A framework for research ethics review during public emergencies

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The global outbreak of the pandemic (H1N1) influenza has refocused international attention on emergency preparedness for urgent threats to public health. Such threats have included the outbreak of severe acute respiratory syndrome (SARS) of 2003, the emergence of multidrug-resistant tuberculosis, the spectre of avian influenza, the terrorist attack on the World Trade Centre and the aftermath of hurricane Katrina.[1–5]

During the outbreak of SARS in Toronto, clinical researchers noted that the need for approval from research ethics boards had resulted in "delays and missed opportunities" for their research protocols.[6] Such emergencies have illuminated the challenges of combining speed and flexibility with intense scrutiny in conventional research ethics reviews. In response to requests for guidance from research ethics committees around the world, the World Health Organization (WHO) recently held a special technical consultation titled "Research ethics in international epidemic response."[7]

Approaches that emphasize time-sensitive review have been adopted by the research ethics board of Health Canada.[8] Also, in response to the pandemic (H1N1) 2009 in Canada, the Public Health Agency of Canada has developed a pilot project titled Streamlining Ethics Review of Multi-Centre Pandemic Influenza Research.[9] However, these approaches do not explicitly address the need for enhanced scrutiny during unusual circumstances, and may not be applicable to all public emergencies. Both approaches represent considerable departures from the procedures normally followed by institutionally based research ethics boards, making their widespread application doubtful.

The federal Interagency Advisory Panel on Research Ethics Review has developed a new section on research ethics review during public emergencies for the revised draft second edition of the *Tri-Council Policy Statement: Ethical conduct for research involving humans*.[10,11] The new section emphasizes that the substantive ethical requirements of the *Tri-Council Policy Statement* are expected to be applicable during public emergencies, but recognizes the potential need for procedural flexibility in response to the demands of specific emergency circumstances. However, the new section stops short of outlining a specific procedural framework, leaving this process to the discretion of research ethics boards and their institutions.[10]

We propose a new framework to guide departures from normal research ethics review during emergencies. It has its roots in the concepts of proportionate review, special scrutiny (i.e., enhanced diligence) and expedited review (i.e., relaxed procedural requirements). It is also informed by our experiences as researchers[12] and as research ethics board members during the Toronto SARS outbreak, and by a subsequent unpublished study of the experiences of researchers and research ethics board members during the SARS outbreak.

Key points

- Public emergencies have illuminated the challenges of combining speed and flexibility with intense scrutiny in research ethics reviews.
- A framework is proposed for emergency review of research protocols based on a combination of increased diligence and enhanced procedural flexibility in proportion to risks and circumstances.
- Emergency ethical review is a tool to help research ethics boards and institutions plan emergency procedures in ways that reconcile the procedures of research ethics review and special circumstances.
- Emergency ethics review may also represent a useful model for general improvement of procedures in research ethics review.

Literature review

We searched MEDLINE and Embase databases (Appendix 1, available at www.cmaj.ca/cgi/content/full/cmaj.090976/DC1) to capture relevant articles in the scientific literature as well as Google Scholar and WorldCat (www.worldcat.org) for relevant books and grey literature. These searches did not reveal any publications with a primary focus on guidance for research ethics review in emergency circumstances. Publications that addressed some of the issues are summarized in Table 1.[11,13–18]

From the Joint Centre for Bioethics (Tansey, Lavery) and the Institute of Medical Sciences (Tansey, Herridge, Heslegrave), University of Toronto; the Department of Medicine (Tansey, Herridge), University Health Network; the Interdepartmental Division of Critical Care (Herridge) and the Department of Medicine (Herridge), University of Toronto; the University Health Network (Heslegrave), the Centre for Inner City Health and Centre for Global Health Research (Lavery), Keenan Research Centre in the Li Ka Shing Knowledge Institute of St. Michael's Hospital; and the Dalla Lana School of Public Health (Lavery), University of Toronto, Toronto, Ont.

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Elements of ethics review in emergencies

Three key elements of a model of research ethics review in emergency circumstances are proportionality, special scrutiny and expedited review.

