



Impacts of COI



Biomedical Research

- If Institution has financial interest in a compound and investigator from that hospital conduct clinical trial on it – may compromise trial (biased design/ data-collection or recording, statistical analyses, or reporting and interpretation of the data)
- Distort research priorities
- COI in enrolment in conflicting parallel trials.



Impacts of COI



Biomedical Research

- Compromise in appointment or promotion
- Undermining morale of staff not involved
- Public confidence in institutional research can get eroded

Teaching

- Student asked to conduct research in which institution had financial interest (even if not useful to students career development)




What should be done about COI?

- Prevent secondary interest from dominating primary interest in making professional decisions
- Not to eliminate secondary interests

1. Conflicts can never be eradicated from professional life
 2. Their existence must be accepted
3. Must *not* be equated with professional misconduct




Remedies: by Whom?

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- Relying on the good character of individual physicians to avoid COI or deal with them judiciously when they arise
 - maintains conditions of mutual trust
 - effective in small communities
 - Less adequate in large organizations and impersonal relationships



Remedies: by Whom?

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- Regulation by the profession
 - provides more assurance
 - involves those who know and care personally about professional practice
 - “Ownership” leads to compliance




Remedies: by Whom?

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- American Medical Association 2002
 - American College of Physicians 2002
 - Accreditation Council for Continuing Medical Education 2002
 - Pharmaceutical Research and Manufacturers of America 2002
 - Office of the Inspector General of the Department of Health and Human Services 2003



Remedies: by Whom?

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- Government regulation of COI
 - A response to the failure of physicians to self-regulate
 - Includes more people in the process and reduces the problem of COI on the part of the profession
 - Is uniform (and therefore may not pick up some aspects) and procedurally complex that normally characterize the legal process.



Remedies: How?

- Disclosure of financial interests to
 - colleagues,
 - co-investigators at other institutions,
 - IRB,
 - administrators,
 - professional or state boards,
 - funders that have supported the clinical research,
 - the general public,
 - readers of articles that report research results
 - audiences at oral presentations of the research results.



Disclosure to journals



Journal policy (NEJM)

- disclosure by authors of any association with businesses that could be affected by their work
- reviewers do not have access to this information
- At time of publication decision is made whether to disclose the information to readers
- Editors could have no financial interests in any business relevant to clinical medicine
- Not to publish review articles or editorials by authors with financial holdings in a company (or its competitor) whose product figured prominently in the article.



Perlis et al, Industry Sponsorship and Financial Conflict of Interest in the Reporting of Clinical Trials in Psychiatry. Am J Psych, 2005; 162:1957-1960

- Examined funding source and author financial conflict of interest in all clinical trials published in the *Am J of Psych, Arch of Gen Psych, J Clin Psychopharmac,* and *J Clin Psych* between 2001 and 2003
- 60% reported receiving funding from a pharmaceutical company or other interested party
- 47% included at least one author with a reported financial conflict of interest.
- Of 162 randomized, double-blind, placebo-controlled studies examined, those that reported conflict of interest were 4.9 times more likely to report positive results;
- Association significant only in subset of pharmaceutical industry-funded studies.



Disclosure in CTs



Potential participant in CT:

- must be told about the COI
- stated in the informed-consent form.
- institutional COI also should be disclosed: IRB has important role
- Other safeguards adopted by the institution should also be disclosed to the patient.
- Allows those who would be affected to assess the risks and to make their own decisions.



Remedies: How?



Disclosure: Problems

- Disclosure only reveals a problem, without providing any guidance for resolving it
- Recipient of information may not know how to interpret it and may not have reasonable alternative courses of action



Remedies: How?



Disclosure: Problems

- May increase levels of anxiety: causing suspicion without allowing for constructive ways to restore trust
- Often institutions lack monitoring systems that can act on the basis of a disclosure of a conflict of interest



Remedies: How?



Internal Monitoring

- Internal reviews of patient care and research by an IRB, ad hoc committee or chief of service
- In institutional COI: have to ensure independence of the committee



Remedies: How?



Internal Monitoring by IRB

- Advantages

- independent of institution,
- no direct financial interest in hospital (should declare)
- has members from outside the institution,
- has a mandate to review research protocols,



Remedies: How?



