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ORIGINAL RESEARCH

Disclosure is Inadequate as a Solution to Managing Conflicts of Interest in Human Research

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Abstract Disclosure is a common response to conflicts of interest; it is intended to expose the conflict to scrutiny and enable it to be appropriately managed. For disclosure to be effective the receiver of the disclosure needs to be able to use the information to assess how the conflict may impact on their interests and then implement a suitable response. The act of disclosure also creates an expectation of self-regulation, as the person with the conflicting interests will be mindful of their own potential biases and aware that their decisions may be monitored. This article discusses some of the problems of relying on disclosure as a solution to address conflicts of interest in research, including the added complexities around institutional conflicts of interest. The case of Dan Markingson illustrates these issues and highlights the vulnerable position relying on disclosure as a solution leaves research participants in.

Keywords Research ethics · Disclosure · Conflicts of Interest · Dan Markingson

Introduction

Conflicts of interest arise in all professions and across many areas of life. They are not peculiar to the human research industry, and the issue of conflicts of interest is not new. Whilst conflicts of interest do not necessarily result in impaired judgement or wrongdoing, a growing number of scandals and evidence of questionable conduct and practices, coupled with a growing public expectation of transparency, demand a serious response to how these conflicts are managed.

Conflicts of interest can undermine scientific integrity as well as damage public trust (Shamoo and Resnik 2009), and so they need to be addressed in a way that protects these core foundations of ethical research. Conflicts of interest have the potential to influence a number of areas of the research life cycle, including the industry–academia agreement, research design, approval processes, trial execution, participant recruitment, and reporting. The impact of any impaired judgment may of course linger as medicines are approved for market and prescribed to patients.

Disclosure is a common solution to the problem of conflicts of interest and its purpose is to "sunlight" conflicts so that they can be scrutinized and managed. The act of disclosure also creates an expectation of self-regulation, as the person with the conflicting interests will be mindful of their own potential biases and aware that their decisions may be monitored. Where conflicts of interest exist for an individual within an institution, there is an opportunity for internal policies and oversight processes to also respond to the disclosure. However, these may be challenged where the institution has its own conflicts of interest, particularly where these conflicts flow in the same direction as the individual's conflicts of interest.

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In this article I use the case of Dan Markingson to explore the effectiveness of disclosure in managing conflicts of interest in human research, including whether scientific integrity and public trust can be preserved. This case illuminates problems in relying on disclosure to address the problem of conflicts of interest in research, including that: 1) research participants cannot effectively manage the conflict of interest as they are not in a position to accurately assess the impact; 2) self-regulation is problematic because often the person is not aware their decisions are influenced; and 3) individual solutions rely on institutional support, but this may be lacking where the institution has its own conflicts of interest. It is not within the scope of this paper to explore alternative conflict-of-interest management solutions.

About the Case of Dan Markingson[1]

Dan Markingson was a participant in a research trial at Fairview Medical Centre, run by the University of Minnesota's Psychiatry Department. The research trial, known as the CAFÉ study, compared the effectiveness of three antipsychotic drugs. AstraZenca, the study sponsor, manufactures one of the drugs, Seroquel. At the time, Dan was under the care of Dr Stephen Olson, who was also co-investigator of the trial. Six days after successfully petitioning the court to have Dan committed to state care, Dr Olson requested the court grant a stay of commitment. The stay was granted on the condition that Dan follow the treatment plan provided by his physician (Dr Olson). The next day, the study coordinator, Jean Kenney, read out the CAFÉ study consent form to Dan and secured his signature.

Dan's mother, Mary Weiss, objected to her son's involvement and raised concerns on numerous occasions, including providing specific details about her observations of Dan's deteriorating mental health. These were either ignored or dismissed. Her concerns escalated to the point where she left a desperate phone message for the study coordinator asking whether they had to wait until Dan killed himself, or someone else, before any action was taken. Less than two weeks later, 26-year-old Dan violently committed suicide.

