Conflict of Interest in Human Research Ethics

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"In the particular context of research ethics, conflict-of-interest policies are thus designed to: (a) promote the unbiased assessment of the risks and benefits of proposed research; (b) minimize self-serving conduct harmful to the subject; (c) promote truth telling; (d) preserve public trust and confidence in scientific and clinical research; and (e) deter misconduct."

Introduction

Conflict of interest has become an increasingly ubiquitous concept in the research ethics community. Funders of health and social sciences research in Canada and the US have recently issued new policies on conflict of interest. Creative research collaborations between universities, governments and the private sector have compelled some universities to revise standing policies on conflict of interest. In the literature, analysts have advanced important reflections about applying the concept beyond professional to institutional conduct. In research ethics practice, ethics review committees have expressed a need for guidance on conflict of interest and proposals to pay fees to university or ad hoc commercial committees for ethics review have raised concerns in Canada. Even legal actors have recently pronounced on conflict of interest in novel areas of research.

As a step toward understanding the context and meaning of these developments, this article explores some of the basics of the definition, evolution and resolution of conflicts of interest. It begins with a discussion of definitions and underlying elements of the concept. It next sketches the evolution of basic conflict of interest concerns in the research ethics community and notes associated legal cases and harms. It then identifies common approaches to the resolution or management of conflicts of interest. Though some of the principles discussed apply to other research ethics domains, the analysis focuses on health and medical research issues. It is intended to be read in conjunction with a companion document in this journal that collects various excerpts on conflicts of interest.

Definition & Elements

What is a conflict of interest (COI)?

The short response is provided by reference to a typical dictionary definition: "a conflict between the private interests and the official responsibilities of a person in a position of trust." The definition captures the classic collision between self-interest and public duties that are intended to protect the common good. Some definitions further distinguish COI from professional conflicts of obligations. Others define some financial liaisons as COI when they exceed a threshold burden of money, such as $10,000. Still other definitions employ an effects approach. They define COI to include personal, intellectual or professional interests that have ill effects on professional duties. These varying approaches demonstrate that the clarity, scope and function of COI definitions matter, if they are meaningfully to guide research ethics thought and conduct.

What, for example, should be required when a stellar researcher who has no financial interest in an objectively meritorious research protocol submits a proposal for review to a research ethics committee of which she is a member? Intuition may tell us that the researcher should not be involved in the review of her project. If the applicable definition of COI were limited to "financial interests," however, then the scenario would seem to pose no COI issues. If the definition of COI were broadened to "private interests," then it, too, would not indicate COI issues. Only if the definition were broadened to reach the researcher's conflicting "professional interests" or involvement in the committee would it indicate a COI issue. Indeed, under research ethics guidelines from Health Canada, the World Health Organization (WHO) and laws and policies from other countries, COI issues would arise in the scenario because the independence of the committee might be compromised. Finally, even if the researcher were uninvolved in the review, would the committee be considered "independent" if its composition is restricted to fellow researchers? The issues raised in the scenario suggest that the answer to the question of what a conflict of interest is merits a longer response that explores deeper dimensions and the underlying rationale of COI. For it is a term of art that consists of several elements.

Relational Analysis: First, and most basically, conflict of interest concerns relational analysis. COI tends to arise when interests in one part of life intersect and risk compromising the responsibilities borne in another part of life. The tension arises from the multiple roles, relations and responsibilities that professionals assume. Though such multiple roles and responsibilities evidence robust living, they may still raise ethical and legal questions when tensions between them materialize into a conflict that risks impinging on professional duties.

Impartiality: A second common element implicit in COI definitions is

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the duty of impartiality. The duty typically arises from a professional responsibility to exercise independent professional judgment. Adherence to the duty is thought to promote rational, unbiased, disinterested decision-making. It has long been an explicit and distinguishing element of the services provided by self-regulating professions, in contrast to the unabashed self-interest classically associated with mercantilism. Impartiality is also thought to be one of the hallmarks and creeds of learned disciplines like science: "The demand for disinterestedness has a firm basis in the public and testable character of science and this circumstance, it may be supposed, has contributed to the integrity of men of science." To exercise unbiased professional judgment effectively means having to recognize and respond to threats to impartiality in a diversity of contexts.

