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Submission to the National Health and Medical Research Council: National Statement on Ethical Conduct in Human Research
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ISSUES PAPER: REVIEW OF NATIONAL STATEMENT SECTION 4 – ETHICAL CONSIDERATIONS SPECIFIC TO PARTICIPANTS

PART ONE: SHOULD THE NATIONAL STATEMENT CONTINUE TO REFER TO VULNERABLE GROUPS?

Question 1: Should the National Statement continue to be organised around categorising or specifically naming groups of potential research participants as requiring special consideration due to their (presumed) vulnerability?

Generally, ACEM considers that it is reasonable for the National Statement to continue to be organised around categorising or specifically naming groups of potential research participants as requiring special consideration due to their (presumed) vulnerability. At the same time, the College also considers that in the context of emergency medicine research, the National Statement could be rephrased to guide a requirement for researchers to give further consideration when the research involves individuals in circumstances that compromise their ability or capacity to fully engage in an ethical discussion of benefits and risks related to research participation. In these cases, the focus should always be on the ethical nature of the proposed research, rather than on vulnerability as an organising principle for potential participants. The College agrees with the comments in Part One of the Issues Paper, in that categorising certain cohorts as vulnerable may limit and/or impede important health and medical research, especially in individuals who are unable to consent. The College supports the Canadian Tri-Council Policy Statement (TCPS2) approach, in which the application of Article 4.7 states that 'individuals should not automatically be considered vulnerable simply because of assumptions made about the vulnerability of the group to which they belong … [but rather consideration of] … their particular circumstances … in the context of the proposed research project.[1]

Question 2: Do you support a focus on vulnerability as existing on a spectrum and on the characteristics and circumstances that may limit an individual participant's ability to fully safeguard their own interests in the context of a specific research project?

In the context of our response to Question 1, ACEM retains support for a focus in the National Statement on vulnerability as existing on a spectrum, and on the characteristics and circumstances that may limit an individual participant's ability to safeguard their own interests in a specific research project. ACEM recognises that each individual participant's circumstances will have an effect on how much their vulnerability impacts this ability. Their vulnerability may also be a characteristic targeted by a specific research project, and participation may lead to personal and societal benefits, as per research in paediatric emergency medicine. However, ethical guidance that clearly conceptualises the spectrum of vulnerability must be included in the National Statement. ACEM considers that any ambiguity may exacerbate the current situation in emergency medicine research ethics, in which different Australian jurisdictions, or even the same human research ethics committee (HREC) in one jurisdiction, make different assessments and interpretations of research proposals against the National

[1] Panel on Research Ethics. The Canadian Tri-Council Policy Statement. Fairness and Equity in Research Participation. Ottawa ON: Government of Canada; 2014. Available from: http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/chapter4-chapitre4/

Statement. These differences place an additional regulatory burden on researchers, and limits Australia's ability to successfully conduct multi-jurisdictional and multi-site emergency medicine research studies.

Question 3: Is there merit in preserving explicit reference to categories of participants in Section 4 who may warrant additional or special consideration? If so, which groups merit inclusion and what is the best way to describe these groups of participants?

ACEM agrees there is merit in preserving explicit reference to the categories of participants in Section 4 that may warrant additional or special consideration. In emergency medicine research, these categories should be based on health related characteristics that compromise individual ability or capacity, e.g. in individuals with critical illness/injury, cognitive impairment, or mental illness. The College believes there is merit in the National Statement continuing to include particular participant groups, such as infants, children aged under 12, victims of crime (past or present) and people potentially participating in illegal activities. Prisoners and persons in police custody warrant additional or special consideration because of potential coercion risk, although this will depend on research design. Researchers need acknowledgement in the National Statement that the group under study is 'vulnerable', 'special' or 'at risk', with a clear set of ethical guidelines and actions that must be taken to accommodate this vulnerability. This gives members of these groups the opportunity to participate in research, rather than denying them the right and potential benefit of doing so. On the other hand, while there is merit in abandoning categorisation of racial groups such as Aboriginal and Torres Strait Islander (ATSI) Peoples as 'vulnerable', the College defers to consensus among ATSI Peoples regarding their inclusion or exclusion.

PART TWO: EXPLORING ALTERNATIVE FRAMEWORKS

Question 4: Does the identification of characteristics and circumstances that merit 'ethical consideration specific to participants', such as decision-making capacity, potential for exploitation and other inequalities, sources of vulnerability or unique sensibilities, provide a useful framework for organising the content of Section 4?

The identification of characteristics and circumstances that merit 'ethical consideration specific to participants', such as decision-making capacity, potential for exploitation and other inequalities, source of vulnerability or unique sensibilities, is considered by ACEM to provide a useful framework for organising Section 4, and particularly important in the consideration of ethical research by HRECs.

Question 5: Does a focus on two core considerations: (1) characteristics of participants and (2) contextual features of the research (see page 7) provide a useful framework for organising the content of Section 4?