The study was found to have numerous financial and non-financial conflicts of interest at the institutional level, as well as at the individual level. The main financial conflicts of interest related to the financial relationships between AstraZeneca, the university, and individual researchers. The university financial relationship with AstraZeneca earned the university a total of US$327,000 (Elliot 2010). Both Dr Olson and also Dr Schulz, the head of the psychiatry department, personally received substantial amounts of money from AstraZeneca before, during, and after the CAFÉ study.[2] The Institutional Review Board (IRB) chair, Dr Adson, reported directly to Dr Schulz and was also personally receiving money from AstraZeneca. They key non-financial conflict of interest arose from the dual role of Dr Olson as Dan's physician and co-investigator of the study. Other non-financial conflicts of interest included the reporting relationships between the investigators as well as study recruitment pressures. These factors added complexity to the situation. Further intangible conflicts may have included reputational and relationship management issues that were in the interest of the doctors involved as well as of the university as a whole.

Following Dan's death, some internal and external investigations were undertaken, although these were later found to be deficient. Carl Elliot, a professor of bioethics at the University of Minnesota, made repeated efforts to encourage the university to have the matter properly investigated, and after numerous failed attempts he went public with the issue. Still, it took years, countless articles, and a 3500-signature petition to the Governor of Minnesota, as well as a deluge of professional support including that of ex-Governor Arne Carlson and international academics, for any proper scrutiny to occur. Meanwhile the university continually denied any wrongdoing and refused to take any further action.

In 2015, the Office of the Legislative Auditor conducted an independent review, finding numerous ethical and conflict-of-interest issues. These included the potentially coercive conditions under which Dan was recruited, inadequate follow-up of Mary Weiss's complaints, inadequate supervision of the research assistant,

[1] Information sourced from Mother Jones (Elliot 2010), Pioneer Press (Olson and Tosto 2008), and Office of the Legislative Auditor (2015). I have left out aspects of the case that, whilst raising ethical issues, are less relevant to the issue of managing conflicts of interest through disclosure.

[2] During the period 2002–2008, Dr Olson received $149,344 from AstraZeneca. Dr Schulz received $112,020 over the same period, although it is unclear whether these amounts relate to research grants and therefore ended up in university coffers or whether they were accepted personally (Elliot 2010). Either way, there is a clear financial conflict of interest, whether direct or indirect.

concerns that the advocate was not present during the informed consent process despite investigator undertakings, the inadequacy of the IRB review of Dan's death, and the Minnesota Board of Medical Practice board review being compromised by conflicts of interest. The Office of the Legislative Auditor also raised concerns about the university response to the calls for further investigation and its lack of commitment to addressing the associated ethical issues.

Conflicts of Interest

Conflicts of interest arise where there is a conflict between an individual's professional role and their private interests (Sah, Lowenstein, and Cain 2013). In a given situation or set of circumstances, the risk is that professional judgement of a primary interest, such as research integrity or participant protection, can be unduly influenced by the secondary (private) interest, such as personal financial gain (Thompson 1993). The person must also be in a position where the decisions they make impact in some way on the ethical conduct of the research or its outcome. Importantly, conflicts of interest are those situations where the secondary interest poses a risk to a person's judgement, not those where judgement has been impaired. As such, conflicts of interest exist irrespective of a person's underlying motives and do not depend on an assessment of them (Lemmens and Singer 1998).

There are sometimes differentiations made between real conflicts, potential conflicts, and apparent conflicts (Davis 2012; Williams-Jones and MacDonald 2008). These definitions seek to differentiate between situations where there are current conflicting interests, those where there is a risk that conflicts of interest will arise, and those where it appears there are conflicts of interest. Whilst it may be clear that actual or potential conflicts need to be managed, it may be assumed that situations where there is an apparent conflict do not warrant the same response, because there are no actual conflicting interests that threaten to impair judgement. However, such differentiations can be problematic because to an outsider apparent and actual conflicts appear the same. Appearances matter because they can threaten public trust. In research, if public trust is eroded this will have implications for future participant involvement as well as impact on the confidence in the outcome and overall scientific research enterprise (Resnik 2004).

