RESEARCH SERIES

Ethical considerations in accident and emergency research

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This is the third paper on research in accident and emergency medicine. It discusses the ethical issues in emergency medicine with particular regard to informed consent and the privacy of subjects and patients.

In a recent article Lewis *et al*, North American emergency physicians defined good research as “any research that enhances our ability to prevent illness or injury, to improve the quality or decrease the cost of care, or to improve the lives of our patients”.¹ These benefits flow only from good research, and while Lewis drew his definition from an outcome perspective one might equally define the term as research that protects subjects and patients from harm, preserves confidentiality, and is freely entered into by participants. Subjects and patients must be allowed to make an informed choice on participation without fear that their treatment might be compromised if they decline. For a research project to be ethical it must also be well designed, it must investigate an issue that is important and for which the available literature does not already provide satisfactory analysis. Protocols must be scientifically robust and likely to yield meaningful conclusions that add to the body of knowledge on a relevant clinical topic. Good research is therefore ethical research and bad research is unethical.

In this paper we discuss the ethical issues in emergency medicine (EM) research with specific regard to issues of informed consent, including vulnerable groups, avoiding harm and protecting the welfare and privacy of subjects and patients. We discuss funding and sponsorship of clinical trials as well as integrity in reporting results and aspects of scientific fraud. Finally, we discuss the structure and role of ethics committees and derive a checklist with which to evaluate the ethical foundation of a study. The properties of a well designed study are discussed elsewhere in this series.

A MORAL BASIS FOR RESEARCH IN EMERGENCY MEDICINE

It is a central theme of EM practice that patients are cared for solely on the basis of need.

Patients attending an emergency department (ED) are entitled to assume that they will be treated in accordance with the best available evidence. The emergency physician (EP) has a responsibility to expand the fund of knowledge that underpins best evidence by means of clinical studies of new technologies and interventions. However, there are inherent difficulties in undertaking clinical research in an ED setting. Patients

are usually frightened, often in pain, and sometimes have impaired cognition because of injury or intoxication. Treatments such as opioid analgesia may change the patient's critical faculties and affect their ability to give informed consent. The ED attendance is usually the first contact between the physician and the patient, there is no long term relationship such as might be seen in the GP surgery or outpatient department.

Randomisation to treatment must occasionally be completed in the context of a clinical emergency. For example, the major trials of thrombolytic therapy in acute myocardial infarction demonstrated substantial mortality gains with treatment and so were soundly ethically based. And yet the data would not have been garnered without the recruitment of thousands of patients with life threatening illness into major multicentre studies. The agents under investigation themselves carried significant side effects, including fatal and disabling strokes with an incidence of 3–7 per thousand treatments.²

Over and above the ethical code that is embraced by all doctors the EP must therefore accept “enhanced ethical duties, moral requirements and social contracts”.³ In a research context the EP must reconcile these two moral imperatives; the obligation to participate in studies that may yield benefit to patients or enhance the appropriate use of limited resources and the protection of a vulnerable group of patients from exploitation.

BALANCING BENEFICENCE AND NON-MALEFICENCE

Patients take on trust the fact that the clinician will act in a professional manner and not misuse the authority of his position. The EP must be committed to the principle that self promotion must not take precedence over the best interests of the patient. Self promotion may take many forms but the kudos of publication in peer reviewed journals is a particular temptation and is essential to those who are writing a thesis or planning an academic career. Integrity and accountability are essential elements in research as in all aspects of clinical practice. The moral obligation of doctors to do good, beneficence, must be tempered by non-maleficence. That is, the expected bad effects of an intervention must be weighed against the anticipated benefits. The type, amount, and probability of harm should be effectively communicated to subjects and the doctor should take account of the fact that what constitutes a harmful effect, or a beneficial effect, may be particular to the individual subject.⁴

Justice and equality of access are inalienable rights that must be respected in participants and