Proportionality

The *Tri-Council Policy Statement* explicitly calls for proportionality as a guiding norm for research ethics review. According to this statement, "Proportionate review is intended to reserve the most intense scrutiny, and correspondingly more protection, for the most ethically challenging research."[19] For example, the first human use of a new drug during an emergency would require greater intensity of review compared with a survey examining the impact of exhaustion on emergency service workers during the emergency.

Special scrutiny

Levine and colleagues[20] have argued that research protocols that present novel or ethically challenging questions, situations and strategies or that pose a challenge to the status quo warrant "special scrutiny." Special scrutiny entails increased diligence in review by a research ethics board, such as more frequent or sequential reviews, increased monitoring or enhanced oversight of the informed consent process.[20] As well, special scrutiny recognizes that additional expertise may be required to review scientific or methodologic aspects of novel proposals, or to assess the researchers' account of the proposed study's risk–benefit ratio, including the impact of the proposed research on the study community.

Three criteria that may trigger special scrutiny are proposed by Levine and colleagues.[1] The first criterion is that the research involves initial experiences of translating new scientific advances to studies in humans (e.g., implantation of artificial hearts). The second is that a known or credible risk exists for significant harm to humans as a consequence of experimental intervention without the off-setting potential for direct medical benefit (e.g., sham surgery). The third criterion is that the protocol raises ethical questions about research design or implementation for which no consensus exists or for which guidelines are conflicting or ambiguous (e.g., placebo trials when effective treatment exists).[20]

Expedited review

Expedited or delegated review is a process normally applied to studies of minimal risk with no novel or worrisome ethical issues. Although widely understood to mean "speed up the process of,"[21] the word "expedite" etymologically denotes a removal of restrictions or impediments.[22] In this sense, expedited review can be thought of as relaxing the usual procedures of a full review by a research ethics board. This relaxation of restrictions generally makes expedited review faster and administratively less cumbersome than full review. While some debate remains about the circumstances under which such relaxation of procedures should be applied,[23] research ethics boards generally employ expedited review when research protocols are deemed to present no more than minimal risk[19,24] (admittedly a difficult standard to operationalize consistently).[25–27]

Framework for emergency ethics reviews

Our proposed framework for emergency ethics reviews explicitly combines increased diligence (similar to that of special scrutiny)[10] with enhanced procedural flexibility (consistent with expedited review) in a manner that is proportionate to the perceived risks and specific circumstances associated with the research protocol. Although each of these guiding concepts focuses on a specific dimension of research ethics review, they have not been combined explicitly. Yet in emergency circumstances, precisely this combination of speed, depth and proportionality of review is required.

An emergency ethics review would be triggered by an official declaration of a public emergency, as has been proposed for any exemptions to normal review procedures during emergencies in the revised draft second edition of the *Tri-Council Policy Statement*.[10] This restrictive application would limit arbitrary demands on research ethics boards and help to reinforce the notion that any exemptions to normal practices in research ethics review should be rare and should require a high level of justification. Protocols submitted to a research ethics board under a designation of emergency review would immediately be assessed (either by the chair of the research ethics board or, ideally, by an

Table 1: Summaries of some literature related to research ethics review under emergency circumstances

Author	Summary
Whitley[13]	This commentary from the *Wall Street Journal* highlights how worldwide research efforts were hampered during the SARS epidemic because of inability to obtain REB approval.
Quick[14]	Although some issues of the research ethics review proposed after the Oklahoma bombing in 1995 are discussed (e.g., the potential value of a centralized single Institutional Review Board model), this report does not discuss details of the procedures or mechanisms used in Oklahoma.
Black[15]	Internationally, research during humanitarian emergencies has been characterized as ad hoc and unregulated.
Ford et al.[16] and Schopper et al.[17]	Médecins Sans Frontières, which provides humanitarian aid and conducts research in public emergencies,[16] recognizes three levels of research ethics review: full board review, expedited review, and exempt from review.[17]
Exploratory Committee on Research Ethics and Public Emergencies[11]	A range of legal principles and general frameworks is cited (e.g., *Siracusa Principles on the Limitations and Derogation Provisions in the International Covenant on Civil and Political Rights, 1984),*[18] but no specific guidance related to research ethics procedures during emergencies is identified.