Institutional Conflicts of Interest

An institutional conflict of interest is defined as the condition where financial, political, or other interests are likely to undermine an institution's ability to fulfil its professional, legal, ethical, or social responsibilities (Shamoo and Resnik 2009). For universities conducting research, financial conflicts may include direct funding for a clinical trial or agreements for future donations. Non-financial institutional interests may include the desire to enhance the institution's reputation, develop new treatments, originate innovative new technologies, win prestigious research awards to attract the best staff, and secure future funding (Barnes and Florencio 2002). All of these secondary interests can be critical to institutions' ongoing viability, so their protection can effectively become everybody's business.

Conflict of Interest Management Policies

Responses to conflicts of interest fall into three main categories: disclosure, management, and prohibition (Emanuel and Thompson 2011; Hampson, Bekelman, and Gross 2011). In the area of human research, the recipients of the disclosure can include the potential research participant, ethics committees, peers, and managers as well as journal and report readers. Policies that aim to manage conflicts of interest might use strategies to minimize the risk of impaired decisions, such as recusal from decision-making responsibilities, transfer of certain tasks to independent colleagues, or additional oversight and reporting requirements. Prohibition of conflicts of interest is clearly the most stringent solution and leaves no room for doubt. Prohibition may be applied variably; for example, all financial relationships with industry, or those over a set amount, might be disallowed or researchers with those conflicts might be prevented from working on a particular clinical trial (Hampson, Bekelman, and Gross 2011).

Disclosure as a Solution to Conflicts of Interest

Disclosure is the most basic and historically most invoked mechanism to deal with conflicts of interest (Lemmens 2011). The Declaration of Helsinki requires that participants be informed of any possible conflicts of interest as well as institutional affiliations (World Medical Association 2013). Disclosure is intended to

mitigate the risk of improper influence, thereby protecting the research integrity and maintaining public trust. As well as allowing the recipient to discount the advice to the extent that it seems contaminated, it is thought that disclosure also restrains the person with the conflict of interest from indulging their secondary interest (Cain, Loewenstein, and Moore 2005). This means that upon disclosure, the responsibility for management of the conflict of interest will rest with the recipient of the disclosure, but some self-regulation could potentially be invoked. If disclosure is to be effective, it needs to be received by the right people, and those enlightened by the contents of the disclosure need to be able to manage the potential impacts appropriately.

Some Problems with Disclosure as a Solution to Conflicts of Interest

Concerns around the effectiveness of disclosure as a solution to conflicts of interest generally relate to whether the disclosure is sufficient to trigger an appropriate response. The factors influencing this include what information is disclosed to the recipient, the ability of the receiver to respond to the disclosure, and how the disclosure is made. For the receiver to assess the conflict of interest, they need an understanding of the nature of the conflict and the likely impact on the judgement or decisions of the researcher, as well as the possible consequences of those decisions. If the audience of the disclosure cannot understand the threat or respond appropriately, essentially the disclosure is futile (Davis 2012). The disclosures made in the case of Dan Markingson illustrate concerns about the challenge of provision of adequate information and highlight the vulnerable position disclosure leaves participants.

Research Participant's Ability to Respond to the Conflict of Interest

Level of Information Disclosed to the Participant

As a starting point, disclosures of the conflicts of interest need to be sufficient. The disclosure needs to be sufficiently specific to enable participants to effectively identify the reach of the conflicts and evaluate their severity (Lo and Field 2009). Even though the focus of disclosure requirements might usually be on financial ties or professional relationships, other interests may have just as much influence and perhaps even more. For example, personal relationships, career aspirations and pressures, and competitiveness, as well as religious beliefs. These factors also have the potential to significantly impair judgement, and as such if a participant is expected to manage the impact of conflicts of interest, they need to have the relevant information. Whilst it is difficult to know what a participant might see as important to their decision, it is possible to disclose what research participants are likely to consider as significant in making their decision, even if this is somewhat of a guess (Wilkinson 2001).

