Commentary

# Monitoring and oversight in critical care research

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## Abstract

Institutionally based research ethics review is a form of peer review that has – for better or worse – become the norm throughout the world. The vast majority of research ethics review takes the form of protocol review alone, conducted in advance of the research. Although oversight and monitoring in clinical research have long been recognized as essential features of sound research ethics, they are seldom exercised in ways that fulfill their motivating goals: to ensure that research is conducted as planned; that research participants comprehend the information presented to them in the consent process; and that the potential benefits and risks of study participation remain acceptable. Annual review of continuing research, monitoring informed consent, monitoring adherence to approved protocols and monitoring integrity of research data comprise the main types of monitoring and oversight activity. We believe that our institutionally based systems of research ethics review and responsibility require greater engagement and participation from researchers and research administrators. The appropriate role of critical care researchers and research administrators is to provide leadership to move toward a greater recognition of the importance of monitoring and oversight for ethical and high quality clinical research.

**Keywords** critical care research, institutional accountability, institutional review boards, oversight and monitoring of research, research ethics, research ethics board, research ethics review, research integrity

## Introduction

The quest for important medical knowledge – the kind that clarifies understanding of or that leads to successful interventions for important clinical problems – has always required departure from accepted norms of medical practice. Innovation in medicine (i.e. trying out new or revised clinical practices to improve health outcomes for individual patients) remains a central feature of medical practice and varies from minor adjustments to 'radical new procedures' [1]. It is doubtful that any thoughtful physician or surgeon has not at some time tailored a patient's treatment to fit specific circumstances, or adjusted a standard dose of a medication in an attempt to maximize the patient's benefit. When Thomas Percival [2] suggested, in 1803, that some of these departures from accepted practice were sufficiently bold to warrant seeking the opinion of medical colleagues before conducting them in patients, he ushered in the age of peer review in medicine.

As recently as the early 1960s, peer review in research was viewed by many investigators and research administrators with the same suspicion that Percival undoubtedly encountered in the 1800s. However, in the wake of the thalidomide tragedy of the late 1950s and early 1960s, revelations in 1963 of researchers injecting elderly indigent patients with live cancer cells at the Brooklyn Jewish Chronic Diseases Hospital, and in the same year an ethically dubious and unsuccessful chimpanzee to human kidney transplant at Tulane University [3], the specter of lost public trust in the research enterprise forced two critical issues onto the agenda. First, how should the risks associated with medical research be dealt with, and,

NIH = National Institutes of Health; REB = research ethics board.

second, how should the burgeoning research enterprise be governed [4]? In 1965, the US National Institutes of Health (NIH) director Dr James Shannon championed a policy whereby the NIH would fund research in human subjects only if, 'the judgment of the investigator is subject to prior review by his [sic] institutional associates' [5]. This policy formalized the practice of institutionally based research ethics review, a form of ethics peer review that has – for better or worse – become the norm throughout the world.

The vast majority of research ethics review takes the form of protocol review alone, conducted in advance of the research. The goal of these reviews is to determine the ethical acceptability of the proposed research. When this has been done, authorization may be given to the investigators to proceed with their proposed research. Investigators are required to conduct the research according to the approved protocol and to give regular status reports (at least annually) in order for approval to be extended. However, research ethics scandals have shown that the limited scope of research ethics review can provide sufficient opportunity for those few investigators who choose to take shortcuts, proceed carelessly, and even occasionally engage in willfully unethical conduct to avoid the scrutiny of their peers. Such deviations from the approved protocol can have grave consequences, both in terms of the safety of research participants and in public trust in the research enterprise.

## Challenges in oversight and monitoring

The lack of effective oversight and monitoring in clinical research makes it similar in many respects to clinical practice, especially that by independent, individual physicians. The similar levels of latitude and independence of action raise the question of whether oversight of clinical research may be sufficiently served, *post hoc*, through litigation by injured parties – a familiar mode of oversight in clinical practice [1]. Since Shannon's institution of peer review at the NIH, the process of ethics approval for research studies by institutional research ethics boards (REBs; also known as institutional review boards or research ethics committees), including formal informed consent procedures as well as annual status reports, have been widely accepted as a sufficient institutional response to ethical challenges in research. According to McDonald [6], '(t)he REB process (and with it the focus on the research proposal and the consent form) has become the reification of the sum total of responsibilities and accountabilities for researchers, research institutions, research sponsors, and research regulators. In effect, this rationalizes the avoidance of major responsibilities that arise before, after and on the peripheries of the REB review process.'