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Box 1

- Research should be valid and should benefit patients and society ahead of all other considerations.
- Study protocols should be well designed and use appropriate methodologies to examine an important issue within your area of practice to refute or strengthen existing theories.
- Informed consent should be obtained and, where exceptions are allowed, the EP must act in the patients best interests
- All patients should have equal access to high quality care regardless of race, creed, colour, sex, or sexuality and care should not be compromised by non-participation in any research project.
- The comfort, safety, and confidentiality of participants and non-participants should be respected.
- Declare funding and conflicts of interests. Publish only accurate results. Publish comprehensive data including those that compromise the hypothesis as well as those that support it.
- Respect coinvestigators, colleagues, and subordinates and treat all those involved with the research with fairness.
- Scientific fraud or misconduct must be reported promptly.

non-participants alike. The researcher must be a good communicator, demonstrating openness and effective listening. When discussing the potential risks of a proposed procedure it is essential to quantify *minimal, low, or high risk* using experiences from everyday life. For example, a minimal risk procedure may be described as one that presents a risk of death of less than one per million and a risk of serious adverse event of less than 10 per million.⁵

Benefits may flow from a research study in favour of the patient or to society. When discussing the benefits of a proposed study one must distinguish between *therapeutic* and *non-therapeutic* research. Researchers are obliged to consider the potential benefit *to the patient* when balancing potential risks associated with any protocol. No matter how great the benefit to society it would not be ethical to expose the subject to anything greater than minimal risk if there is little direct benefit to the patient.

Box 1 contains suggestions for a code of practice, modified from a recent statement from the Society for Academic Emergency Medicine.⁶

CONFIDENTIALITY/MEDICAL RECORDS

All patient information, whether collected for clinical indications or for research purposes is confidential and NHS employees are legally obliged to control its dissemination. The investigator should only obtain personal data that are essential to the research. It is not for the investigator to determine what information is sensitive and which persons are authorised to share that information. The circumstances in which patient identifiable information may be disclosed should be the subject of a specific clause in the consent document. Patients and subjects are entitled to ask to what use the information about them is to be put and their wishes are to be respected if they request that some information about them is not used. Confidential information obtained for one purpose must not be used for another.

Patient identifiable information should be secured against unauthorised access in accordance with the Data Protection Act of 1984. Data should be aggregated or anonymised where possible and information from which individual patients may be identified should not be retained any longer than necessary.

The anonymity of the subjects of case reports must be protected. Many biomedical journals require that the subject of case reports sign a standardised consent form prior to publication.⁷ Where projects require the investigator only to

access patient records without any procedures being performed it is not required that individual patients are consented about their records being scrutinised. Directors of Research, Audit and Development within an NHS Trust and Local Research Ethical Committees (LREC) will ensure that the investigator is an authorised person, that only relevant data are collected, and that the data are handled and presented in accordance with the above principles. Examination of past patient records, essential for audit as part of clinical governance, does not require LREC approval.

CONSENT

Fifty years ago the Nuremberg Declaration recognised that the voluntary consent of human subjects was absolutely essential in the conduct of clinical investigation and established the principles of informed consent, namely that the person should be legally competent and entitled to give consent and be "able to exercise free power of choice without the intervention of any element of force, fraud, deceit, duress, overreaching or other form of restraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision".

In the UK consent is required by law before a person is subjected to any procedure whether for treatment, investigation, or for research purposes. The doctor determines whether the patient is competent to give consent. It may not always be necessary to obtain written consent as the patient may be deemed to have implied his consent by voluntarily submitting to a minor procedure. However, it is good practice to obtain written consent for major interventions and unusual treatments as a defence against a charge of assault and battery. Written consent is required for all but the most trivial interventions such as measuring height, weight, etc. Written evidence of consent does not reduce the rights of the subject or the responsibilities of the investigator. Consent must never be *assumed*.

All people who are subjects of research, whether healthy or sick, should be aware of the fact and the nature of the research. This can be difficult or impossible in some clinical circumstances. For consent to be valid it must be informed, understood, and voluntarily given. Subjects should have enough information in comprehensible form to enable them to make a proper judgement on whether or not to participate. Normally this requires time for reflection before a decision to enroll.

