



Special issue highlighting research at RPH

REVIEW AND COMMENT

THE CHALLENGES OF OBTAINING CONSENT IN EMERGENCY CARE RESEARCH

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Abstract

It is not possible to consent a patient for emergency research in advance of their acute illness, as the clinical events are not predictable. We discuss the problems of undertaking research in an emergency care setting, where patients lack the capacity to provide consent but require time critical interventions. There is no settled definition of what constitutes 'research' as distinct from 'treatment'. In fact their relationship is a continuum that demands similar level of oversight for both. We provide examples where the usual requirement for written informed consent means the trial underestimated benefits, because the treatment would normally be given without delay. Consent rituals that delay the start of trial treatments may in fact be unethical and offend against the Declaration of Helsinki. Clinical research delivers improved patient outcomes irrespective of the randomised group. This is currently under threat by a lack of consistency across jurisdictions in the interpretation of the relevant legislation. *Tasman Medical Journal 2020; 2(1): 11-14*

INTRODUCTION

Each year there are over 8 million attendances at emergency departments (ED) in Australia. The ED is the interface between the community and the hospital, and patients either self-refer, attend by ambulance, or are referred by GPs and other agencies, for example, police. Emergency Medicine (EM) is concerned with the assessment and management of the acute and urgent aspects of all physical and behavioural disorders in all age groups. The wide range of presentations is matched by the wide spectrum of severity, from life-threatening to self-limiting conditions.

In Australia and internationally, EM seeks to advance knowledge through scientific research. EM research is often undertaken in collaboration with other disciplines within the hospital, community and in pre-hospital (ambulance) care. Research improves clinical outcomes irrespective of the group to which the patient was randomised.^{1,2,3} Like other areas of clinical practice, a substantial proportion of established emergency care is based on consensus and expert opinion rather than robust high-level evidence from research trials. Undertaking research in the pre-hospital setting or ED presents specific challenges.

Assessing eligibility for research participation of an undifferentiated patient who presents acutely and may have time-critical and potentially life-threatening illness or injury requires skill and a pragmatic approach. This can be achieved ethically with good study design, robust research infrastructure and a supportive organisational culture.²

CHALLENGES IN EMERGENCY CARE RESEARCH

One of the biggest challenges is obtaining consent. The standard procedures for obtaining written informed consent for research participation have been developed for situations where there is time for the patient to digest information and ask questions, for example in an outpatient clinic setting with an already-established doctor-patient relationship. These circumstances do not apply in emergency care. It is not possible to consent someone in advance of their acute illness or injury, as the events are often unanticipated, as in major trauma. Patients are often too unwell to provide informed consent. Obtaining proxy consent from next-of-kin, who may or may not be present, can be impractical for a time-critical situation, and presenting a distressed family member with a multi-page information and consent document is intrusive and unreasonable.⁴ Indeed, there have been calls for special training or accreditation for ethics committees considering emergency care proposals.⁴ In some jurisdictions, these difficulties have resulted in bureaucratic or legal impediments to undertaking essential research in an ED and prehospital setting. This also applies to essential research activity in intensive care units, where similar circumstances apply.

Research not only leads to better treatments, but also identifies practices found to be ineffective or harmful. Relevant examples include steroids for acute spinal cord injury, gastric lavage for toxic ingestions and activated protein C for sepsis. Examples of current treatment uncertainties relate to the use of intravenous fluids in shock resuscitation, the dosing of oxygen following cardiac arrest resuscitation, and the early use of fibrinogen concentrate in major trauma-related bleeding. These are a few examples of a plethora of everyday clinical situations where high-level evidence that would be available from quality research is lacking. All of these situations require

timely intervention in circumstances where the patient is likely to lack capacity to provide written informed consent. Community attitudes are supportive of waiver of consent in such circumstances.^{4,5} For this to be considered ethical, the ED researcher has to assume responsibility for both the conduct of the trial AND the waiver of consent, as well as the treatment of the patient. This concept is controversial and can be the cause of the impediments mentioned above. In order to determine what is in the best interests of patient care, however, it must be thought through and overcome.

