Ethical and professional conflicts associated with the conduct of clinical trials

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Disclosures
Conflict of interest defined

- **Conflict of interest**: According to the IOM report, *Conflict of Interest in Medical Research, Education, and Practice*, a “conflict of interest is a set of circumstances that creates a risk that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest.” (p. 46)
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- “… making methodological choices that are biased by interests that are at odds with the established goals of science…”

  *Studies in History and Philosophy of Science* 46(2014):18
Overview

• Why do we care about conflicts of interest in the context of biomedical research?
  – We care mainly for two chief reasons
• How well do existing mechanisms in place for managing conflicts work?
  – We’ll look at some examples that should worry us about their effectiveness
• Can we do a better job at recognizing and managing them?
  – It’s critical that we learn how to
Why do we care about conflicts of interest in the context of biomedical research?

• We care about conflicts of interest because they can impede efforts to:
  – conduct scientifically sound studies capable of shedding light on how to understand and treat disease
  – conduct ethically responsible studies in a way that does not exploit or hurt people
What are the mechanisms in place for managing conflicts and how well do they work?
## Managing Conflicts of Interest

<table>
<thead>
<tr>
<th>Competing Interests</th>
<th>Categorization of Interest</th>
<th>Risk</th>
<th>Risk Management Resources</th>
<th>Strength of Risk Management Resources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good Science</td>
<td>Primary</td>
<td>Inaccurate data or bias that can lead to dangerous, ineffective treatments</td>
<td></td>
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<tr>
<td>Ethical Research</td>
<td>Primary</td>
<td>Exploit or hurt people</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Making Money</td>
<td>Secondary</td>
<td>Not making money</td>
<td></td>
<td></td>
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<tr>
<td>Personal Prestige</td>
<td>Secondary</td>
<td>No reputational benefit</td>
<td></td>
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## Managing Conflicts of Interest

<table>
<thead>
<tr>
<th>Risk</th>
<th>Types of Bias</th>
<th>Risk Management Resources</th>
<th>Strength of Risk Management Resources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bias</td>
<td>Selection Bias, Publication Bias, Biased investigators</td>
<td>Research Design, Peer Review, Disclosure of financial relationships, Other??</td>
<td>Weak, Strong??</td>
</tr>
</tbody>
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## Managing Conflicts of Interest

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</thead>
<tbody>
<tr>
<td>Exploit or hurt people</td>
<td>Investigator sense of responsibility, IRB review, threat of litigation</td>
<td>???</td>
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### Managing Conflicts of Interest

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How well do current mechanisms for managing conflicts work?

Some considerations and examples that should give us pause
One troubling consideration:
The culture of Academic Health Centers

• The best way to identify, avoid, and/or manage conflicts is to promote a safe environment that encourages open communication about problems
  – Academic health centers are characterized by silence about problems and fear of reprisals by those in a position to report them
• Apart from some financial conflicts, we have no centralized focus on identifying and managing conflicts
  – We are our own worst enemy at times because we generate many troubling conflicts ourselves
Troubling examples: The case of bias

• To know whether current mechanisms work for preventing bias we need to know:
  – If some kinds of bias are more injurious to producing studies that can improve health care than others
  – If so, whether our prevention/management strategies are weighted toward those that are most injurious
  – If not, whether our prevention/management strategies are weighted toward those that are most prevalent?
How well do current mechanisms work for preventing bias?

- Bias is bias and the bias introduced by poor study design, publication bias, and the like are more prevalent than that introduced by financial relationships yet our prevention/management methods for preventing or reducing such bias are largely ineffective.

- We continue to rely upon them while we ramp up efforts to shine more light on financial relationships.
Bias in the published scientific record: Animal studies and excess significance bias

- A comprehensive review of 160 meta-analyses of animal studies related to six different neurological disorders, most of which showed a statistically significant benefit of an intervention, concluded that only 8 of the 160 favorable findings could be supported.
  - The study assessed 4,445 animal studies for 160 candidate treatments of neurological disorders,
  - 1,719 of them had a “positive” result, whereas only 919 studies would a priori be expected to have such a result.
  - Authors concluded that only 8 of the 160 evaluated treatments should have been subsequently tested in humans.

Some more troubling examples, close to home

UC Davis marketing efforts
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<td>Respectful treatment of patients and research participants</td>
<td>Primary</td>
<td>Deceit, Lack of informed consent</td>
<td>Ability of people to recognize conflict, IRB ??, Research Ethics Consultation Service</td>
<td>????.</td>
</tr>
<tr>
<td>Making enough money</td>
<td>Primary or Secondary?</td>
<td>Loss of NCI CCC designation, financial loss</td>
<td>Employment of people tasked with this</td>
<td>????.</td>
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The table above outlines different components related to conflicts of interest, their categorization, associated risks, risk management resources, and the strength of these resources. The categorization includes primary or secondary interests, and the risks range from deceit and lack of informed consent to loss of designation and financial loss. The resources and strength vary, indicating the complexity and importance of managing such conflicts effectively.
Can we manage conflicts of interest better?

• Do “one size fits all” institutional or federal sponsor coi policies help or hinder management of coi that impinge on primary interests in rare diseases research?
  – Who is best responsible for fulfilling/guarding primary interests in rare disease research and how capable/committed are they to doing so?
  – How well do current coi policies and practices guard these primary interests?

• Do onerous levels of compliance with current (inadequate) policies and practices provide a false sense of security that conflicts of interest are being avoided/appropriately managed?
  – Institutional focus of coi processes are designed to assure regulatory compliance rather than prevent secondary interests from trumping primary interests
  – If this is true, what can be done about it to better ensure sound and ethical research?
Questions??