Loyalty: A third, and often determinative, element of COI obligations is the duty of loyalty. It is not simply that many professional responsibilities include an obligation to provide impartial professional judgment in the abstract; rather, one's professional judgment is to be exercised in the context of human relations and human needs. As suggested by the phrase "divided loyalties," conflicts of interest generally do not arise in the absence of some underlying duty of loyalty. Thus, an actual conflict of interest tends to occasion "perplexities of conscience" by posing the question of loyalty to whom. Basic answers about how to resolve such perplexities and conflicts may well come from the source that imposes the duty of loyalty — that is, from the professional canons, codes of ethics, guidelines, law, policy, reasonable expectations of the parties, which will often oblige one to exercise professional judgment on behalf of an individual or undertaking. For example, codes of ethics or conduct for Canadian psychologists, physicians and engineers indicate that (a) the professional is engaged by the public to exercise specialized knowledge, skills and advice to advance the best interests of the client or patient, and (b) that conflicts of interest should be resolved consistent with the higher duty of loyalty — that is, often in favor of the client/patient. Such specified duties of loyalty are intended to serve both individual needs and the public good.

Honesty & Good Faith: Fourthly, a corollary of the duties of loyalty and impartiality is the duty of honesty and good faith. Duties of honesty and good faith appeal to professional virtue. They discourage untruthful or deceptive behavior. The duties imply a general obligation to be forthright and forthcoming about factors that may impair one's duty to exercise independent professional judgment on behalf of an individual or undertaking. Accordingly, they raise communication and disclosure issues.

Trust & Confidence: Final elements of COI obligations are the duties of trust and confidence. Often formulated in codes of ethics, practice or conduct, these duties convey respect for special professional relations. They also encourage individuals to confide personal information and entrust their welfare to professionals who possess special expertise and experience. Similarly, at the macro level, the legitimacy and viability of science and human research reside on the confidence and trust of the public. Canadian society has thus, through formal Acts of Parliament, delegated and entrusted to government research councils general authority for the oversight and funding of research. These powers, monies and responsibilities are held in public trust — that is, strictly for the benefit of the public, who have a vital interest in the ethics of human research. Predictably, if scandals over research ethics begin to seed public distrust, then formal scrutiny and corrective measures may prove necessary to restore public confidence and participation.

COI in Research Ethics: Evolution, Cases & Harms

The companion document to this article, Divided Loyalties: An Anthology of Conflict of Interest Duties, indicates that COI has become a term of art that broadly affects the research ethics community. This is a relatively recent and evolving phenomenon. For as will be shown, the term COI first appeared in North American policies on human research in the last decades, whereas it has been part of the canons of ethics of some professions since before World War I. While general dictionaries, encyclopedias of bioethics and legal dictionaries offer definitions of the term, leading medical and population-based research dictionaries have only begun to do so. Thus, the 1988 edition of the Dictionary of Epidemiology did not include the term; the 1995 edition does.

Yet, if explicit use of the term "conflict of interest" is a recent phenomenon in research ethics, concerns associated with the concept are comparatively ancient. For example, the Hippocratic Oath from the 4th or 5th century BC continues to enjoin western physicians to act for the benefit of their patients. How are physicians to discharge this implicit duty of loyalty if they undertake experimentation with current patients largely to advance medical knowledge for the benefit of future patients? This tension between the healer and experimenter roles materialized in law centuries later in the 1767 case of Slater v. Baker, one of the first medical malpractice cases in Britain. There, the court upheld damages against a physician who had treated a patient with a novel and injurious technique, declaring that "many men very skilful in their professions have frequently acted out of the common way for the sake of trying experiments." The case indicates the early role the law began to play in regulating COI. The remarks of the court express concern about the perils
and divides that inhere in the “dual capacity” roles of some professions.

Beyond the early reference to dual-capacity concerns, COI in research ethics has since progressed through at least two more recent phases. One critical phase began with the influence of COI concerns in structuring modern research ethics. Since the early declarations by the US government and the World Medical Association (WMA) some 25 years ago, for instance, it has become a national and international norm in research guidelines, human rights policies and law to require prospective review of the ethics of proposed research by an “independent” committee. This attests to the growing importance of applying COI concepts to institutions. In theory, then, research ethics committees are to be composed of disinterested individuals who exercise independent professional judgment as an element of COI duties discussed above. In practice, the calls for more lay members and interdisciplinary diversity on research ethics committees have arisen from a realization that ethics review strictly by one’s professional or institutional peers can yield bias, by excluding other relevant and legitimate expertise, voices and values, to the detriment of the public good. Another phase in the evolution has emerged largely within the last decade, with explicit use of the term “conflict of interest” in a proliferation of pronouncements by diverse members of the research ethics community. Hence, research funding guidelines, policies and laws increasingly articulate explicit COI definitions, standards and procedures for researchers, universities, publishers, professionals and research ethics committees.

