
Physicians and the Pharmaceutical Industry: Interests and Conflicting Interests

Dr Anne Holbrook, MD, PharmD, MSc, FRCPC
Director, Division of Clinical Pharmacology & Toxicology
McMaster University
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Learning Objectives

- What is Conflict of Interest?
- What do the regulators have to say about COI and you?
- Why does COI matter?
- How can you avoid COI (or not)?

Disclosures

- ▶ Clinical Pharmacologist/Internal Medicine specialist
- ▶ Drug policy advisor
 - Federal, provincial, regional expert advisory committees for decades
- ▶ CIHR Investigator
 - ▶ Research funding all from public sources
 - ▶ 13 current peer-reviewed grants

Which Scenarios Represent COI?

1. You are a Rheumatologist

A young, attractive sales representative of Bigco pharmaceutical company asks your office receptionist if she can bring lunch for the whole office, in order to spend 30 minutes discussing a great new oral biologic agent for your RA patients.

2. You are a Clinician Researcher

Your fabulous research project on Device X failed to win a CIHR grant and will die without funding. The manufacturer is willing to pay more than your CIHR budget for a study, but requests some major revisions to the protocol. The extra funds can be used for your research.

3. You are a Drug Policy Advisor

In a government-funded clinical guideline which you helped author, your expert team concluded that all drugs within a family are equally effective and safe. On behalf of one of the involved companies, a threatening lawyer's letter arrives, accusing you of breaking the law. COI is implied.

- a. Scenario 1 and 2
- b. Scenario 1 and 3
- c. Scenarios 2 and 3
- d. All of the above
- e. None of the above

What is Conflict of Interest?



'A conflict of interest is created any time a reasonable person could perceive that a physician's personal interest or relationship with industry is at odds with the physician's professional responsibilities. It is important to note that a conflict of interest can exist even if the physician is confident that his or her professional judgment is not actually being influenced by the conflicting interest or relationship.'

- Premise that perception is as influential as reality
- COI usually subdivided into financial and intellectual

Background

- Interactions between physicians and the pharmaceutical industry are frequent
 - Sales rep visits, CME, research, advisory boards, presentations, social events
- 83% of physicians have some type of interaction with the pharmaceutical industry
- Estimated \$4.5 billion spent annually on drug promotion in Canada
 - Vs \$1.5 billion on R&D

Background (2)

- The interests of the pharmaceutical industry are transparent
 - Drugs are made by industry
 - Industry wants to maximize profits
- The ‘interests’ of physicians are a problem, due to multiple roles and unique expertise
 - Diagnosticians, prescribers, counsellors, researchers, teachers, policy advisors, administrators, business owners, entrepreneurs
 - ‘where there is no conflict, there is no interest’

COI Guidelines

■ Rationale

- “...when physicians are seen or perceived to be in conflict of interest there is an inevitable erosion of public trust which is fundamental to our patients and society.”

■ Regulatory and advisory bodies

- Canadian Medical Association, Royal College of Physicians & Surgeons, College of Family Physicians of Canada, Common Drug Review, College of Physicians and Surgeons of Ontario, Canada’s Research-based Pharmaceutical Companies

■ Universities and Medical Schools

- McMaster has COI guidelines

CPSO: Guidance on Physicians & Industry

- Avoid COI
 - Avoid interactions with industry
 - Take no gifts
 - Patient teaching aids ok but should not be product-specific
 - 'Modest' meals are ok, information should be critically appraised
 - Drug samples have handling rules
 - CME content should be based on learning needs

CPSO: Guidance on Physicians & Industry (cont'd)

- Disclosure of COI – any educational activity or research
- Consultations or advisory boards
 - Written agreement, providing unique advice
- Research
 - Follow norms of TCPS-2 and REBs
 - Finders fees only allowed if additional work
 - ‘gag’ rules unethical, as is ghostwriting

Application of COI Guidelines

- Financial (receipt of funds)
 - Primary financial conflicts of interest include grant funding, consultancies, advisory board membership and the like from industry
 - Requires disclosure, often precludes involvement
- Intellectual conflict of interest
 - authorship on articles or commentaries, representing a special interest group
 - Infrequently requested or acted on

COI Influence on Outcomes

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"Try this—I just bought a hundred shares."