In the Dan Markingson case, a key issue was that the conflicts of interest were not adequately disclosed. A cursory disclosure of the financial conflict was made in the introduction of the informed consent form, stating "The investigator is being paid by AstraZeneca to conduct this study. AstraZeneca is the pharmaceutical company that manufactures and markets the medication quetiapine (Seroquel)" (University of Minnesota 2003, 1). This disclosure lacked detail: it was silent on the extent and exact nature of the financial relationship and failed to mention the other existing financial relationships. It was also unclear that this was a disclosure as such, because the sponsorship was not indicated as a potential issue or mentioned in other parts of the form such as in the section on risks. The fact that a pharmaceutical company is paying for the study is not likely in itself to alert the participant (in this case Dan) to scrutinize the possible impacts more thoroughly, rather it sounds as if it is usual—funding for the study has to come from somewhere.

In addition to the financial conflicts of interest, there were also non-financial conflicts of interest such as both Ms Kenney—the study coordinator—and Dr Olson being under pressure to secure and retain participants. They were under such pressure because the study had previously been on probation because of its poor recruitment (Elliot 2010). The relationship with AstraZeneca could also be considered a conflict of interest. As a senior member of the psychiatry department, Dr Olson would have been expected to maintain a good working relationship with AstraZeneca, and this had the potential to influence his decisions, particularly if the outcome was not supportive of AstraZeneca's interests. The disclosure to Dan did not mention any such conflicts.

The Way the Information is Disclosed to the Participant

The effectiveness of the disclosure is also influenced by who is making the disclosure and how it is made. Even where disclosures are complete, it is unlikely that people can appropriately discount advice from biased sources (Cain, Loewenstein, and Moore 2005). For example, the way the information is disclosed can give a false impression about the seriousness of the conflict of interest and what options are available to the participant to respond to it. Disclosure can normalize the general presence of disclosures or lead participants to believe that the specific conflicts of interest are "approved" (Emanuel and Thompson 2011, Elliot 2009). This can lead to an inadequate scrutiny or an increased risk that the secondary interest is indulged (Sollitto et al. 2003).

In Dan's case, the financial disclosure statement was part of the introduction of the ten-page consent form and was read out to Dan by Ms Kenney (Office of the Legislative Auditor 2015). The consent form shows that Dan signed the form in the presence of Ms Kenney; Dr Olson witnessed his signature (University of Minnesota 2003). It is possible that the consent process was thorough and discussions were had with regards to the meaning of the disclosure, the associated conflicts of interest, and their potential impact, and there is no evidence indicating otherwise. However, it is also reasonable to conclude that the oral delivery made it easy to skim over or play down any issues, including the issue of sponsorship, and it is possible that the purpose of the disclosure was more to "tick a box."

Ability of the Participant to Assess the Contents of the Disclosure

It is argued that research participants are generally not in a good position to interpret or evaluate the contents of a disclosure (Foster 2003, Emanuel and Thompson 2011, Lo 2012). One problem is that it is difficult for people without experience in managing conflicts of interest, or knowledge of the research industry, to understand the potential impact that impaired judgement may have on them (Lo 2012). As well, without knowledge of all of the secondary interests and strength of those, participants cannot make a proper assessment of the likelihood that those interests will adversely impact them. The strength of the "pull" of secondary interests would vary between individuals and depend on context. The direction and magnitude of influence is extremely difficult for an expert to estimate, let alone a "lay person" (Cain, Loewenstein, and Moore 2005).

Whilst disclosure of non-financial conflicts of interest may be necessary to allow the participant to fully assess the risk, there would clearly be difficulties for the participant in managing such conflicts of interest. Non-financial conflicts are particularly subjective and often not easy to assess, let alone manage; for example, it is unclear how ambition could be assessed or managed even if it were disclosed. Also, interests such as management pressure can impact on individuals differently. Some people are able to sustain such pressures, while others succumb to their influence.