Note: REB = research ethics board; SARS = severe acute respiratory syndrome.

emergency review subcommittee established in advance) for the risks associated with the proposed research, as well as the identification of important novelties or uncertainties that might require enhanced scrutiny. A summary of the framework for emergency review and its application is presented in Table 2.

Enhancing diligence

Complex protocols and those assessed as involving a high level of risk to the participant or to the community would be assigned a greater number of principal, or "in-depth" reviewers, representing relevant expert perspectives. The chair of the research ethics board would be free to call on nonmembers of the board for special expertise. Reviewers could also be directed to focus their attention on aspects of the proposal that align directly with their expertise and to limit their reviews to very specific questions. Such an approach would not only enhance attention to ethically relevant aspects of the study, but would also improve the availability of members of the research ethics board for other time-sensitive reviews related to the emergency. The use of nonexperts by research ethics boards in addition to expert members would provide redundancy in the review, which is a key measure for enhancing scrutiny.

Research submitted to a research ethics board for review during an emergency may not have outside funding and thus may not have been peer reviewed for scientific merit.[14] The research ethics board may decide that there is a greater than usual requirement for both scientific and ethics evaluations in emergency circumstances, such as whether sufficient animal or preliminary human safety data are available for a new application of an existing therapy. Research ethics boards could also require heightened monitoring of a proposed study as a means of enhancing ongoing assessment of risks and potential benefits. This requirement might be particularly appropriate for protocols in which understanding of the risks and benefits of a novel intervention is expected to evolve quickly (e.g., in a treatment trial of an acute, life-threatening disease). Early detection of toxicities or other harmful effects of a research intervention could help to reduce research-related harms by leading to adjustments in protocol or, if necessary, termination of the intervention.

Increasing procedural flexibility

Rather than providing a broad suspension of the usual procedural requirements of national and international guidance documents, emergency ethics review would require that any

Table 2: Application of an emergency ethics review process triggered by declaration of public emergency

Procedural requirements that may be altered	Procedures that may increase diligence	Factors relevant to diligence and speed of review
REB membership		
• Variable number of reviewers • Public representation changes according to the issues raised in protocol • Expertise of reviewer varies by protocol	• Redundancy of review • Multiple perspectives	• Complexity of protocol • Assessment of risk
Review time		
• Time to initiate review occurs within hours of receipt of protocol • Time to carry out the review changes according to the issues raised in protocol • Streamlined format for communicating with researcher decreases waiting time	• Prioritization of relevant protocols • Reduction of competing demands on REB members	• Urgency of the proposed research • Risk–benefit ratio
Assignment burden for reviewers		
• Expert reviewers review only protocols directly related to their expertise so that overall burden of review may be reduced	• Reduction of competing demands on REB members	• Complexity of protocol • Urgency of the research
Meeting format		
• Face-to-face or virtual depending on availability of reviewers or physical limitations imposed by the emergency	• Redundancy of reviewers • Multiple perspectives	• Complexity of the emergency • Urgency of research
Scientific peer review		
• May or may not be needed depending on what review has already occurred	• Assessment of value and validity	• Risk of protocol to participants • Complexity of protocol • Controversial nature of proposal
Monitoring		
• May be increased where risk is high or uncertain	• Ongoing assessment of risks and benefits	• Complexity of protocols • Difficulty in assessing future risk • Risk to participants or research staff

Note: REB = research ethics board.

relaxation or alteration of these requirements be proportionate to the complexity and urgency of the emergency and to the risks posed by the specific research proposals under review. Depending on the volume of submissions to a research ethics board, protocols related to an emergency may either be reviewed individually by the chair of the board or the chair's delegate (as is usually done in expedited or delegated review), or examined by the chair or a specific triage committee and prioritized according to applicable substantive ethics guidelines. Where protocols are deemed to be beyond minimal risk, judgement would be required to determine the necessary number and expertise of reviewers. Teleconferences or video conferences[28, 29] could accommodate reviewers' schedules and possible restrictions on reviewers' mobility — a circumstance that prevented many meetings of research ethics boards when isolation and quarantine procedures were applied during the Toronto SARS outbreak. The aims of the proposed procedural flexibility would be to enhance scrutiny wherever possible and ensure timeliness of review.