If the proliferation of COI pronouncements reflects heightened sensitivity to the issues, such sensitivity may stem from a broader appreciation of the harms associated with COIs. Harms may occur at two levels. Firstly, and irrespective of consequences, an intrinsic wrong may lie in the simple breach of a duty, especially in professional relations clothed with a covenant of trust, honesty and loyalty. The law formally regards such relations as “fiduciary” and imposes professional obligations to act with honesty, loyalty and utmost good faith. Thus, under the Criminal Code of Canada, the breach of trust by a public servant may constitute an offense, whether or not the public servant benefits from the breach. Secondly, from a consequentialist view, a range of avoidable harms may flow from research conduct driven by divided loyalties. When divided loyalties are not identified and actively managed, they may lead to a lack of candour in professional relations, bias, nonconsensual research, bodily harm or psychological injury, financial misconduct, and a range of community harms, such as a loss of public confidence, trust or participation in the research enterprise. Of course, concurrent breaches of loyalty, trust and honesty do little to diminish the risk of fraud. A few cases illustrate the point.

**Dual-Capacity Harms:** The harms that may flow from dual-capacity roles percolate through the annals of human experimentation law. Perhaps due to the kind of risks and the established duty of loyalty in the medical profession, dual-capacity concerns have proved central in a number of cases involving the physician-researcher since the 1767 *Slater case*. For example, in *Halushka v. University of Saskatchewan*, a court upheld a damage award for a research participant who had survived a cardiac arrest that partially resulted from a physician/researcher’s nondisclosures about research. *Halushka* remains the leading Canadian case on informed consent to medical research on the 30th anniversary of the judgment, because the court made clear that, in general, research participants are entitled to “full and frank disclosure of the facts, probabilities and opinions that a reasonable man might be expected to consider before giving his consent”; the disclosure duties arise, in part, from the special obligation of loyalty, honesty and trust in fiduciary relations. More recently, in *Green v. Matheson*, a former New Zealand patient alleges to have been subjected to non-consensual cervical cancer research and denied standard treatment due to a physician’s/researcher breach of the duty of patient loyalty. Such allegations prompted a public inquiry which (a) substantiated many of the allegations, (b) found that applicable ethics committee procedures lacked impartiality and (c) deemed the research unethical. Finally, in the landmark ruling of *Moore v. University of California*, the California Supreme Court recently held that conflicts of interest in biotechnological research may ground liability for a breach of fiduciary duties. Though the case was eventually settled, a cancer patient had alleged that his physician had, without his knowledge or consent, converted tissues from the patient’s excised spleen into a multi-million dollar drug in which the physician-researcher had an undisclosed financial interest. The case suggests that when experimentation cases involving dual-capacity professionals come before the courts, they tend to resolve the conflict in favour of applicable ethical duties of loyalty. More generally, *Moore, Green, Halushka* and *Slater* offer a broader lesson: that professional adherence to the duties of loyalty, honesty and trust helps avoid the dignitary, mental, physical and financial harms too often suffered by research participants.

**Familial & Community Harms:** In a recent judgment upholding a professional misconduct sanction against a physician who had conducted non-consensual experimentation on a dead patient, the highest court of France found that the physician-researcher had violated the ethical principle of respect for the human person. Beyond distressing the patient’s family, the case
prompted commentary from the President of France, a written opinion from the National Bioethics Committee\(^6\) and a new legal text to govern research on persons who are brain-dead.\(^9\) Inspired by the principle of respect for the person, the reforms signify an attempt to redress and prevent harms at the individual, familial and community levels.

**Financial & Integrity Harms:** The US government recently found that a non-physician member of a Canadian research team had engaged in scientific misconduct through the falsification of data entries in an international clinical trial.\(^30\) The finding of falsification is alleged to have been associated with pressures to maximize the recruitment of patients into the study through “finder fees”\(^31\) – that is, paying recruiters for persons recruited. Such *per capita* payments provide clear financial incentives to maximize enrollment. But they may also induce the recruitment of those who do not precisely match the medical profile needed. The incentive pits loyalty to the patient against personal financial gain. Any resulting wrongful enrollment may skew the scientific validity and compromise the integrity of research; it heightens the risk that enrolled patients will suffer harm. For such reasons, finders’ fees have prompted recommendations that either they be subject to strict scrutiny by research ethics committees\(^20\) or that they, in effect, be prohibited.\(^53\)

**Managing COI**

COI guidelines share a common intent to avoid the foregoing risks and ills. They do so by establishing standards and procedures for identifying, preventing and managing COIs. COI duties thus serve to arbitrate value disputes and define norms of ethical conduct.