Ability of the Participant to Assess Extent of Potential Harm

To ensure the participant has a full appreciation of the potential risk of the secondary interest, they must be aware of what damage the impaired judgement may cause. This hinges mainly on how much control the researcher has over their care during the trial, including decisions about their enrolment status and treatment should issues arise. At least in a general sense, this would likely be known at the time of obtaining consent; however, it seems that this is generally not required to be included in conflict-of-interest disclosures.

In Dan's case, Dr Olson's influence was substantial, so the extent of potential impact was sizeable. Dr Olson had the power to keep Dan in the study and to control his medications (Office of the Legislative Auditor 2015). Others in positions of significant influence included Dr Schulz, Ms Kenney, Dr Adson, and, at the highest level, the university president. All of these people had a financial relationship with AstraZeneca, directly or indirectly, as well as numerous non-financial conflicts of interest. Understanding of this complex hierarchy of influence would have been essential to Dan's understanding of the harm that could have resulted.

Overall, the disclosure to Dan was clearly deficient, given that key information was absent, in particular the extent of the financial relationship and the recruitment pressures that had the potential to significantly influence judgement. He was not made aware of the amount of money at stake or the number of people in positions of power receiving it. The information that was provided was at best superficial and therefore did not enable Dan to make a proper assessment of how the conflict of interest may have affected his care. As a result, Dan

was not able to use this information to manage the conflict of interest and as such disclosure was inadequate in this case.

Should Participants Be Responsible for Managing the Conflict of Interest?

Even if it were clear that disclosure could equip participants with the necessary knowledge to scrutinize decisions and manage their impact, there is a question over whether it should be their role to do so. That is, should participants hold the responsibility of managing the potential impact on their own interests? Research participants are volunteers agreeing to be involved in research that carries no guarantee of therapeutic benefit. Through the course of research, they are also subjected to interventions or procedures, and often these carry risk (Council for International Organizations of Medical Sciences 2016). Much of this is outside their control, and they are in a position where they need to trust that researchers will protect their interests. Participants are not involved in accepting conflicts of interest; they do not benefit from them, yet they bear some of the risk of the consequences of judgement that has been influenced by them. At least morally speaking, this position should afford them a significant level of respect and protection. It has been argued that transferring the burden of responsibility for managing conflicts of interest to research participants who have no control over the researcher's judgement is inappropriate and unfair (Angell 2000; Cain, Loewenstein, and Moore 2005). Furthermore, the Declaration of Helsinki specifies that the protection of research participants should never rest with the participants themselves (World Medical Association 2013), and managing the impact of conflicts of interest is part of participant protection.

Can Researchers Self-Manage Their own Conflicts of Interest?

Self-management is an assumed secondary benefit of disclosure, because the transparency creates an expectation of self-regulation. Effective self-management of conflicts of interest relies on the conflicted person being consciously aware of the impact that the secondary interest has on their thought processes and then being able to adjust accordingly (Cain, Loewenstein, and Moore 2005). However, it is argued that individuals are largely unaware of their biases, and consequently the problem relates to unintentional and unconscious bias (Dana and Lowenstein 2003, Shamoo and Resnik 2009, Elliot 2009). Evidence of this is provided by the Orlowski and Wateksa (1992) study, at a particular healthcare institution, on the impact on prescribing practices when a pharmaceutical company gifted doctors an "all expenses paid" seminar at a resort. They found that there was a significant increase (two to three times) in the prescribing of the promoted drug even though doctors believed that such inducements would not have an impact on their level of prescribing. Their prescribing behaviour changed even though they were aware that their participation in the trips was "known."

A lack of self-awareness of bias may be exacerbated where the professional culture is tolerant of conflicts of interest or perhaps even promotes them. For example, where financial conflicts of interest are common and maintaining good relationships with funders is necessary for ongoing viability, this is just the normal working landscape. Researchers' reality may then be skewed so that bias is as not as obvious to identify.