Information is usually given by means of an information sheet (IS), written in plain English and in terms that could be understood by a child aged 10–12 years. It should set out:

- Purpose of the investigation
- The procedure
- All potential risks
- Pain, suffering, psychological distress
- Discomfort, inconvenience, expense
- Benefits (or lack of) to the individual and to others
- A statement to the effect that the person is free to choose not to participate or to withdraw at any time without incurring displeasure or disadvantage
- An invitation to ask questions
- Reference to non-availability of payment
- Reference to non-availability of compensation for injury
- Name and contact address of researcher(s)

Subjects should, where possible, be given plenty of time to study the IS and to consult with relatives or their family doctor. Both parties should sign the document, an independent person should witness the signature. The IS should be filed in the case notes.

In the case of a child under the age of 16 it is common to obtain the consent of a surrogate, usually a parent, as well as the child. Children who are intelligent enough to understand the consequences of their action may grant or withhold consent regardless of their age. It is good practice to seek parental consent in addition when the subject is under 18. Children should not be involved if the research could equally well be done in adults. And there must be no financial or other incentive offered to child, parent, or guardian.⁸

How much information is necessary?

The researcher must exercise professional skill and judgement in deciding what constitutes adequate disclosure of potential risks. Clearly the patient/subject must be warned of any substantial or unusual risk or a danger that may be special to the particular person. This issue was considered by the House of Lords in the *Sidaway Case*.⁹ Ethical committee approval for a research proposal will require the demonstration of a satisfactory patient information document.

Questionnaires are often sent to patients by mail. It is assumed that the subject is consenting when he completes the questionnaire. However, a clear explanation is necessary as to the utility of the information and the confidentiality. LREC will disapprove of "cold calling" vulnerable groups. A pre-questionnaire telephone call from a named individual may be proposed. Where intimate, intrusive, or distressing details appear on the questionnaire advanced informed consent is required.

Consent in incompetent patients

A working group on ethics lamented the plethora of policies focusing on informed consent (IC) that are designed to protect the individual rather than promote or facilitate research that may benefit society as a whole. The group pointed to circumstances where IC is not available (cardiopulmonary resuscitation, collapsed or obtunded patients, ventilated patients in intensive care). There is an ethical obligation to carry out research in these patients if treatment is to be improved and lives saved.¹⁰

Where physical or mental incapacity renders a subject incapable of giving informed consent the Declaration of Helsinki¹¹ allows for a surrogate to give their consent to an intervention, requiring that the surrogate use prior knowledge of the subject to determine the decision that he would have made, if competent. The clinician is obliged to disclose fully to the surrogate all available data on the risks and benefits of the proposed intervention. Foex sets out the options for proceeding without consent, which include the "reasonable" use of consent by proxy, retrospective consent, and waived consent. The last is appropriate to research in the emergency setting, where the patient may be incompetent by reason of critical illness or injury and the proposed alternative interventions carry similar profiles in terms of potential benefit and risk.¹²

In emergency situations the clinician may be forced to act in the patients best interest and to *presume* consent on the basis of necessity. Clearly this is only appropriate for interventions that will benefit the patient directly, and consent should be obtained as soon as practicable afterwards. In a research context the intervention must be part of a protocol approved by an independent ethical committee and should represent no more than minimal risk to the patient.

Children

The Ethics Advisory Committee of the British Paediatric Association acknowledges that research involving children is an important means of promoting child health and wellbeing. Research involving children may include the study of normal development, the aetiology, assessment and treatment of disease, and the validation of the results of research conducted in adults.¹³ It is essential that protocols are well designed and

Box 2

• Fraud

Deliberate deception, usually the invention of data, dishonesty in data collection, or falsification of results

• Piracy

Deliberate exploitation of ideas from others without acknowledgement

• Plagiarism

Copying ideas, data or text without permission or acknowledgement

• Other

Misleading statements during the presentation of data
Misrepresentation of authorship
Misuse of Trust premises and facilities

involve statistically appropriate numbers of subjects and so the A&E department of a district general hospital is an appropriate setting for this type of study.