Internal Monitoring by IRB

- Disadvantages
 - Some members are internal and may themselves have a COI
 - Public usually perceives IRBs as internal bodies.
 - IRBs already burdened by a heavy workload
 - Need competence to address COI issues



Remedies: How?



External Monitoring

- Best safeguard against the potential harm due to COI e.g. multi-centric studies are monitored and audited by external agencies
- Committee (with authority to monitor and stop if needed) of people outside the institution to review without COI



Remedies: How?



External Monitoring: Problems

- Commitment of committee members
 - Time-consuming
 - Compensation?
 - Awkward position of criticizing colleagues.
- Investigators
 - External review is time-consuming
 - Adversarial relationship with external reviewers



Remedies: How?

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- Mediation
 - Abstention
 - Divestiture
 - Prohibition



Remedies: Researchers

Association of American Medical Colleges (AAMC)
and the Association of American Universities (AAU)
core principles

- Disallow individuals who hold significant financial interest in research involving human subjects from conducting the research except under compelling circumstances
- Coordinate COI and IRB processes with adherence to a more stringent determination
- Promote disclosure and transparency of financial interests.




Remedies: Organisations

Association of American Universities (AAU)

1. Disclose always,

2. Manage the conflict in most cases (e.g. Segregation of research endeavors from financial and technology transfer, develop guidelines

3. Prohibit the activity when necessary to protect the public interest or the interest of the university.



Van McCrary et al, A National Survey of Policies on Disclosure of Conflicts of Interest in Biomedical Research, NEJM; 2000, 343:1621-1626


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- 127 medical schools
 - 170 research institutions receiving > \$5 m in total grants annually from NIH
 - 48 journals in basic science and clinical medicine
 - 17 federal agencies

Substantial variation among policies on conflicts of interest at medical schools and research institutions.

Many journals (57%) and funding agencies (76%) do not require disclosure of conflicts of interest



*Lo et al, Conflict-of-Interest Policies for Investigators in
Clinical Trials; NEJM 2000; 343:1616-1620*

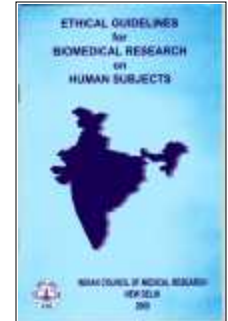
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- Analyzed policies governing COI at 10 medical schools in the US that receive the largest amount of research funding from NIH
 - All required faculty members to disclose financial interests to university officials
 - 6 required disclosure to the IRB, and a committee on conflicts of interest or a university official.
 - 4 had stricter requirements for investigators conducting clinical trials than required by federal regulations.
 - 7 specifically addressed violations of COI policies including censure, suspension of grants and of IRB approval of studies, non-renewal of appointment, and dismissal.

ICMR Guidelines



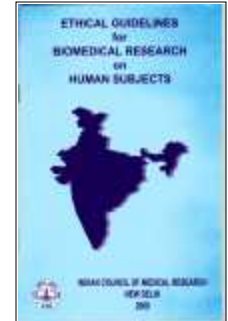
- VII Principles of accountability and transparency ... full disclosure is made by those associated with the research or experiment of each aspect of their interest in the research, and any conflict of interest that may exist
- SPECIFIC PRINCIPLES: 9. In all situations where there is likely to be conflicts of interest it must be ensured that the interest of the individuals involved in the study are protected at all cost.
- GENERAL GUIDELINES: Guidelines developed to handle situations where there is COI between an individual, and that of family and society at large.

ICMR Guidelines



- *DECISION MAKING PROCESS:* A member must voluntarily withdraw from the IEC while making a decision on an application which evokes a conflict of interest, which should be indicated in writing to the chairperson prior to the review and should be recorded so in the minutes

ICMR Guidelines



Institutional Policy in COI:

- Academic institutions conducting research in alliance with industries/ commercial companies require a **strong review** to probe possible conflicts of interest between scientific responsibilities of researchers and business interests.
- In cases where the review board/ committee determines that a **conflict of interest may damage the scientific integrity of a project or cause harm to research participants**, the board should advise accordingly.
- Institutions **need self-regulatory processes to monitor, prevent and resolve such conflicts of interest.**

ICMR Guidelines



- Prospective participants in research should also be informed of the sponsorship of research, so that they can be aware of the potential for conflicts of interest and commercial aspects of the research.



Thank you