ACEM considers that a focus on two core considerations, (1) characteristics of participants and (2) contextual features of the research, provides a reasonable and useful framework for organising the content of Section 4. However, if these two core considerations are too broad, there is potential for 'ethics committee creep', leading to foreseeable increases in individuals being identified as potentially vulnerable and requiring special consideration. Specific measures should be included in the National Statement to protect groups where there is consensus on vulnerability that simultaneously provides for their research participation, and subsequently advances knowledge in the care of similarly vulnerable populations.

Question 6: in addition (or in preference) to the concepts, issues and frameworks described in this section of the Issues Paper, are there other concepts, issues or frameworks that you consider to be useful in organising the content of Section 4? If so, what are these concepts, issues or frameworks?

In addition to the concepts, issues and frameworks described in Part Two of the Issues Paper, ACEM considers that Section 4 of the National Statement should directly address and provide clear guidance on the concept of situational incapacity in emergency medicine research, the time-critical nature of emergency medicine research

and the specific constraints in obtaining prospective informed consent in emergency medicine research. The College also considers that an expert on emergency medicine research from which HRECs can seek advice would form part of any useful alternative framework.

PART THREE: PROMOTING OPPORTUNITIES FOR INCLUSION

Question 7: If guidance is provided in Section 4 that promotes the inclusion of groups of people often excluded from research, should those participant groups be listed?

ACEM applauds the NHMRC and AHEC on efforts to promote inclusion of groups often excluded from research in Section 4 of the National Statement, and supports the listing of participant groups. Any list in Section 4 should include people requiring and receiving emergency medical care, people highly dependent on medical care, victims of crime (past or present), infants, children aged 12 years and under, and pregnant women and the foetus.

Question 8: Would it be useful for the guidance provided in Section 4 to address the most common constraints and impediments on participation or those that have the greatest impact on their exclusion or lack of participation? If so, which constraints and impediments should be addressed?

ACEM considers that Section 4 should provide clear guidance regarding the inclusion of acutely ill and injured patients in emergency medicine research. Emergency department patients are often excluded from research because they are often unable to participate in a prospective informed consent process. Section 4 of the National Statement should address specific constraints and impediments to research participation in emergency medicine, such as cognitive impairment or acute loss of capacity in unconscious patients and people in cardiac arrest.

It is pertinent to highlight here the dearth of evidence supporting many established emergency medical treatments – see adrenaline in cardiac arrest – and the urgent need to undertake high quality, ethical research trials to establish questions of efficacy and harm. The overriding principle for participation should be the scientific merit of the research and the relative balance of the benefits and risks to participants, which is best addressed by a properly constituted HREC together with local research governance systems. Depending on the nature and design of the research, options in these circumstances include (1) waiver of consent, (2) abbreviated verbal consent to allow initiation of care, followed by more formal consent processes to continue/withdraw participation once stabilised, (3) proxy consent from the patient's next of kin (NOK) or guardian, and (4) delayed/deferred consent under an initial waiver or NOK consent. In ACEM's view, the Department of Health and Human Services Victorian-Specific Modules[2] provide a sensible approach to this dilemma (see guidance on page 3 of 17 for research that involves a "medical research procedure" and Section 1.3 emergency medical research procedure on page 5 of 17).

Question 9: Guidance on ethical considerations specific to participants applies to the targeted, intentional recruitment of identifiable groups of participants and to those whose participation in significant numbers is likely or foreseeable. Should this guidance also apply to the incidental involvement of individuals in a research project? If so, how should 'incidental involvement' be defined?

Guidance on ethical considerations specific to participants should also apply to the incidental involvement of individuals in a research project and be defined in the National Statement. Incidental involvement could be defined as becoming enrolled in a research project by virtue of being a member of the broader population of interest, with an equal chance of being targeted by the research project as any other member of that broad

[2] Department of Health and Human Services. Victorian-Specific Module Guidelines. Melbourne: State Government of Victoria; 2018. Available from: https://www2.health.vic.gov.au/about/publications/formsandtemplates/Victorian-Specific-Module-Guidelines.

population.

PART FOUR: GUIDANCE FOR RESEARCH INVOLVING ABORIGINAL AND TORRES STRAIT ISLANDER PEOPLES

Question 10: Is the scope of guidance provided in Section 4 related to research involving Aboriginal and Torres Strait Islander Peoples appropriate and is the guidance adequate? If not, what is the more appropriate scope of this guidance and/or what ways is the guidance not adequate?

ACEM considers that the scope of guidance provided in Section 4 related to research involving Aboriginal and Torres Strait Islander Peoples is appropriate and adequate. However, as per our response to Question 3, the College defers to consensus among ATSI Peoples regarding the scope of this guidance.

PART FIVE: EMERGENCY CARE RESEARCH AND OTHER ISSUES IN CHAPTER 4.4

Question 11: In what ways, if any, should guidance for the conduct of emergency care research differ from guidance for other research involving people highly dependent on medical care who may be unable to give consent (such as intensive care research and research with unconscious people)?

