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Refining the Enrolment Process in Emergency Medicine Research

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Abstract

Research in the emergency setting involving patients with acute clinical conditions is needed if there are to be advances in diagnosis and treatment. But research in these areas poses ethical and practical challenges. One of these is the general inability to obtain informed consent due to the patient's lack of mental capacity and insufficient time to contact legal representatives. Regulatory frameworks which allow this research to proceed with a consent 'waiver', provided patients lack mental capacity, miss important ethical subtleties. One of these is the varying nature of mental capacity among emergency medicine patients. Not only is their capacity variable and often unclear, but some patients are also likely to be able to engage with the researcher and the context to varying degrees. In this paper we describe the key elements of a novel enrolment process for emergency medicine research that refines the consent waiver and fully engages with the ethical rationale for consent and, in this context, its waiver. The process is verbal but independently documented during the 'emergent' stages of the research. It provides appropriate engagement with the patient, is context-sensitive and better addresses ethical subtleties. In line with regulation, full written consent for on-going participation in the research is obtained once the emergency is passed.

Keywords

informed consent; emergency medicine research; consent waiver; assent; mental capacity

Introduction

Research in the emergency setting involving patients with acute clinical conditions (including acute myocardial infarction (AMI) and stroke) is needed if there are to be advances in the diagnosis and treatments of those conditions. Despite its importance, research in these areas poses several ethical and practical challenges, not least in the area of patient consent. Fully informed consent, a central pillar of research ethics, cannot, for the most part, be obtained where the patient is in severe pain, incapacitated or under influence of powerful analgesic or sedative medication and where treatments need to be given very rapidly.

Regulatory frameworks have been developed to allow this research to proceed with a consent waiver but these frameworks miss important ethical subtleties. The process of enrolment described below applies to research involving patients who may be unable to provide written, fully informed consent because of an acute clinical condition and for whom there is no time to contact an approved representative. It represents a significant refinement of the simple consent waiver because it captures important ethical nuances without jeopardising the conduct of research.

Emergency Medicine Research

Well-known clinical trials such as ISIS (1, 2, 3), TROICA (4), CRASH (5,6), PAD (7) and PolyHeme (8) have all contributed significantly to acute patient care but they have also raised the profile of the ethical issues. Including UK patients in the international TROICA trial was initially prohibited by the UK Medicines for Human Use Act as this did not permit consent waivers. TROICA prompted an amendment to the Act (9, 10). In the US a range of trials and the generally recognised need to conduct research on resuscitation led to the production of the US Federal Regulations on the exception from informed consent in emergency research (11, 12).

There is a definite and continued need for research studies and clinical trials involving patients who are in the most acute clinical conditions in the emergency setting. For example, thrombolysis and emergency percutaneous coronary intervention (PCI) have yielded major benefits for patients compared with the pre-thrombolytic era. Further advances in the management of AMI require new experimental medicine studies and clinical trials, which are likely to be conducted within the context of immediate diagnosis and treatment by emergency PCI.

Ethics and regulation

There are two conventional principles of research ethics that conflict in the emergency medicine research context. First, it is ethically important that research in emergency medicine should proceed. As outlined above, without the knowledge that such research generates, emergency medicine clinicians are unable to discharge their obligations to continue to increase benefit and reduce potential harm to their patients. Second, it is usually considered imperative that participants give fully informed consent to be enrolled in the study (13, 14, 15).

Regulatory systems across the globe recognise that often both of these requirements cannot be satisfied in the emergency context. Patients require treatment urgently so there is little time for explanation, discussion and reflection. Patients may also be in extreme pain or shock, suffering from hemodynamic compromise, have already received opiates or be terrified thus compromising their capacity to make a considered decision. Both time and capacity are required for fully informed consent (16, 17). As a result the regulatory systems generally grant, under certain conditions (see Figure 1), an exemption from the requirement to obtain informed consent. Most importantly this exemption is based on the idea that informed consent requires capacity and that capacity will be lacking in many of the potential subjects of this research.