Situational Challenges to Researcher Self-Management

It is often assumed that a person behaves in a way that reflects their disposition and character, underplaying the role situation has in determining behaviour (Cain, Loewenstein, and Moore 2005). However, outcomes of social science experiments, such as the Stanford prison experiment,[3] have shown that ethical behaviour is shaped by a person's disposition as well as situational factors (Master 2014). A person who ordinarily behaves in an ethical manner can be swayed to behave questionably under the pressure of certain conditions. In this way, influence of circumstance may also compromise a person's ability to effectively self manage their conflict of interest, resulting in impaired decision making. This is not necessarily about being tempted by direct bribes. In the research setting, it could be pressure to recruit participants, the appeal of prestige, subordination issues, or simply positioning oneself for future work.

In the case of Dan Markingson, there are some situational factors that may have influenced Dr Olson's self-

[3] The Stanford prison experiment was a psychological study conducted in 1971 simulating prison life and examining the impacts of power, or lack of it, on individual's behaviour (Stanford University 2011).

management. He was under pressure to keep participants in the study and he may have had other concerns such as damaging his relationship with AstraZeneca or his reputation as an investigator. For example, despite numerous requests to review Dan's regression, Dr Olson did not act on Mary Weiss' concerns (Office of the Legislative Auditor 2015). This may have been because in his professional opinion the concerns were unfounded, or it could be that he assessed Dan and determined that he was not in particular danger. However, it is possible that his judgment was influenced by the situational factors. These pressures may have been a disincentive to look seriously at Dan's involvement in the study. The lack of management of the conflict of interest means that this will remain an open question.

Difficulty of Proving that Self-Management is Effective

For self-management to be recognized as effective, there needs to be evidence that it works. This is problematic given that is extremely difficult to distinguish between cases in which conflicts of interest have improper influence and those where it does not (Barnes and Florencio 2002; Lemmens 2011). This is largely due to the problem of obtaining indisputable evidence that can clearly connect the conflict with the impaired decision. Questionable decisions or conduct can be explained away simply as mistakes, errors, or poor record-keeping, as in the misconduct case against Thereza Imanishi-Kari.[4] Judgement may also be impacted due to tiredness, pressure of other deadlines, or personal issues, so it is difficult without any admission to prove whether or not it was the conflicting interest that unduly influenced the questionable decision. Essentially this means that there is no way of knowing if self-management is effective or not.

Further to the problem of establishing that self-management actually works, there is also the need to preserve public trust, and this is impacted by how the situation appears. Dennis Thompson (1992) promotes the importance of what he calls the "appearance standard" in the context of ethics in government. As the name suggests, this standard is concerned with how conduct might be perceived and holds that simply doing the right thing is not enough. Thompson (257) says "appearing to do wrong while doing right is really doing wrong," and this is because appearances can damage public confidence as well as accountability. He points out that even if people with conflicts of interest do overcome any personal biases, reasonable doubt can remain. If it cannot be demonstrated that conflicts of interest do not impair judgement, and if there is the possibility for reasonable doubt about whether it has or not, then public trust cannot be reliably preserved.

In the case of Dan Markingson, from an outside perspective it is impossible to ascertain whether decisions were unduly influenced. Mary Weiss (Dan's mother) lodged a complaint to the Minnesota Board of Medical Practice regarding Dr Olson's conduct in this case. To review the matter, the board hired an independent consultant, Dr Adson (Elliot 2017). However, Dr Adson was not impartial—he had a long list of conflicts of interest pertaining to the case. He was a colleague of Dr Olson, he reported directly to Dr Schulz who was the co-investigator of the study alongside Dr Olson, he was the Chair of the IRB at the time the CAFÉ study was approved, as well as when the adverse event (Dan's death) was investigated, he was the Director of the research centre where the drug trial took place, and he was also receiving payments from AstraZeneca throughout this entire period (Office of the Legislative Auditor 2015, Elliot 2013). Dr Adson disclosed his conflicts and acknowledged being very familiar with the case prior to commencing the review, but after considering the "possible" conflict the Board determined that it was acceptable so long as the consultant felt he could review the materials objectively (Office of the Legislative Auditor 2015).