FUNDING AND PAYMENT

Although there is a tradition of altruism in UK based clinical research many companies, institutions and organisations offer financial rewards to participants, especially where healthy volunteers are being recruited into studies of pharmacokinetics. It is ethical to cover reasonable costs, but not ethical to offer heavy payments to induce patients/subjects to participate. LREC must be made aware of any financial arrangements with subjects. Acceptance of payment does not impair the ethical or legal rights of the subject.

The nature of payments to individuals, departments, and institutions by sponsoring companies must also be declared to LREC as well as any investment or other relationship between the sponsor and the investigator. Investigators must ensure that the proposed study funded by a legitimate source and that funding is not contingent.

What if things go wrong?

Patients and subjects who are harmed as a result of participation in research in an NHS institution are covered by NHS indemnity. Substantial payments in compensation may be made to victims of accidents but this depends on a demonstration of negligence, including a deviation from approved protocols. Alternatively there may be an offer of "ex gratia" payment, limited to £50 000, for non-negligent harm.¹⁴ Where the research is sponsored by independent sector organisations there may be an advanced contract of indemnity between participants and sponsors. Payment of compensation does not depend on a demonstration of fault, it is sufficient that harm resulted from participation.¹⁵

RESEARCH FRAUD AND MISCONDUCT

Researchers are entitled to expect that their work is regarded as honest until shown to be otherwise. Misconduct is uncommon but occurs in most countries, even in sophisticated systems. The elements of scientific misconduct are described in box 2, modified from the report of a Working Party of the Royal College of Physicians.¹⁶

Several causes of misconduct have been described, including pressure to publish, financial inducements, and simple vanity. In addition, heads of department may append their names to manuscripts without proper scrutiny or critical appraisal. It follows that, to avoid the risk of accusations of misconduct, researchers must abide by a code of practice. Senior researchers should ensure the proper supervision of juniors and should not append their names to any work without

Box 3

- Review proposals for research to be carried out in the health district, including the hospital Trust and local general practitioners
- Consider protocol amendments
- Consider allegations of misconduct in research that may be put before it and ensure that appropriate information is passed to appropriate authority (Royal College, GMC)
- Ensure proper investigation of adverse effects among research subjects and consider the implications for continuing a study
- Ensure that subjects are able to comment on and withdraw easily and without penalty
- Advise its appointing authority on all matters pertaining to the ethics of research
- Make an annual report of its decisions to the health authority, the report is then made available to the public

regular and proper scrutiny of raw data. Guidelines on authorship have been drawn up by the Vancouver group.¹⁷ It may be a condition of LREC approval that raw data are retained on file for 10 years. LREC should be aware of simultaneous work by the same investigators to determine if sufficient time can be devoted to the project to merit a meaningful contribution by authors. Local investigation of improbably high output may reveal evidence of questionable authorship.

Misconduct in other researchers must not be tolerated and must be reported promptly. There should be a named person within the organisation who is responsible for the receipt of complaints of research misconduct. This will usually be the director of a research institution, the dean of a university, or the postgraduate dean in an NHS setting. Alternatively, investigation of complaints may be initiated by bodies such as pharmaceutical companies, who may have funded the study, or their agents. When complaints are received by the nominated person they may be rejected at the first stage or investigated further, perhaps leading to referral to the General Medical Council (GMC), grant giving body, or journal editor.

LOCAL RESEARCH ETHICS COMMITTEES

All research on human subjects should conform to the principles outlined in the CIOMS and WHO guidelines.¹⁸ Investigators cannot be the sole judges of conformity and Research Ethics Committees (REC) were established in all health authorities in the mid-1970s after recommendations by the Royal College of Physicians and the Department of Health. All medical research is subject to ethical review. The Medical Research Council and other major grant giving bodies require REC approval prior to making a grant.

Each health authority has one or more LREC. The committee has a responsibility to conduct ethical review of all research involving patients or healthy subjects. All research investigations involving human subjects come before it for mandatory review. Fast track mechanisms exist for selected proposals that pose no ethical problems because they involve no risk of distress or injury and no issues of confidentiality.