The new EU Clinical Trials Regulations No 536/2014 (18) with application from May 2016 accepts a “derogation” from written informed consent in certain emergency situations where it is not possible to obtain informed consent prior to an individual’s participation in a trial. In the UK the Medicines for Human Use (Clinical Trials) Amendment (No.2) (19) and the Mental Capacity Act (20) both allow research to be conducted on patients who lack capacity, with a ‘waiver’ of consent. In the US, the Federal Regulations allow an exception from the requirement to obtain informed consent (12, 21). In both cases, the authority to approve the use of the waiver is granted to Research Ethics Committees (RECs) subject to certain constraints (see Figure 1). More broadly, both the International Council for Harmonisation Good Clinical Practice Guidelines (ICH-GCP) and the Council for International Organizations of Medical Sciences (CIOMS) explicitly permit research on patients with acute clinical conditions subject to conditions very similar to those in place in the UK and the US (14, 15).

The problem

Research in the emergency context may need to be conducted even when the potential subject is incapable of giving their consent. For patients who are unconscious and when the relevant regulatory conditions (see Figure 1) are met, the requirement to obtain informed consent for these interventions can be waived. There will however be a group of patients who are conscious but will clearly lack capacity; others will remain on the edge of capacity; while still others will maintain the ability to make decisions. In ethical and legal terms, for this group of patients, the important issue is capacity: if the conscious patient has the capacity to decide, the regulations (and hence the consent waiver) do not apply. Not only is the capacity of patients in this group variable and often unclear, but because they are conscious they are also likely to be able to engage with the researcher and the context to varying degrees.

One option is to formally assess the capacity of potential research participants. This faces several serious difficulties. First, there are practical difficulties with requiring a suitably qualified individual always to be available for the formal determination of capacity. Second, such an assessment would take time where little or none may be available. Third, requiring a determination of capacity presumes that capacity is a binary concept. Capacity is usually taken to involve the ability to comprehend, retain and use information in making a decision (22). But clearly each person’s ability to satisfy these conditions will vary with context and

content and hence, that capacity will be a matter of degree (23). In considering issues of research ethics, there is a mismatch between the binary operation of the consent waiver and the extent to which individuals are able to comprehend what is happening to them. The problem here is that an individual may fail the ‘capacity test’ and yet be conscious enough to know that something different is happening about which they have not been informed, and / or to which they may not agree. By insisting on a strict determination of capacity this approach fails to take into account the realities of the situation and the nuances of the ethical relationships within them.

Refining the process

In what follows below we describe the key elements of an enrolment process for emergency medicine research that refines the consent waiver and addresses the challenges outlined above. These elements serve as an explanation of the flowchart of the process depicted in Figure 2. The key points of the process are summarised in text format (Figure 3).

1 Verbal consent

Overall, the emergency context provides a good justification for a consent process which is primarily verbal. As Roberts *et al* suggest there is evidence to suggest that requiring a detailed, written consent process in this context is potentially detrimental to the patient’s health (17, 24).

What matters ethically for consent is that the autonomous (and so competent) person makes a voluntary decision having been given (and understanding) the relevant information. Importantly, there is nothing in this that requires consent to be written. It is an artefact of regulation and the need for evidence in this context. In the emergency context there is good reason to avoid unnecessary steps. However, it remains important, for the same reason that regulation is important, to have a record of the process that is independent of the researcher (25). Instead of requiring written consent, a verbal¹ but independently documented process is one that is sensitive to the context of the research and the ethical issues surrounding consent.

2 Unconscious patients are enrolled on the consent waiver; Conscious patients go through a consent/assent process

The important ethical feature of the group of patients who are conscious but with unclear capacity is that they can, to varying degrees, engage with the researcher. There is a clear obligation on the part of both clinicians and researchers to engage with those patients who can, to the extent that the patient is able. The UK Mental Capacity Act acknowledges this obligation: “Nothing may be done to, or in relation to, [the patient] in the course of the research to which he appears to object (whether by showing signs of resistance or otherwise) except where what is being done is intended to protect him from harm or to reduce or prevent pain or discomfort” (26).

¹A verbal process does not exclude non-verbal communication (gestures, expressions, head movements) which could also indicate consent or assent to study inclusion.