**Identification:** Practically, the management of COI begins by imposing on research professionals a duty to identify a potential, apparent or actual conflict of interest. Such identification will depend either on the specific definition outlined in applicable guidelines, codes, policies, etc., or on the generally recognized definition and elements of COI described above. In either instance, the definition should express the underlying elements of loyalty, honesty, and good faith to an individual or enterprise. Once a COI has been identified, it may be addressed through such resolution or management measures as prohibitions, disclosure, withdrawal or monitoring.

**Prevention & Prohibitions:** Policies or codes that seek to prevent COIs may outline both prohibited and regulated conduct. Such prohibitions impose a duty to avoid certain financial liaisons, personal involvements or professional collaborations, on the rationale that in cases of real conflict an individual cannot serve the best interests of two masters. Again, this bespeaks higher duties of loyalty. Prohibitions thus serve to prioritize one’s professional obligations. To be an effective deterrent, prohibitions will typically outline incentives or sanctions for enforcement, such as reprimand, conditional continuation of the professional activity and suspension or loss of particular privileges.

**Disclosure & Consent:** Disclosure requirements give practical effect to the duty of candour. The rationale for imposing a duty to disclose potential or actual COIs is plain. Firstly, disclosure duties, by obliging professionals to be transparent about the limits of their loyalty, are responsive to an ethic of truth-telling. They convey respect, honesty and good faith in one’s relations to an individual, entity or undertaking. Secondly, the duty to speak enables the person in the potential conflict and those likely to be affected by it to explore in detail the contours, significance and implications of the collision of interests. Thirdly, honest and full disclosure enables those whose interests might be adversely affected to make informed and self-protective choices that advance their best interests.\(^94\) Disclosure duties are thus designed to work in tandem with established consent standards in research ethics. In doing so, they advance autonomy and informed decision-making values.

**Administrative Mechanisms & Structures:** A variety of mechanisms may be employed for monitoring and administering COI. If a professional declares a potential conflict and parties potentially affected by it agree to his or her continued involvement, the provision of intermittent reports or submission to external audits and monitoring are common mechanisms for managing the potential conflict. Logically, the precise administrative mechanism should depend on the nature, scope and risks posed by the conflict. At the institutional level, for example, administrative structures will sometimes be instituted to isolate particular services and decision-making from information, relations or incentives that risk compromising the independent judgment or integrity of the service. Hence, requiring institutional research ethics committees to include sufficient diversity and numbers of non-institutional lay members helps to ensure the impartiality of a committee that might otherwise become captive of vested institutional, professional or financial interests. Similarity, so-called blind trusts financed partially by pharmaceutical companies have been proposed in Britain as one means of financing independent regional ethics review committees.

**Withdrawal:** As a duty to avoid COI will preempt participation in some activities, withdrawal duties will curtail some personal and professional undertakings. Withdrawal may sometimes be advised or required. For example, withdrawal becomes appropriate when, by objective standards, it is clear that disclosure and consent will not cure
the breach of loyalty, will not ensure disinterested behaviour, or will not preserve the integrity of the undertaking. In this respect, judges, peer reviewers and research ethics board (REB) members share similar ethical duties. Those who have COI in a case, article or protocol typically have a duty to recuse themselves, or may be forced to withdraw from consideration of the merits, so as to preserve the independence and integrity of the review process.

Miscellaneous Remedies: What might generally be called remedies refers to a class of miscellaneous initiatives — beyond disclosure, monitoring and withdrawal — undertaken to minimize risks or rectify harms associated with conflicts of interest. In essence, they are corrective measures specifically designed to cure or minimize harms associated with a COI. Such remedies may be imposed before or after the COI materializes. Thus, preventive financial divestiture or transfers may be required as a condition of appointment to research posts in academia or policy positions in government. By contrast, if an undisclosed conflict of interest is discovered after the fact, an editor may require the restriction of an article contaminated by significant bias, a funder of research may compel disgorgement of research monies, a university might require re-review of a protocol tainted by COI in a REB. Basic notions of justice counsel that remedial initiatives should be commensurate with the harms and instituted through fair and reasonable proceedings.