It would be difficult to prove whether Dr Adson's judgement was influenced by his myriad of conflicts of interest, although it would be hard to argue that none of these interests distorted his judgement in any way. They were not insignificant conflicts, and combined they could seem insurmountable. The Office of the Legislative Auditor (2015) pointed out that just one of those conflicts of interest should have been enough to excuse him from this investigation and concluded that the review was compromised as a result. Even though there is no way of telling whether or not the conflict was effectively self-managed, the perception of bias undermined the integrity of the report and therefore public trust in the outcome.

[4] Thereza Imanishi-Kari was accused of fabricating or falsifying data after a student discovered that trial data documented in her notebooks was inconsistent with the published report, but she only admitted to poor record keeping and was exonerated by an appeals board (Resnik 2004).

What Impact Do Institutional Conflicts of Interest Have?

Institutional conflicts can exacerbate the threat to the integrity of the research posed by an individual's conflict of interest. Individual's decisions can be impaired, as well as those made collectively by oversight bodies. The responsibility for maintaining and promoting institutional interests can be delegated through inference, for instance appearing in corporate goals as well as specifically documented in individual performance agreements. As Schafer (2004, 21) claims, "When the University becomes a business, its top officials are virtually required to adopt commercial values as an adjunct to their academic values." Institutional conflicts of interest can then become an individual's conflicts of interest, adding further complexity to the management of conflicting interests. The main concern is that oversight and management of the conflicts could be impaired, particularly when individual conflicts align with the institutional conflict.

In the case of Dan Markingson, the institution of the university had a conflict of interest relating to the CAFÉ study. AstraZeneca was funding the CAFÉ study, and the risk of the conflict was intensified as the university's budget relied on revenue from such research grants (Office of the Legislative Auditor 2015). As well, the university president repeatedly stated that his top-level goal was to make the University of Minnesota one of the best public research universities (MPR News 2015). Together, these secondary interests had the potential to take priority as well as discourage transparency and stringent oversight.

Institutional Conflicts Impact on Individual Decision Makers

Institutional pressures can lead researchers and decision makers to compromise their primary responsibilities of participant protection and scientific and institutional integrity (Barnes and Florencio 2002). It is not that these professionals are necessarily directed to act one way or the other, as the organizational goals and interests can be well embedded in the institutional culture with even individual performance measured against contribution towards those goals. If research laboratories and career prospects depend on renewed industry funding, individual interests can start to align with those funding their work (Lewis et al. 2001). Impaired decisions could potentially impact all stages of the research, including approval, monitoring, and review, thereby impacting participant safety and integrity of the results.

In the case of Dan Markingson, the institutional interests may have impacted on the researchers conduct during the study. For example, whilst the CAFÉ study research protocol gave an undertaking that an independent advocate would be available to the participant, Dan was not provided with an advocate until four days after he signed the consent form (Office of the Legislative Auditor 2015). Ms Kenney and Dr Olson both had numerous reasons to press ahead with obtaining Dan's consent, and they did. It appears that Dan's right to access independent advice and his fully informed consent were not a primary consideration, nor was serious attention given to how vulnerable this may have left him.

Institutional Conflicts Influence Over Research Oversight

Institutional conflicts of interest can also jeopardize the integrity of oversight boards, as institutional pressures may bias individual members. Members may be part of the institution leadership team, for example, and as a result may have concerns about the ongoing viability of the organization as well as its reputation. There also may be some members that benefit directly or indirectly from financial relationships with industry. Often ethics committee deliberations are confidential, and this reduces transparency (Gillam 2003). Where decisions are suspect, the confidentiality of the content of discussions inhibits discovery and thereby accountability. Given that any resulting harms are not easily discoverable and there is less accountability, the risk to research integrity is greater (Barnes and Florencio 2002).