ACEM considers that guidance for the conduct of emergency medicine research differs from guidance for other research involving people highly dependent on medical care who may be unable to give consent. Much current clinical emergency medicine practice is not based on gold standard, level one evidence. Guidance on alternative consent models must be included in the National Statement to improve patient safety and best practice in emergency medicine. ACEM emphasises that the overwhelming majority of clinical researchers have strong and altruistic drives to improve patient safety and care. Without clinical research that examines key treatment options for critically ill and injured patients, advances in safety and efficacy are not possible.

ACEM considers that the worst scenario for emergency medicine is for changes in clinical management to occur within a scientific vacuum. As one example, different doctors can clinically choose to prescribe two different treatments for the same condition, based upon their personal preferences. However, if this random clinical approach were to be structured into a clinical trial, the ethical governance and regulatory burden would be problematic and difficult. Such an approach can lead to perverse situations in which the sickest and most vulnerable patients continue to be given outdated, unproven and possibly harmful treatments, because they are denied the right to participate in research that seeks to test new treatments and address questions of efficacy or harm. This approach also denies future emergency department patients – or the same patient re-presenting with future episodes – and the public the chance of better health and medical outcomes from earlier application of innovative techniques and insights. It is of substantial concern to ACEM that the most sick and injured people in the community often receive established treatments that are of unproven benefit and possibly even harmful. ACEM considers that this is unethical; while scientifically valid research with appropriate safeguards to resolve this situation is not. Rather than these circumstances being a barrier to research, the NHMRC and AHEC need to be proactive in this area and make clear positive statements in the National Statement that articulate the ethical imperative to undertake research among patients in these circumstances.

The unique aspect of emergency medicine research is the time critical nature of the intervention, or the short therapeutic window. This may also be true in critical care settings, and in other persons highly dependent on medical care. Time is always a major consideration, often precluding next of kin (NOK) involvement for consent. When immediate lifesaving treatment is required in cardiac arrest or major trauma, it is simply impractical to seek proxy consent from a family member or guardian. Such events are unplanned and therefore, research into improving diagnosis and treatment cannot be scheduled or consented in advance. The same principle applies to obtaining research data and blood samples in rapidly changing clinical situations involving dynamic conditions such as anaphylaxis.

In other situations, when interventions do not need to be administered immediately, it is often not reasonable for patients (or proxies) to make truly informed decisions about participation, and alternative strategies need to be employed. Moreover, the emotionally charged settings of sudden adverse changes in a loved one's health status are very difficult environments to introduce a discussion about research participation. In some circumstances, a waiver of consent may be more appropriate, or a modified consent process, but most traditional approaches for obtaining informed consent are neither appropriate nor valid in many emergency medicine research contexts.

There are clearly vulnerable groups that present to emergency departments with permanent vulnerabilities, e.g. people with dementia. Section 4 must include guidance for groups like these. Other groups are temporarily vulnerable, and guidance may differ from guidance for the permanently vulnerable. Both groups should be allowed to be included in supervised research, with appropriately defined safeguards. The concept of incremental risk may be of value. Feasible alternatives for emergency medicine research must be an essential element of the revised Section 4. Guidance for deferred versus waived versus proxy consent may differ depending on the particular group and research design, but these differences are warranted. Again, the overriding principle should be the merits of the research question and the potential benefits and risks associated with research participation, balancing the principles of equity and justice. A properly constituted HREC is capable of making this determination, with appropriate guidance from the National Statement.

Question 12: If Section 4 were to include guidance related to (non-clinical) emergency or disaster research, what, specifically, should be the content of that guidance?

ACEM considers that content in Section 4 should also include guidance related to non-clinical emergency and disaster research. Guidance should recognise that data collection and outcome evaluation for these rare events is essential to inform emergency and disaster responses to future events. The unpredictability and timing of non-clinical emergencies and disasters precludes prospective HREC approval, but the global nature of these incidents require study and publication in the literature to disseminate findings and translate lessons learned. For example, recent international mass casualty incidents have published detailed operational clinical information about the emergency response, which helps agencies elsewhere review and implement appropriate preparedness initiatives and programs.

Question 13: Should the National Statement permit the use of non-HREC review pathways for research involving participants (groups, cohorts or individuals) who otherwise merit special consideration in the current Section 4?

According to ACEM, the National Statement should permit the use of non-HREC review pathways for research involving participants who otherwise merit special consideration in the current Section 4.

STATEMENT

On Friday 11 May 2018 at 15:17 this paper was submitted by Shelley Cogger (via the policy@acem.org.au email address) to the National Health and Medical Research Council (NHMRC) Online Services website: https://online.nhmrc.gov.au/consultation/nhmrc-targeted-consultation-issues-paper-review-national-statement-section-4.

Submission received:
https://online.nhmrc.gov.au/node/33018/done?sid=548&token=6d5ddf0d66120e9ccf5372adbd4bdc9d

Reviewed by Doctor Simon Judkins, ACEM President, on 10 May 2018.