Conclusion

The foregoing discussion suggests a number of points that are relevant to developments in the Canadian research ethics community. Firstly, over the last decades, conflict of interest has evolved from a comparatively amorphous concept of relational analysis into a tool for identifying and managing interest conflicts in research ethics. Secondly, the concept consists of several elements, including implied duties of loyalty, candour, impartiality, trust and good faith in the exercise of particular professional relations. Thirdly, because these duties are often articulated in codes, guidelines, policies or laws, they impose norms and standards of ethical conduct about to whom or what one owes special and paramount obligations. Fourthly, the inference is that clear duties bespeak clear roles, particularly when conflicts arise. In contrast, silence or ambiguity on these matters heightens the likelihood of role confusion, of inconsistent identification and resolution of COIs, and of associated harms.

These points prompt important questions. In the continuing evolution of the concept of conflict of interest, for instance, how should the professional model of COI precisely apply to institutional COP? On the other hand, the relational analysis may seem similar: that is, the duties of loyalty, impartiality, candour and good faith should help to identify conflicts, their depths, and help to define or refine duties in varying institutional contexts. Such identification sets the stage for employing the disclosure, prevention, monitoring, structural or administrative and procedural mechanisms, to manage and resolve COIs.

On the other hand, questions of institutional COI may seem significantly different when we ask whether those with responsibilities for promoting research should also have responsibilities for ensuring the ethics of research. If such a dual capacity structures an inherent institutional conflict of interest, then how may it be prevented, resolved or managed? That such questions are regularly before universities, funders and research ethics committees underscores the urgent need for further understanding and discussion of how best to define, identify and manage institutional COI.

In this spirit a final ‘institutional’ question lingers: should Canadian REBs be clothed with special or fiduciary duties of loyalty, candour, impartiality, in the discharge of their functions? If so, to whom or what should such duties be owed? Some might point to the literature and international norms to argue that REBs already have such special duties and that they are owed to research participants and the public. The argument may seem paradoxical: to discharge special duties that arise from the public covenant between government, scientists, research institutions and the citizenry, it is argued that in the best interest of society REBs must provide a community voice, structural conscience and impartial forum for arbitrating the value conflicts inherent in research ethics review. Though such arguments are persuasive, questions on the role and duties of REBs still reverberate in Canada, in part from funding shifts that are restructuring the research ethics community, in part from silence or ambiguities in current federal guidelines on conflict-of-interest matters for REBs, and in part from the ongoing unprecedented federal initiative to establish common ethical guidelines for biomedical, health and social science research involving human participants. If REBs are asked to function in conflicting capacities or if they are given duties that divide their loyalties, then they are less likely to prove effective and less likely to garner the long-term public trust. Clarity and precision on the basic purpose, duties and roles of REBs will best enable them to discharge their unique societal tasks. To define precise, paramount duties sometimes necessitates difficult value choices and rankings. But better to cultivate clear norms and resolve the choices in guidelines, policies, codes, conduct, than to cloud them in ambivalence that sometimes showers upon the research enterprise and research participant the avoidable harms sparked by divided loyalties.
References

Note: The Anthology referred to in some of the notes appears in this issue of Communiqué, pp. 11-16. For further reading, see NCBHR Selected Bibliography: Bioethics Research with Human Subjects in the Health Sciences (1985-1993). NCBHR Communiqué CNBHR 1995; 6(2) suppl: 10.


4. Harvard University, Faculty of Medicine. Faculty Policy on Integrity in Science, 1994.


6. NCBHR, op cit. p. 16.


10. US NIH op cit.


12. See Anthology, op cit., sec. IV.


17. See, e.g., Code of Ethics of the Professional Engineers of Ontario, sec. 77, Ont. Reg. 941.


20. Anthology, op cit., sec. IV.


22. Anthology, op cit., sec. I.


29. NCBHR op cit. pp. 5-6.


35. Anthropology, op cit.


38. Halushka, op cit.

39. ibid, 444-445.


44. Moore v. University of California, 753 P. 2d. 479 (Cal 1990), cert. denied 111 S. Ct. 1388; excepted in Anthology, op cit., sec. III.


50. Federal Register 1995; 6047448.


54. Halushka, op cit.