According to Lewis et al. (2001, 784) "Industry funding creates an incentive to promote the positive and suppress the negative." The outcome could be that instead of attracting serious scrutiny, issues supportive of those institutional level secondary interests are overlooked. Perhaps decisions unfavourable to institutional interests become difficult to make and maintain. The risk is that the purpose and benefit of the review board is undermined, because they cannot be separated from the conflict of interest. The whole idea behind ethical review boards was that research protocols ought to be reviewed by a committee independent of the study (Elliot 2009).

In the Dan Markingson case, the institutional conflicts may have impacted the research oversight. As well as possible pressures flowing from the institutional conflict, the IRB Chair Dr Adson had numerous personal conflicts of interest relating directly to the case. These conflicts were possibly tolerated because of the university's own financial relationship with AstraZeneca. The IRB investigation of Dan's death clearly needed to be impartial; it was a serious issue. However, Dr Adson served as one of the two primary reviewers of the adverse event, although he claimed that he refrained from making decisions in the case due to IRB conflict of interest policies (Office of the Legislative Auditor 2015).

It is unclear why Dr Adson was allowed to serve as one of the two reviewers when he was prevented from making decisions in the review process. Whilst he may not have held the power to make decisions, he would have still had considerable influence as one of only two reviewers, as well as due to the power he enjoyed as the chair of the board. The Office of the Legislative Auditor (2015) found that the investigation into Dan's death was lacking, particularly given that reviewers did not seek information from anyone other than Dr Olson. Whether or not the conduct of the investigation was impaired by the conflicts of interest is not clear. However, the facts are that the conflict existed and the outcome was defective. The research oversight in the Dan Markingson case was clearly inadequate. Knowledge of Dr Adson's conflicts of interest did not invoke an effective management response, and any disclosures made were ineffective in upholding research integrity. Public trust was also damaged when the inadequate investigation was revealed.

Conclusion

This exploration of the adequacy of disclosure as a solution to conflicts of interest has highlighted some problems of, and limits to, this approach. Whilst the act of disclosing factors that could impair judgement may rise to the challenge of transparency, it does little to tame the influence of those interests. The disclosure itself does not "do" anything; it relies on someone else doing something about it. However, those receiving such disclosures may not be equipped to do anything about these conflicts of interest and therefore leave management of them wanting.

This is particularly so in the case of disclosures to research participants. Rather than being a straightforward concept, some of the conflicts are a complex web of interests and pressures, coexisting in an environment entirely unfamiliar to that person. This is not a strong starting point for effective management, so the content of the disclosure has a big job to do. Generally, however, particularly where those conflicts are multilayered and interwoven, full disclosure of the nature and extent of those conflicts is problematic at best, perhaps even unachievable, and therefore cannot meet such a challenge.

Given that the types of conflicts of interest considered here cannot be eradicated, particularly as the funding arrangements of universities are unlikely to change in a hurry, some self-management of conflicts of interest will always be necessary. However, this is largely unreliable and would need to be complemented by alternate strategies that enjoy more control over the influence on judgement. Any potential for disclosure to be effective on its own is further challenged when those conflicts are supported by institutional conflicts of interest. Where this is the case, effective oversight can be hampered and there is little hope for this to be exposed. It is not in an institution's interest to be transparent when that may hinder their financial relationships with industry and therefore their very existence. The potential severity of these conflicts needs to be met with a robust conflict management response, one that can meet the challenge of preserving research integrity and maintaining public trust. Disclosure is a simple solution and just not adequate to deal with the complexity of conflicts of interest in research.

In the Dan Markingson case, the superficial disclosure of the financial conflict did not bring about effective management of the conflict of interest. Although no precise link was established between Dan's participation in the CAFÉ study and his death, it seems that his safety and well-being were overshadowed by the power of other interests. The conflicts of interest were left unaffected, ultimately compromising Dan's care.

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