Medical research involving patients or healthy volunteers is required to enable new therapies to be developed and evaluated prior to their widespread introduction. All research is performed within a strict framework of guidelines and regulations, including the requirement that a participant’s informed consent be obtained before any part of the research protocol is undertaken. The intention of prospective consent is to uphold the respect for autonomy and to ensure the wellbeing of the research participant. This has been re-emphasised in the most recent version of the Declaration of Helsinki [1].

There are a number of life-threatening emergencies, such as major trauma and cardiac arrest, where the need for immediate treatment means that consent for treatment cannot be obtained. The same consent problem applies to new therapies being evaluated for emergency conditions. Whilst new therapies for emergency conditions must be assessed within the normal research framework, the normal consent process cannot apply when the patient is incapacitated and there is no time to contact the patient’s legally authorised representative. Alternative methods of obtaining a person’s consent for emergency research have been tried and found wanting.

Prospectively consenting sufficient numbers of an ‘at risk’ group to provide enough participants for research is expensive, time-consuming and unworkable. Deferred consent whereby a person is recruited to a research project and then their consent requested at a later date is also inadequate. Here the consent can only be for continued participation, as it is not possible to consent to something that has already occurred. Requesting consent retrospectively is meaningless. Obtaining consent from an appropriate proxy is a well-established principle that enables decisions to be made on behalf of patients lacking the capacity to make their own decisions. In the emergency scenario the proxy needs to be immediately available (which they often are not) and to be in a fit state to make a decision on behalf of the patient. Furthermore, a relative’s decision-making ability may be compromised by their concern for the patient. Requiring proxy consent can also lead to delays in administering trial drugs. Kompanje reviewed the time from injury to drug administration in a traumatic brain injury trial where proxy consent was used [2]. In over 85% of cases the time from injury to drug administration exceeded 4 h (over 5 h in 60%). Had the need for consent been waived then most patients could have been recruited and received the drug within 3 h of their injury. In this particular trial the time window for receiving the drug was 6 h from time of injury but for some drugs a shorter timeframe may be necessary but might be very difficult to meet.

Where enrolment to an emergency research protocol occurs without prior consent, a number of participants will die before consent is obtained. There has been debate as to whether these patients’ data might be retained and analysed. These patients must be included in any analysis of the trial results; to do otherwise risks biasing the results so that either a promising therapy is lost or a harmful one adopted. All of these alternative methods of gaining consent have developed out of a desire to give due respect to the person’s right of autonomy.

Emergency care research in Europe

Research in Europe is regulated by Directive 2001/20/EC that was intended to harmonise regulation across Europe [3]. Article 5 addresses research involving patients lacking capacity and requires consent to be obtained from a legally authorised representative prospectively. Emergency research is included in this need for proxy consent but the Directive does not indicate who may, or may not, act as a proxy. The Directive has been interpreted differently across Europe and, as a result, research permitted in one country may not be possible in another.
Emergency care research in the UK

In the UK the Directive only applies to research involving an investigative medicinal product (that is, a drug trial) [4]. Under the UK regulations two types of proxy decision maker are allowed. One is the personal legally authorised representative (pLAR) who is usually a relative of the patient. For research involving an incapacitated adult, where discussion with the pLAR may not be possible, then a professional legally authorised representative (prLAR) may be appointed by the health authorities. This person may be anyone the health authority feels is appropriate. There is no requirement for this person to have any particular training or expertise in order to be appointed.

For emergency research there may be a designated prLAR who the researchers can approach for permission to recruit patients. Exactly how the prLAR can give meaningful consent on behalf of people he has not previously met is unclear. In reality the prLAR can only confirm that the potential participant fulfils the inclusion criteria and none of the exclusion criteria. How this improves the wellbeing or protection of patients is not apparent.

As already stated, in the UK the Directive only applies to drug trials. Therefore any other form of emergency research is impossible in the UK under current legislation.

Emergency care research in the US

In the USA a waiver of informed consent is permitted for emergency research under specific circumstances [5]. In order for the waiver to be permitted the researchers must first demonstrate that the planned research can only be performed using incapacitated patients, that the planned intervention might benefit that group of people and that waiting for proxy consent would not be feasible. The risk for the participants must also be reasonable in relation to the severity of the condition being investigated.

Despite the need for emergency research the waiver of consent has not been applied as often as initially expected. This is partly because interpreting and applying the criteria has proven difficult. One major sticking point has been around the obligation for ‘community consultation’. Here the researchers are expected to ‘consult’ with the ‘community’ that will be recruited to the trial. Exactly who constitutes a ‘community’ and what form the consultation should take is open to interpretation.

Public opinion

For emergency research without consent to be successful it is paramount that it has the support of the public. In general public opinion appears supportive [6]. There are several surveys looking at patients’ views on the acceptability of emergency research, most of which are generally in favour. There is one more in-depth study where sudden cardiac death survivors were interviewed about their understanding and perceptions of performing research when consent was not possible [7]. Again their views were, in the main, positive. One area that patients did struggle with was that of randomisation. It appeared that allocating patients to treatment groups by chance was unsettling.

Is emergency care research ethically acceptable?

Autonomy, beneficence, non-maleficence and justice are the four principles of medical ethics that are widely accepted as guiding medical practice. In general, autonomy is given precedence over the others. The balance amongst the principles changes in the emergency scenario. If the individual’s autonomy cannot be upheld then the other principles become more important.

Many of the treatment protocols used in emergencies have not been assessed to the same level as other treatments. The principle of beneficence, however, requires that any intervention must be expected to benefit the recipient. Where there is a genuine lack of knowledge about which therapy will produce benefit then entering the patient into a randomised controlled trial to find out would be justified. The principle of justice obliges clinicians to use finite resources at their disposal prudently. This necessarily means knowing which treatments are effective and which are not. Such information can only be obtained by research.
Improving emergency research in Europe

The first step in improving research would be to recognise that emergency research is different from the norm in so far as there is no-one in a position to provide prospective consent. And that despite this emergency research is necessary for the common good. The second issue is to consider how respect for the individual’s autonomy and protection of their wellbeing might be addressed.

The Declaration of Helsinki already permits research without prospective consent (subject to national legislation). This is limited to situations where the proxy representative is unavailable and the research cannot be delayed, i.e. emergency research. Protecting the interests of the research subjects is not directly mentioned in the Helsinki Declaration in relation to emergency research other than to say that a REC should have approved the specific reasons for allowing the research to go ahead.

In 2002 Löjtönen suggested criteria that would allow a research ethics committee to grant an exemption to prospective consent [8]. These should include: there being no alternative patient group who could consent; no delay in treatment is possible; informed consent not possible in the necessary timeframe; the risks associated with being in the study are reasonable when compared with the risks of the disease process being studied; and that the proposed intervention should potentially be of benefit to the group being recruited. There should also be no reason to believe that the individual would object to being in the study and that consent for continued enrolment is obtained as soon as possible. Whether these, or similar, criteria will ever be introduced on a Europe-wide basis only time will tell.

Conclusion

Improving the treatment and care of people suffering from life threatening emergencies will depend upon research. Unless research without consent is permitted then this vulnerable group will be disadvantaged. Emergency research is ethical but needs its legality clarified, which if done at a European level would enable the necessary large clinical trials to go ahead.

Key learning points

- Emergency research is necessary for the common good.
- Prospective consent is not possible.
- Enrolling patients into emergency research is ethical.
- The Declaration of Helsinki supports emergency research without prospective consent.
- Uniform European legislation is needed to permit large trials to improve the management of life threatening emergencies.

References