The current state of oversight and monitoring of clinical research make them the Achilles' Heel of research ethics, the flaw that fatally weakens the rest of the operation. Although these practices have long been recognized as essential features of sound research ethics, they are seldom exercised in ways that fulfill their motivating goals, which are 'to ensure that research is conducted as planned, that research subjects comprehend the information presented to them in the consent process, and that the potential benefits and risks of study participation remain acceptable' [7]. In part, this reflects the fact that, despite important improvement in awareness and interest in research ethics within the research community, the review and oversight of research are still viewed by many investigators as an intrusion on their professional discretion and as obstacles to research, rather than integral and complex challenges for enhancing research conduct and governance. As such, research ethics review, oversight and monitoring remain among the small handful of essential research related activities that are conducted on an almost entirely voluntary basis. Institutions either lack the resources or the motivation (or both) to ensure that these activities occur and are done well.

## Oversight and monitoring practices

Research monitoring and oversight encompass four types of activity [8]: annual review of continuing research, monitoring of informed consent, monitoring of adherence to approved protocols and monitoring the integrity of data. These activities are intended as means of quality assurance in research, and as means of establishing expectations of rigorous and ethical conduct in research. However, there are very few empirical research data to demonstrate how well these practices fulfill these functions [9,10], and the few epidemiological studies of monitoring and continuing review suggest much room for improvement [8]. Furthermore, it is also taken on faith that when these activities do occur they contribute to the higher order aims of protecting human participants and promoting ethical conduct in research, but similar deficits in empirical evidence make these claims increasingly suspect and raise a deeper question about what we are trying to achieve through research ethics review, monitoring and oversight practices, and how.

According to the Canadian Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans [11], '(p)rinciples of accountability require that, regardless of the review strategy, the REB continue to be responsible for the ethics of all research involving human subjects that is carried out within the institution.' In interviews with REB members at several major Canadian universities, however, McDonald [6] found them to be apprehensive about monitoring. This seems a reasonable response to the ambiguous message of the Tri-Council Policy Statement, which, in a subsequent section, states that '(b)eyond scrutinizing reports, the REB itself should not normally carry out the continuing ethics review, except in specific cases where the REB believes that it is best suited to intervene' [11]. So, the committees most responsible for research ethics continue to be given few, if any, resources and little helpful guidance on these matters.

Our own hospital, St. Michael's Hospital, has taken the unusual step of implementing a monitoring programme with a

full-time research ethics monitor. Through judicious use of skill, diplomacy and diligence, and with strong support from the hospital's research administration, we are forging what we believe is a fruitful new direction in research monitoring and oversight. We are working to create a climate and culture within the institution that support investigators with the myriad technical requirements of research, particularly the Canadian and US regulatory requirements for clinical trials, but also to provide them with meaningful opportunities to discuss and examine the complex ethical and regulatory issues that arise in the conduct of their research.

Our monitoring programme places strong emphasis on education. We provide investigators with detailed information about research responsibilities through regularly scheduled rounds and a variety of other educational activities, such as courses in the International Conference on Harmonisation's Good Clinical Practice guidelines [12]. We conduct internal quality assurance audits of ongoing trials, initiated either by random selection, investigator request, or in response to specific events or concerns. We have also monitored informed consent discussions between research staff and prospective research participants, and we are currently planning to survey research participants themselves in order to gain a better understanding of their perspective.

These activities not only engage investigators with the issues, but they also provide the REB with a real and meaningful set of mechanisms to help it fulfill its obligations for monitoring and oversight. The REB members receive feedback about the actual conduct of the research that they approved, and this constitutes an important learning loop for their review of future proposals. The institution is also exercising due diligence by gathering more details about the conduct of its research, especially for investigator-initiated drug studies, in which the institution must assume sponsor responsibilities. Our researchers have responded very favourably to acknowledgement and support for the high standards of their conduct, and to recommendations for improvement, when these are warranted.

## Conclusion

Given the many ethical challenges inherent in critical care research, it would be tempting to propose a separate and distinct approach to their monitoring and oversight. We do not see it that way. Although perplexing challenges related to monitoring and oversight in critical care research will invariably arise [13–15], such as informed consent from a substitute decision maker for those patients whose capacity changes over time [16,17], similar challenges are equally likely to arise in other clinical research fields. We believe that our institutionally based system of research ethics review and responsibility requires greater engagement and participation of researchers and research administrators so that they can help to compensate for the limitations of the ethics review process, rather than ignoring or taking advantage of them. We need better professional ownership of these issues by investigators and clinical departments, and institutional pride in affording these issues the time, resources and intellectual commitment that they deserve. The appropriate role for critical care researchers and administrators in this respect is to help provide the necessary leadership to move beyond the limits of current research ethics review practices and toward a greater recognition of the importance of monitoring and oversight for the performance of ethical and high quality clinical research.

## Competing interests

The author(s) declare that they have no competing interests.

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