Ethics approval requirement for *CJEM* research publications: a step forward for Canadian emergency medicine

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Every emergency medicine researcher has, on occasion, cursed a Research Ethics Board (REB). The ethics approval process is both complicated and time-consuming. REBs frequently request seemingly arbitrary changes to protocols that took months and sometimes years to develop. Research in the emergency department (ED) or in pre-hospital settings pose unique ethical challenges,[1,2] and REBs are frequently unfamiliar with these environments. This can lead to delays in obtaining ethics approval, as researchers educate their REB and negotiate acceptable approaches.[3]

In light of these concerns, it may seem surprising that *CJEM* recently formalized a policy that all research published in the *Journal* must be approved by an REB (see CJEM Instructions for Authors online at http://www.caep.ca/). While the ethics approval process can be inconvenient and frustrating, history has shown that it is crucial for the protection of research subjects and that it is necessary to avoid the harm that ill-conceived or poorly executed research can produce. The ethics approval process provides a counter-balance to powerful and pervasive forces that push research forward at any cost; it fosters a trusting relationship between researchers and subjects.

The history of medical research is littered with stories of research gone wrong, and research subjects who have suffered as a result. The unconscionable experiments of Nazi physicians came to light in the mid 1940s during the Nuremberg trials. The Nuremberg Code was subsequently developed in 1947 to articulate the principles of ethical research.[4] Other codes and declarations followed[5,6]; however, unethical research still occurred all too frequently. One particularly egregious example was the Tuskegee Syphilis Study. In 1932, the US Department of Public Health initiated a project designed to determine the natural history of syphilis. Because there was no effective treatment for syphilis, it was considered acceptable to withhold treatment from a group of infected subjects and follow them over time. Four hundred poor and minimally educated African-American men were recruited into the study. Few understood that they were part of a research project, and deceptive means were used to ensure compliance with invasive data collection procedures. In the 1940s, when it was discovered that penicillin was an effective treatment for syphilis, the investigators actively prevented their subjects from receiving antibiotics. The study continued for decades and published results in peer-reviewed journals until 1972, when a series of *New York Times* articles led to public outrage, particularly among minority communities.[7]

It is tempting to view the Nazi experiments and the Tuskegee events as a result of bad men living in a different time. Unfortunately, there are more recent examples of the same phenomenon. In 1988, the Cartwright Inquiry examined the case of a prominent New Zealand gynecologist and researcher who withheld treatment from women with cervical dysplasia in an effort to "prove" that it did not lead to cervical cancer. This took place between 1966 and 1987 and resulted in the deaths of many participants.[8] In 1999, 19-year-old Jesse Gelsinger died after participating in gene

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therapy research based at the University of Pennsylvania. Regulators subsequently discovered there had been unreported adverse events associated with the University of Pennsylvania study that suggested it was unsafe for Jesse to participate in the research.[9] Even today, research can still pose significant risks to subjects.

We must recognize that powerful forces push research forward and we must understand that REBs provide a necessary counterbalance to these forces. Pharmaceutical companies and device manufacturers allocate significant time and money to clinical research. The resources that are invested before research begins, and the potential profits that can be made, lead to tremendous incentives for companies to rapidly complete studies. Protocols and practices that provide robust protection for subjects frequently slow the research process down. It is unlikely that industry would pursue an appropriate level of protection for research subjects without strong, clear direction from REBs. Money, however, is not the only reason researchers go astray. The pressure to publish and be promoted can cause a conflict for academic researchers and may tempt them to act in ways that are not in the best interests of their subjects. All researchers want to complete what they start and see positive results from their hard work. It is human nature to seek the fastest, most efficient way to get results, rather than the safest way.

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While high-quality research requires a well-designed protocol and researchers with integrity, trust is the glue that holds it together. When we ask patients to help us find better treatments for future generations, they need to be confident we are doing everything possible to minimize the risks involved. Studies have shown that many research subjects do not understand the consent process,[10,11] do not read consent forms before signing them[12] or do not have the education necessary to understand consent forms even if they read them.[12] In one study, almost one-third of participants did not even remember being asked to give consent.[13] But when research participants are asked if they would be willing to participate again, the vast majority say yes.[14] This is because they trust us. They trust the research we are conducting will not be trivial or unsafe. They trust that researchers have no conflict of interest and will follow the rules. They trust that someone is looking out for them. If we fail to meet these expectations, the results are more than just a moral failure. The experience of American researchers in the aftermath of Tuskegee demonstrates that trust is crucial for the research process to work and once lost, it is very difficult to regain.

When we recruit research subjects from the ED and prehospital settings, it is particularly important that we are mindful of subjects' unique vulnerability and that we act to protect and empower them, rather than exploit them. In this regard, the *CJEM* policy mandating REB approval is an important one and it is in keeping with other major medical journals. However, some questions remain. Can editors and peer reviewers at *CJEM* assume that if an REB has approved a study, further scrutiny is unnecessary? I don't believe so. REBs sometimes make incorrect decisions, particularly when they deal with unfamiliar research settings. *CJEM* editors and reviewers must continue to scrutinize the ethical elements of submissions, and *CJEM* should reserve the right to reject research deemed to be unethical, even if it has been approved by an REB.

Another challenging question is whether *CJEM* should require quality improvement (QI) projects (also known as quality assurance projects) to obtain REB approval. Although QI and research can appear similar, they have different goals. QI focuses on improving patient care in specific settings, (e.g., determining how often physicians in an ED prescribe steroids to asthmatic patients), while research is a systematic investigation designed to develop generalizable knowledge (e.g., determining whether prescribing steroids to asthmatics leads to fewer return visits).[15,16] Some characteristics of a project that identify it as research rather than QI include subjects who are exposed to more than minimal risk or to untested interventions, interventions that differ from current standard care, interventions that are not intended to benefit subjects and a design that is intended to produce generalizable results.[15,17,18]

Whereas the ethics review process for research is well articulated and established, the rationale and appropriate process for review of QI projects is not. Some have argued that any project submitted for publication requires formal (i.e., REB) ethics review.[19] Others have proposed more selective and rational criteria.[15,17,18] Occasionally, researchers knowingly call research activities QI to take advantage of

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this confusion and avoid REB review. This unethical practice should be strongly condemned and steps should be taken to prevent it. However, requiring all QI projects to obtain REB approval is problematic for a number of reasons. Many QI projects do not need this level of scrutiny as they pose no risk to subjects. Moreover, REBs may resist or refuse to review QI projects given the substantial work they already undertake, and few institutions have a lower level ethics review mechanism in place. QI projects are often not initially intended for publication and, thus, REB approval is not sought. Once completed, however, the findings of such "internal" projects may prove particularly interesting or instructive and, thus, be worthy of publication. In such cases, some REBs will grant "retroactive" approval, or provide written confirmation that REB approval was not required. Most will not. For these reasons, *CJEM* has, on occasion, published select QI projects that have not received REB approval and should reserve the right to do so in the future. Such projects should meet clear predetermined criteria that differentiate them from research, and the authors should demonstrate that they have considered and addressed any relevant ethical issues.

History shows us why research ethics review is so important. Yet, REB approval is about more than addressing past wrongs and fending off industry or academic pressures. It is about the incredible trust that our subjects place in us as emergency researchers and about proving ourselves worthy of this trust.

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