- SRs on physician-pharma interactions and Clinical activities
 - Begins in medical school, continues on average of 4 interactions per month
 - Overall, associated with higher prescribing frequency and costs, and lower prescribing quality
 - One sponsored meal is enough to change prescribing
 - Typically physicians are convinced they are not influenced by these interactions, but that their colleagues are...
 - 61% IM residents believe they were not influenced vs 16% believed their colleagues were not

COI Influence on Research

- SR of 546 trials in 5 drug groups in clinicaltrials.gov
 - 63% primarily funded by industry, 23% nonprofit, 14% government
 - 307/427 (71.9%) of Phase 3-4 trials funded by industry
 - Industry trials more likely to report positive outcomes
 - 85.4% vs 50% government-funded, $P < 0.001$
 - Less likely to be published within 2 years - 32.4% vs 56.2%, $p = 0.005$
 - Selective reporting of results; downplaying harms
 - 5/5 studies on pharma influence on protocols suggest influence to favour Pharma - e.g., more use of placebo
- New Cochrane SR on drug/device studies suggest more favourable conclusions not explained by risk of bias

COI Influences Guideline Outcomes

- SR on guideline author COI and guideline recommendations
 - 56-81% authors had some financial COI
 - No empiric data on influence of COI on recommendations
 - Case studies suggest authors benefit from related recommendations
 - No info on intellectual COI

COI Influences Patient Advocacy

- Investigation of tax returns of 104 US large patient advocacy groups
 - 83% received support from industry
 - 39% (230 of those disclosing amounts, received > \$1million/yr
 - At least 36% had industry executive on the board
 - 27/104 reported a policy on COI, only 12 with policy on institutional COI
- Dozens of public advocacy submissions on new drugs in Canada reviewed
 - Not one is against reimbursement by public plans

Where Does Academia Stand?

- Approx 70% clinical trial funding is from Pharma or biotech industry
 - Decreasing % held in academic HSC's
 - Financial ties between industry, institutions and researchers are common
 - How much influence does this have on results reported?
 - Increase in institutional COI
 - Not much evidence of self-policing on their own COI
 - Many journal editors have COI
- How to regulate without destroying research and development, technology transfer?

When Interests Collide

- Nancy Olivieri vs Apotex (and some of Hospital for Sick Children and U Toronto)
 - Against confidentiality agreement, spoke out against deferipone
 - Hospital and university expecting large donations from Apotex
 - Controversy led to new investigator protection guidelines
- David Healy vs U Toronto
 - Criticized industry over antidepressants and suicide
 - CAMH cancels his job offer, eventually arranged a settlement
- Main teaching resource on treatment of pain underwritten by Purdue Pharma
 - Minimizing harm of opioids (OxyContin)
 - Purdue eventually fined \$0.6 billion in USA
 - Ontario is world's largest users of opioids

Are the Missions Compatible?