As a result, the process requires that the researcher responsible for the patient explains briefly and alongside whatever account of the clinical process is usually given, that research is being conducted and that they are eligible for enrolment. The study will, as far as possible, be discussed with the patient and the risks and benefits explained. Patients will be given the option to participate or not. In cases where capacity is unclear, any sign (verbal or non verbal) either to enrol in the study or not will be registered as assent or dissent. In cases of dissent the patient will not be entered into the study. This explanation and patients' responses do not stand in for a full consent process. It is verbal and truncated because of the emergency and it is delivered to all conscious patients to enable appropriate engagement. Those with capacity will understand and be able to consent in a truncated form while those with limited capacity will be given an opportunity to assent to (or dissent from) participation and so will be involved in the process to an appropriate extent. Judgement is required here to interpret any response on the part of the patient particularly in the negative. So while conscious patients are unlikely to be able to give full consent on this process they are given the opportunity to participate in the decision-making to the extent that they are able.

3 Patient Advocate

The Patient Advocate (PA) role is filled by a health care professional present in the emergency room but independent of the research team, e.g. a clinical nurse or radiographer. The PA plays two important roles in the process: (i) to be an independent witness and to document that the process was undertaken appropriately and (ii) to provide an independent assessment of the patient's willingness or otherwise to participate in the research. The latter role requires the PA to witness the exchange between the researcher and the patient about the research study and to make a judgement in conjunction with the researcher about any affirmative or negative response by the patient. The patient advocate is not a surrogate for the patient or the legal representative of the patient but a trained independent observer who oversees the consent process and is in a position to interpret the patient's condition and responses to the researcher.

4 Consent for on-going participation

In line with regulatory requirements, full written consent for on-going participation in the research is obtained from the patient or their representative once the emergency is passed.

Conclusions

The process that we have outlined represents a nuanced approach to the research ethics around consent in the challenging context of emergency medicine research. The process suggested here does not involve a detailed, burdensome and time-consuming exercise that is often true of informed consent processes.

It balances the pressing need to conduct research in the emergency setting with an ethical approach that strives to inform and consult patients before their participation. It does not require simply withholding relevant information about research from participants and it does not require delays in life-saving interventions. Instead it is firmly embedded within the context of the consent waiver but represents an appropriate refinement of the regulations that

is better able to capture the ethical complexity of the context. It is context and patient sensitive. Most importantly, it is centred on a recognition that treating people well involves treating them honestly and engaging with them at a level appropriate to their specific circumstances.

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Abbreviations List

AMI	Acute Myocardial Infarction
CIOMS	Council for International Organizations of Medical Sciences
DHHS	United States Department of Health and Human Services
FDA	United States Food and Drug Administration
ICH-GCP	International Council for Harmonisation Good Clinical Practice Guidelines
PA	Independent Patient Advocate
PCI	Percutaneous Coronary Intervention
REC	Research Ethics Committee

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Shared requirements for a consent waiver (common to UK, EU and US regulators)

- Either the research can only achieve its aims in the emergency context on incapacitated potential subjects, or the incapacity of subjects and the emergency context must be necessary features of the research design
- It should be impractical to seek an opinion from patient or legal representatives in a timely manner
- It must have IRB/REC approval
- Fully informed consent or advice should be sought from the patient or their representative after the emergency has passed

Figure 1. Shared requirements for a consent waiver.