Adopting special arrangements for consent (eg waiver of consent or delayed consent) is not a theoretical concept, but one that contributes to avoidable mortality and morbidity. In the CRASH trial of corticosteroids for acute severe head injury, waiver of consent improved time to treatment by 1.2 hrs.⁶ In the CRASH-2 trial of tranexamic acid for trauma, it is estimated that a 1 hr treatment delay due to consenting requirements reduced the proportion of patients who benefited from the trial treatment from 63% to 49%.⁶ The requirement for written informed consent means the CRASH-2 trial underestimated benefits, because treatment would normally be given without delay.⁶ Some have argued that consent rituals that delay the start of trial treatments are actually unethical and offend against the Declaration of Helsinki.⁶ The imposition of different standards for consent to treatment prescribed within or outside clinical trials is illogical.⁷

State and territory legislation governs consent for the provision of medical care across Australia, and therefore conditions vary amongst the seven jurisdictions. All jurisdictions allow emergency medical treatment to be delivered without prior consent if the treating doctor believes, in good faith, that the intervention is in the best interests of the patient and necessary in order to prevent death or injury, provided the patient has not previously refused such treatment in an advance directive. However, these provisions do not necessarily extend to consent for research participation. As a result, this question is currently the subject of legislative reviews in several Australian states. The text of the various Australian Guardianship Acts (which contain the legal requirements for consent) varies across the country, and each Act is subject to

different interpretations. This is leading to multicentre ED trials being approved in some states but not in others. For example, the EXACT Study (Reduction of Oxygen After Cardiac Arrest; ClinicalTrials.gov NCT03138005), compares 100% oxygen vs titrated oxygen after a non-traumatic out of hospital cardiac arrest. The rationale is that 100% oxygen (current routine practice) may increase neurological injury compared to titrated inspired oxygen.⁸ This study is funded by the National Health and Medical Research Council (NHMRC) and is currently recruiting in Victoria and South Australia, but cannot achieve institutional research governance approval in Western Australia, despite Human Research Ethics Committee (HREC) approval.

A key problem is that there is no settled definition of what constitutes 'research' as distinct from 'treatment'. Without an agreed approach, attempting to define this in law, and to describe circumstances in which research may or may not be permissible, can lead to confusion and inconsistency. Patients and the community are the losers.

The NHMRC guidelines on the Ethical Conduct of Research in Humans describe the issues surrounding patients who lack capacity to consent for research participation, including those 'highly dependent upon medical care.'⁹ The guidelines state that where a participant lacks capacity to consent, this should be sought on their behalf from a 'guardian, or person or organisation authorised by law'. There are also circumstances specified where, again provided this is consistent with law in the relevant jurisdiction, research participation may be approved without prior consent provided a number of tests are satisfied. These requirements are best assessed by a HREC, which is uniquely placed to weigh all of the competing issues including the clinical importance of the problem, the scientific merits of the proposal, the adequacy of safety and monitoring procedures, and the overarching ethical principles of autonomy, beneficence, equity and justice.⁷ The prospective balancing of these considerations by a properly-constituted HREC should provide public confidence that the authority the HREC assigns to an emergency/critical care researcher to waive consent will be carried out responsibly.

Emergency Physicians, along with others who care for the seriously ill and injured, are strong advocates for their patients. At the heart of this is the delivery of high-quality, evidence-based clinical care. Responsibility for the welfare of our patients is keenly felt, and this is not diminished when it comes to enrolling patients into research.

In a modern, knowledge-driven health industry, the distinction between treatment and research may be arbitrary and anachronistic. In fact, patients are more protected in a research trial than in routine clinical care.¹⁰ Unwarranted practice variation or the introduction of unproven treatments into practice exposes patients to unregulated risk, but researchers who try to study these risks in a risk-reducing way are hampered by burdensome regulation.¹⁰ As a multi-billion dollar enterprise primarily concerned with the health and wellbeing of all citizens, we need to operate within a 'virtuous cycle' of continuous evaluation and improvement. We would be better off thinking about a continuum between clinical care and research and demanding a similar level of oversight for both.¹⁰

The alternative is a situation where it is acceptable to continue to deliver unproven, ineffective, and possibly harmful treatments to patients, but unacceptable to undertake the necessary research to resolve these questions of efficacy and harm. It is not the act of randomisation that confers risk but the nature of the interventions. Patients will be safer and knowledge will be gained when interventions of uncertain value are evaluated in well-designed and properly conducted trials with appropriate ethical oversight.

CONCLUSION

Australia has been a leader in the last two decades in the field of emergency/critical care research, with advances that have resulted in enormous benefits to patients and to wider society. Much of this has been publicly funded, 'common good' multicentre clinical research delivering improved patient outcomes and better value for funders. This is currently under threat by a lack of consistency across jurisdictions in the interpretation of the relevant legislation. Although well intentioned, an absolutist approach denies the sickest and most vulnerable patients the right to benefit from participating in research. Our profession must

advocate strongly on this issue and ensure it is placed on the national agenda.

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Conflicts of interest: All authors are engaged in Emergency Care research and are affected by the circumstances in Western Australia as described in this article.

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