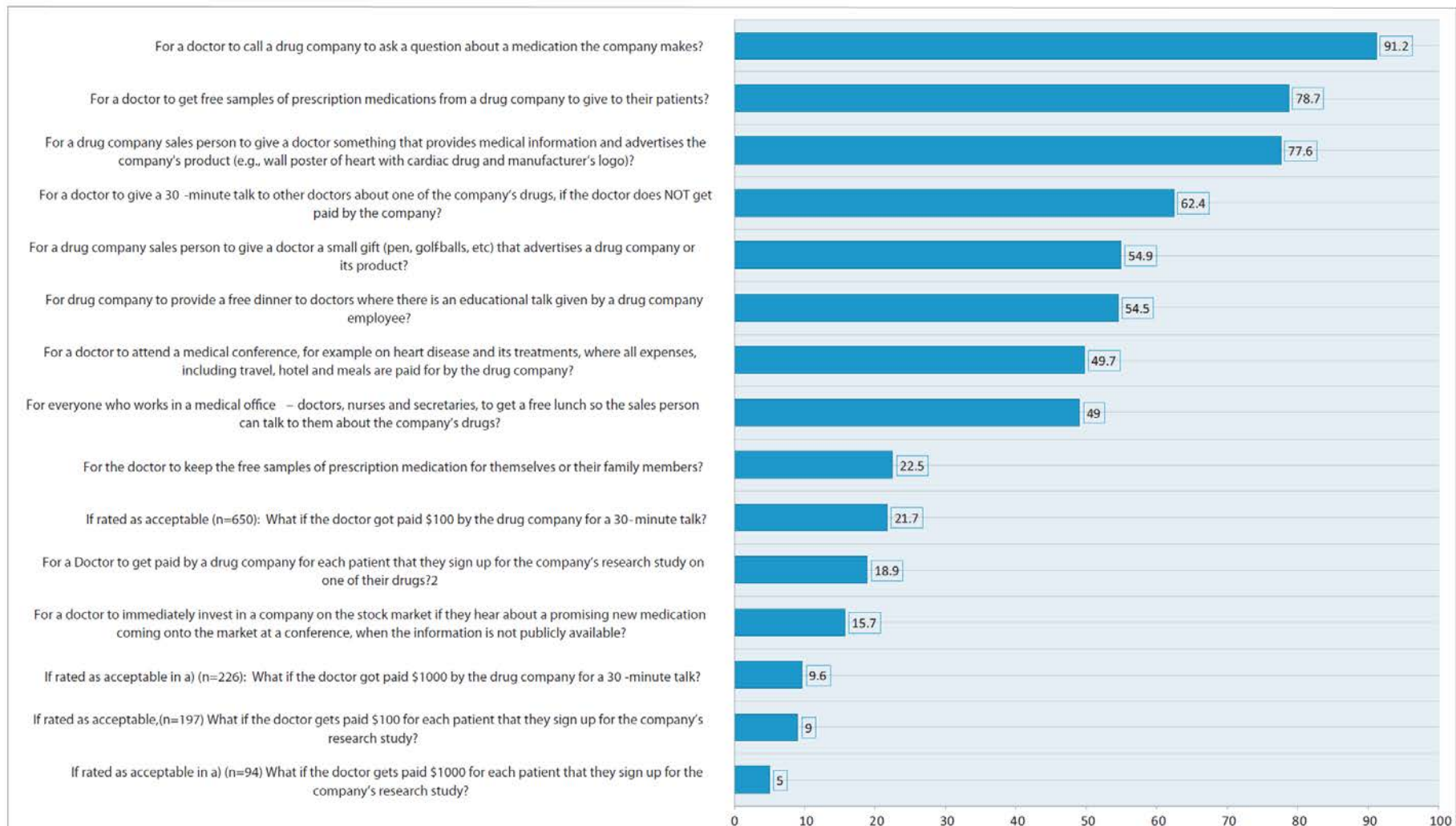
ACADEMIA	PHARMACEUTICAL INDUSTRY
Conduct basic and clinical research to understand human function, diseases and treatments for patients	Develop new products to generate profit
Train students/fellows to be independent investigators who can successfully compete for peer-reviewed funding	Attract trainees to work on company's product(s)
Promote EBM; independent critical judgment by physicians	Develop marketing strategies to increase sales
Provide cost-effective care for patients; generate revenue consistent with the academic mission	Increase profits through increased sales
Improve local health, public health, global health	Work on local/public/global health if it can lead to a profit or a charitable donation which will increase profile.

Public Opinions on Physician-Pharma Interactions



- Survey (n=2059) in USA associated lower trust with belief that physicians accept gifts from Pharma
- Some evidence that 'sunshine rules' also associated with lower trust
- Canadian public opinion phone survey
 - 1041 participants
 - 56.8% female, mean age 52.6 yr, 57.7% post-secondary education. 18.2% francophone

Physician-Pharma Interaction Acceptability (N=1041 Canadians)



Recent Developments

- Recent RCT – physicians more likely to support prescribing based on high quality study
 - If study funded by pharmaceutical industry, lower likelihood of prescribing - odds ratio, 0.52; 95% CI, 0.37 to 0.71; P<0.001).
- USA AHSCs which restricted sales rep detailing vs those that did not
 - > 16 million prescriptions, modest shift to non-detailed drugs
- Sunshine Lists
 - Payments from industry to physicians in USA made public
 - Coming in Ontario by late 2020
- COI guidelines for others in health care
- Pharma in USA attempting to weaken evidence requirements for drugs

Back to Scenarios

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Summary

- COI guidelines gradually getting stricter
 - Some evidence correlating COI with patient outcomes
- Canadian public opinions not in complete agreement with physician guidelines
 - Lack of education on consequences of interactions, or considering medicine like any business?
- COI is a surrogate outcome; Bias is the real concern
 - Combat with Critical Appraisal skills of prescribers and Smart drug policy