Use of the model on a policy level

The main innovation of the emergency ethics review is a merging of three established guiding concepts for research ethics review procedures (i.e., proportionality, special scrutiny and expedited review) into a single framework for emergency circumstances. Emergency ethics review responds to the three main policy challenges of research ethics review, which are likely to be magnified in emergencies. First, research ethics boards and their institutions are responsible, and must be accountable, for thorough and careful review of research proposals. Second, especially in emergency circumstances, failure to conduct a high-quality review with sufficient speed can result in lost opportunities to gain critical knowledge. For example, in the treatment of unknown or poorly understood pathogens, our ability to resolve important clinical questions quickly may be a key determinant of case fatality rates for an infectious disease outbreak. And third, in all cases, the level of scrutiny and flexibility in procedural standards must be proportionate to the risks and uncertainties involved.

Emergency ethics review is not a framework of substantive ethical principles or a how-to guide for research ethics boards to respond to individual emergencies. Rather, we view it primarily as a tool to help research ethics boards and institutions plan their emergency procedures in ways that will ensure the best fit between the procedures of review and the special demands imposed by emergency circumstances. As with any new policy model, the merit of the emergency review will need to be determined by its application and evaluation in real emergency situations. In many countries, regulation of research and research ethics review falls to a national body; thus, acceptance of this framework might need to be incorporated into national research guidelines. Planning and institutional support can allow research ethics boards to have the appropriate documentation and evaluative strategies in place in the event of an emergency and permit the necessary collection and evaluation of data.

Similar tools to enhance the quality and reliability of research ethics review have been applied to good effect. For example, the Alberta Research Ethics Community Consensus Initiative has developed a tool that assigns a numeric estimate of risk in each research proposal.[30] As part of the implementation process, the emergency review process should be formally tested to understand its strengths and weaknesses. This testing could be done initially under normal circumstances using a small proportion of high-risk submissions to a research ethics board. A comparison of two research ethics boards reviewing the same protocols (as would occur in a multicentre clinical trial) might be conducted, with one using the emergency review process and the other its usual procedures. Alternately, a pre–post comparative design might be used, or even a randomized comparison of research ethics boards assigned to either the emergency review process or normal procedures. This type of testing would familiarize research ethics boards with the framework for emergency review and, if shown effective in trials, facilitate its use during a public emergency. Several practical elements, such as a process of electronic submissions and the development of video conferencing capabilities, might be developed concurrently with testing of the emergency review process. The variable capacity among research ethics boards around the country to ensure the kind of scrutiny we envision might prove to be a challenge to implementation. Therefore, our proposal would require some preparedness planning for successful implementation.

The framework for emergency ethics review may also be useful for improvement of research ethics review procedures more generally. Pilot-testing the process of emergency ethical review under normal circumstances may help prepare research ethics boards for emergencies. At the same time, it may offer insights into whether this strategy can improve both the quality and efficiency of review. If so, emergency ethics review might prove to be useful beyond emergency circumstances.

This article has been peer reviewed.

Competing interests: Ronald Heslegrave is employed by the University Health Network of Toronto, where he is chair of the Research Ethics Board, and has received travel assistance to attend academic conferences in this capacity. He has received a grant from CIHR for a study related to research ethics, for which he is co-investigator. He is also ethics delegate for the Institute for Cancer Research of the Canadian Institute for Health Research. None declared for Catherine Tansey, Margaret Herridge or James Lavery.

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