The requirements listed are common to regulators from UK, EU and US

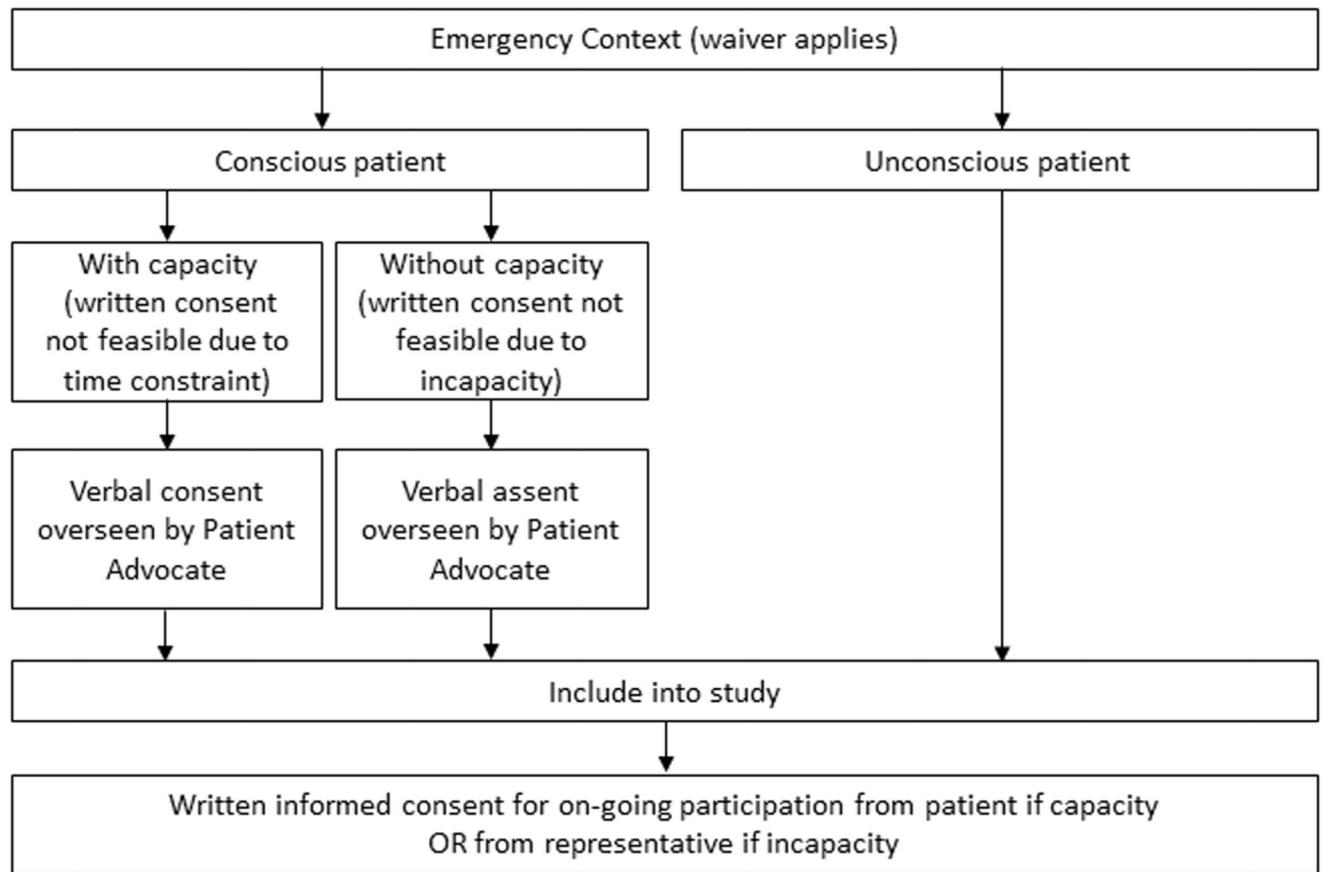


Figure 2. Refined enrolment process in emergency medicine research

Emergency admission patients eligible for inclusion in research follow one of three routes.

An independent advocate oversees the process. Written consent is sought after the emergency is passed.

Key Elements of the new process:

- It is embedded within the context of the consent waiver for emergency medicine research
- It does not require a determination of capacity
- It allows those patients who can engage with the researcher to do so
- Verbal consent or assent is obtained from all conscious patients who are able to engage with the researcher
- Unconscious patients are enrolled in the research according to the consent waiver
- The enrolment process is recorded, witnessed and overseen by the Patient Advocate
- The Patient Advocate is independent of the research team and is able to be an advocate for the patient in the emergency context
- Full written consent for on-going participation in the research is obtained from the patient or their representative once the emergency is passed

Figure 3. Key Elements of the new process

Key elements are described below