LREC are multidisciplinary and include specialists from different fields and at least one nurse, as well as lay people. They should be a manageable size, not more than 12 members, but with the ability to coopt additional professional advisers. Members are unpaid or receive a small honorarium or sessional allowance. The LREC usually meets monthly, its business is carried out in private but the decisions are made public. Multi-location REC (MREC) consider proposals for multicentre studies that cross several Trusts. While the LREC does usually defer to MREC in approving such studies the LREC may refuse approval for a number of local reasons.

Box 4

1 Investigators

Do the investigators have sufficient experience and qualifications relevant to the field of research?

2 Site

Is the site appropriately staffed and equipped?
Are the accommodations for subjects acceptable?

3 Scientific merit

Has the project sufficient scientific merit and value?
Will the study answer the question being examined?
Has the work been done before?
Can the results be obtained in any other way?

4 Drugs and devices

Has the substance or device received the necessary approval for use in human subjects?
Are subjects to be treated in a manner appropriate to their status as healthy volunteers or patients?
Are the subjects in a subordinate relationship to the investigator or are any of them part of a vulnerable group? If so are arrangements suitably in place to protect their interests and cater for their special needs?
Where there is recruitment by advertisement is the advertisement satisfactory?
Is the patient information sheet adequate in terms of form, language, and content?

6 Risks and benefits

What is the nature, severity, and likelihood of hazards?
In non-therapeutic or healthy volunteer research are the risks minimal?
Are they proportionate to the anticipated benefits of the research?
What benefit, if any, is intended to the individual subject?

7 Pain, distress, and discomfort

Are the levels proportionate and acceptable?

8 Statistical value

Is the study capable of producing sufficient meaningful data for analysis?

9 Financial arrangements

Are the arrangements acceptable so that the impartiality of the investigator is not in question?

10 Safeguards and protection

Is appropriate provision made for the monitoring, recording, and handling of adverse reactions and other difficulties?

11 Personal injury or death

Has the company sponsor agreed to abide by the appropriate ABPI guidelines?

12 Confidentiality

Will the subjects' medical and personal details remain confidential?
Will subjects be asked to provide consent to limited necessary access to data by sponsoring company and regulatory bodies?
Will data and results generated during the study be published in a form that avoids the identification of individual subjects?
Will there be compliance with the provisions of the Data Protection Act 1984?

Objectives of REC

"To maintain ethical standards of practice in research, to protect subjects of research from harm, to preserve the subjects' rights and to provide reassurance to the public that this is being done".¹⁹ It is not intended to impede good research, but facilitate it, approving studies of good quality, not badly

planned or poorly designed protocols. Such defective research causes inconvenience to subjects and carries the risk of hazard without producing valid or useful results. Box 3 contains a summary of the functions of the LREC.

ETHICAL FOUNDATIONS OF A RESEARCH PROPOSAL: A CHECKLIST

In clinical research the REC will make an assessment of the risks and benefits represented by the proposal, taking account of the likelihood and severity of any risk to subjects and patients, and weighing this against the potential for benefit. Researchers must show that risks have been kept to a minimum with proper exclusion criteria, no inducements to perform invasive procedures over and above those that are *clinically* indicated and a robust system for dealing with adverse events. The REC will also address the hoped for benefits of the research and will approve the proposal only if it is satisfied that the risks are acceptable in the context of the potential benefit. The researcher must show that the study is capable of answering the question being asked, that proper scientific and statistical methodologies are to be used, and that the dignity and confidentiality of patients and subjects will be respected. The knowledge gained must have demonstrable utility in the understanding or management of important clinical problems. Financial considerations must have been addressed, there must be identified adequate funding from legitimate sources to support the study to its conclusion, including medical, nursing and other staff costs and consumables.

