Editorials

Clinical trials in emergency situations

BMJ 2007; 334 doi: http://dx.doi.org/10.1136/bmj.39097.582130.80 (Published 25 January 2007) Cite this as: BMJ 2007;334:165

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Haleema Shakur, trials manager (crash@lshtm.ac.uk), Ian Roberts, professor of epidemiology, Lin Barnetson, data manager, Tim Coats, professor of emergency medicine

Author affiliations

New guidance allows patients to be enrolled without prior consent

On 12 December 2006 an amendment of the UK's Medicines for Human Use (Clinical Trials) Regulations 2004 came into force.[1] The amendment allows unconscious patients in emergency situations to be enrolled in clinical trials without prior consent provided that this has been approved by the appropriate ethics committee. The amendment has been anxiously awaited by emergency care researchers since these regulations first changed the legal basis for consent for research on medicinal products in the United Kingdom in May 2004.[2]

Researchers have always been concerned about the effects the regulations might have on clinical trials in emergency situations in patients with impaired consciousness, such as those with head injury, major trauma, or cardiac arrest. The regulations imposed the need for prior consent from a personal or professional legal representative before a patient could be recruited into a clinical trial.

The regulations only applied to trials of drugs. Non-medicinal trials and trials of clinical care continued to be governed by common law.[3]

The change in consent procedures was not the only threat to the conduct of clinical trials in emergency care. The increased bureaucracy, reporting, and costs of clinical trials that followed the implementation in 2004 of the European Clinical Trials Directive led to a sharp decline in the initiation of clinical trials and in participant recruitment throughout Europe.[4]

Many important clinical trials such as the TROICA (thrombolysis using tenecteplase (Metalyse) in cardiac arrest) trial foundered because of the new laws.[5] As well as an approved consent procedure, participating National Health Service trusts had to have local procedures, guidance, and training in place to ensure compliance with the regulations. A year after the introduction of regulations, most NHS research and development departments still had no systems in place that would allow emergency care trials in patients with impaired mental capacity.[6]

The CRASH-2 (clinical randomisation of an antifibrinolytic in significant haemorrhage) trial (www.crash2.Lshtm.ac.uk) developed a consent protocol in line with the 2004 regulation, which was

approved by the UK Medicines and Healthcare Products Regulatory Agency and multicentre research ethics committee and has now recruited more than 3500 patients. However, UK hospital trusts have been slow to implement effective procedures for professional legal representatives for unconscious patients in emergency situations.

The first CRASH trial included patients with severe head injuries, who were unable to give informed consent. It was conducted before implementation of the legislation, and the multicentre research ethics committee gave approval for the trial to be conducted using a "consent waiver." With the approval of the ethics committee, the attending doctor took responsibility for enrolling patients into the trial. Patients and relatives were informed about the trial as soon as possible, and written information on the trial was provided. Of the 10 008 patients randomised, only one patient had to be withdrawn from the trial (at the request of a relative).**7**

Efforts are being made in the UK to redesign the environment in which clinical research is conducted. This has resulted in the formation of organisations such as the UK Clinical Research Collaboration (www.ukcrc.org). However, in the two years since implementation of the regulations, recruitment into clinical trials in unconscious patients in emergency situations has been slow in the UK.**8** The evidence base for trauma care was already seriously lacking,**9** and the regulations did not help. Unconscious patients in emergency situations should have the right to benefit from medical research, but the 2004 regulations put this right in jeopardy.

The amendment to the clinical trials regulations will be welcomed by emergency doctors. NHS research and development departments urgently need to develop guidance on how to implement this amendment. In the meantime, emergency doctors can be reassured that the new guidance allows patients to be enrolled without prior written consent if approved by the ethics committee, and that clinical trials once again have the potential to provide the evidence needed to improve emergency care.

Footnotes

- **Competing interests:** None declared.

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