Box 4 contains suggested guidelines in the form of a checklist with which to assess ethical basis for a research project. Guidelines are modified with permission from a 1994 publication.²⁰

SUMMARY AND CONCLUSIONS

The accident and emergency department is an environment well placed to support clinical research. There is an obligation to undertake research to expand the evidence base that is the foundation of clinical practice. Emergency physicians must understand that investigations involving accident and emergency patients entail additional ethical considerations because the patients are a vulnerable group whose critical faculties may be impaired by pain, fear, or therapeutic interventions. Informed consent is a central theme of ethical research, subjects should be afforded adequate time to reflect and consult on participation and should be acquainted with the nature, likelihood, and severity of any risks as well as the potential benefits. Fairness and equality for non-participants requires particular attention. Special arrangements may be called for when experimental treatments are offered in the context of a clinical emergency or to obtunded patients. REC are established to ensure that only properly resourced, well

designed studies with robust methodologies are approved. All proposals involving access to patients should be submitted to the REC. These committees exist to protect patients and subjects from harm and to ensure that their rights, their dignity, and their confidentiality are not jeopardised by any research protocol.

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REFERENCES

- 1 **Lewis LM**, Lewis RJ, Younger JG, *et al*. Research fundamentals: I. Getting from hypothesis to manuscript: An overview of the skills required for success in research. *Acad Emerg Med* 1998;5:924-9.
- 2 **Fibrinolytic Therapy Trials Collaborative Group**. Indications for fibrinolytic therapy in acute myocardial infarction: Collaborative overview of early mortality and major morbidity results from all randomised controlled trials of more than 1000 patients. *Lancet* 1994;343:11-22.
- 3 **Adams J**, Schmidt T, Sanders A, *et al*. Professionalism in emergency medicine. *Acad Emerg Med* 1998;5:1193-9.
- 4 **Gillon R**. *Philosophical medical ethics*. Chichester: Wiley, 1986.
- 5 **Nicholson RH**. *Medical research with children: ethics, law and practice*. Oxford: Oxford University Press, 1986.
- 6 **Larkin GL for the SAEM Ethics Committee**. A code of conduct for academic emergency medicine. *Acad Emerg Med* 1999;6:45.
- 7 **British Medical Association**. BMA web site. www.bmj.com/collections/informed_consent/draft_f
- 8 **The Royal College of Physicians of London**. *Guidelines on the practice of ethics committees in medical research involving human subjects*. 3rd edn. London: Royal College of Physicians, 1996.
- 9 **Sidaway v Governors of Bethlam Royal Hospital [1985] AC 871**.
- 10 **Lemaire F**, Blanch L, Cohen SL, *et al*. Informed consent for research purposes in intensive care patients in Europe – part I. An official statement of the European Society of Intensive Care Medicine. *Intensive Care Med* 1997;23:338-41.
- 11 **World Medical Association**. *World Medical Association Declaration of Helsinki* 1989. (1964, revised 1989). The World Medical Association Handbook of Declarations.
- 12 **Foex BA**. The problem of informed consent in emergency medicine. *Emerg Med J* 2001;18:198-204.
- 13 **British Paediatric Association**. *Guidelines for the ethical conduct of medical research involving children*. London: British Paediatric Association, 1992.
- 14 **HSG (96) 48**. NHS Indemnity – Arrangements for clinical negligence claims in the NHS.
- 15 **ABPI**. *Clinical trial compensation guidelines*. London: ABPI, 1991.
- 16 **Royal College of Physicians**. *Fraud and misconduct in medical research: causes, investigations and prevention*. Report of a Working Party. London: Royal College of Physicians, 1991.
- 17 **International Committee of Medical Journal Editors**. Uniform requirements for manuscripts submitted to biomedical journals. *BMJ* 1982;284:1766-80.
- 18 **World Health Organisation and Council for International Organisations of Medical Sciences**. *International guidelines for biomedical research involving human subjects*. Geneva: WHO, 1993.
- 19 **Royal College of Physicians**. *Guidelines on the practice of ethical committees in medical research involving human subjects*. 2nd edn. London: Royal College of Physicians, 1990.
- 20 **Bendall C**. *Standard operating procedures for local research ethics committees: comments and examples*. London: McKenna, 1994.