Education and debate

Ethics, audit, and research: all shades of grey

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Decisions about the need for ethical review should be based on the morality of all actions rather than arbitrary distinctions between audit and research

Editorial by Abbasi

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Ethical considerations should apply to all medical practice, but many people act as if they apply only to research. For example, all research studies have to be scrutinised by an ethics committee (institutional review board in the United States), but most ethics committees specifically exclude audit studies from their remit. Similarly, journal editors and funding agencies will require evidence of ethical review before accepting research for publication or funding but do not require this for audit studies. Consequently, the distinction between audit and research can have important implications, and the temptation to label research as audit is considerable.¹ Unfortunately, the distinction is at best difficult. This article reviews the distinction between audit and research, and the nature of ethics.

Audit or research?

Research and audit have many similarities. They both start with a question, both expect the answer to change or influence clinical practice, both require formal data collection on patients, and both depend on using an appropriate method and design to reach sound conclusions. The standards expected of audit in terms of design, data collection, and analysis should be at least as high as for research, if only because audit potentially leads to change more often than research does and often much greater change. It is also clear that both audit and research differ from normal clinical practice because clinical practice rarely

achieves a high standard of data collection and analysis.

The major bureaucratic distinction drawn between audit and research is that research investigates what should be done, whereas audit investigates whether it is being done (and if not, why not).² Guidance on making the distinction between audit and research is available,³⁻⁴ but the distinction is difficult to agree or make in actual practice.⁵ Some consequences of this difficulty have been discussed.⁶⁻⁹ The distinction is important because so many consequences follow, often irrationally. One is the need for ethical approval.

At present, responsibility for classification lies primarily with the investigator. Many biases and interests can therefore influence the decision. Local ethics committees may give guidance on the distinction, but some recognise that the distinction is difficult.¹⁰

Documents that discuss the distinction between audit and research rarely consider the moral issues.^{3-4 10} Instead, they give criteria, often based on process—for example, projects using postmortem material always require ethical review. In this situation it is worth considering the ethical aspects of all health care and whether audit and research should be distinguished.

When is additional ethical scrutiny needed?

The Greek word *ethika* (and *ethos*, its root) referred to character, and both referred to the morality of actions. Morality is derived from *mores*, the Latin for character. Thus ethics applies to a person's character, referring to the morality of decisions and actions in all circumstances. Morality relates to any situation in which there are conflicts between different values.

Every clinical encounter has three components¹¹: an epistemic part, when the situation is analysed and potential actions are identified; a pragmatic part, which identifies which of the potential actions are possible; and an ethical part, which identifies which of the potential actions is morally acceptable or preferred (that is, most compatible with the values of society, the patient, and the clinical team). If it is accepted that all clinical practice, including research, should be undertaken ethically, then the main issue is to decide when formal ethical scrutiny might be necessary. To help

decide, the following questions could be asked of any study or change in practice:

- How much does this deviate from current normal (accepted, local) clinical practice?
- What is the (additional) burden imposed on the patients (or others)?
- What (additional) risks are posed to the patients (or others)?
- What benefit might accrue to the patients (or others)?
- What are the potential benefits to society (future patients)?

The answers might determine when additional, usually external, ethical scrutiny should occur. The questions also apply to research on healthy people (because the change is from no clinical practice whatsoever) and to all other interested parties as well as participants. Similar questions could apply to normal clinical care, where some clinical decisions might benefit from additional ethical consideration by an external group.⁹

What factors influence need for ethical review?

Ethical concerns arise when the involved parties have different interests or values in a situation in which a potential conflict exists between the burden and risk imposed on patients or others (including society) and the likely benefit (box). They may also arise when there is a large imbalance in power, as between a doctor and patient, and this accounts both for organisations that scrutinise professional behaviour (such as the General Medical Council in the United Kingdom) and also, in part, for the development of powerful ethics committees.

Change in practice is integral to most formal studies. In audit, the change is usually in the domains of data collection and analysis, although some units advise that audit: "Never involves disturbance of patients over and above normal clinical management. There is no extra data collection and no extra interventions or clinical assessments."¹² Research more commonly involves manipulating interventions.

Minimal changes in clinical practice, such as ensuring a consistent approach towards all patients or collecting some extra information, would rarely require specific ethical consideration. Moderate

changes, such as the introduction of integrated care pathways, might need ethical review because the changes may be ineffective.¹³ Major change, such as deliberate randomised selection between different managements for patients in the same situation, should always have ethical scrutiny.

The degree of conflict arising from the competing interests of the investigator, clinician, or other responsible party is the next important factor. This is coupled with considerations of the imbalance in power between investigators and participants. Most reasonable people can probably judge minor conflicts, but external review will be needed when the conflict between benefit and risk exceeds the threshold at which an interested party can reasonably make an unbiased judgment.

Burden includes the additional time and effort required of the patient or other subjects in data collection; it could also include taking additional tissue samples, etc. Minor burdens, such as filling in a short (5-10 minute) questionnaire or having pulse and blood pressure measured, will not require external ethical scrutiny but any larger burden probably does—for example, if the patient has to make extra clinic visits, have additional home visits, or spend more than one hour extra on giving information. The risks to be considered relate both to any procedures undertaken and to the use of the data collected, especially data that are not collected in routine practice. This will be relevant to audit projects, most of which collect additional data.¹⁴

Minor risks, such as having additional blood taken during a routine venepuncture or the risk associated with revealing data that are commonly collected in standard investigations (such as, urea and electrolyte values) would not normally require external ethical scrutiny. However, if the additional procedure poses any important risk, or if the nature of the additional data might cause any distress or harm, external ethical scrutiny should occur. The burden and risks need to be weighed against the potential benefits. The benefits are usually for others, although sometimes patients may benefit directly—for example, receiving an otherwise unobtainable treatment.

Every study, whether audit or research, should have some prospect of succeeding in its stated aim. The lower the likelihood of an investigation achieving its goal, the less risk or burden that the patient should bear and generally the more it should be subjected to external ethical scrutiny. Interestingly, one consequence of this rule would be that much current audit and NHS routine data collection would require ethical scrutiny because they are rarely likely to achieve their stated goals and the costs and risks are often not small.

Societal benefit can arise in several ways. The study might deliver results that will benefit other patients, although in practice most studies will be incapable of delivering even reasonably certain conclusions. But small studies can be ethically sound¹⁵ through stimulating larger, more definitive studies or contributing to a systematic meta-analysis. In addition, the researcher might learn important lessons about doing research, and this is probably the main benefit of most projects.

External ethical review

If a study requires some form of ethical scrutiny, the next step is to consider what might constitute adequate

Assessing the need for additional ethical consideration in clinical studies

- Change in local clinical practice associated with the study
- Additional burden imposed on the patient or others by the study
- Additional risk imposed on the patient or others:
 - Directly, from the procedure, or
 - Indirectly, from the additional data
- Likelihood of direct patient benefit
- Likelihood of a benefit to society through an increase in knowledge:
 - Directly, from knowledge obtained, or
 - Indirectly, from teaching research methodology, stimulating better studies, or contributing data to (later) meta-analysis

Case scenarios

Below are four examples of ethical dilemmas. We invite readers to respond to the questions raised through bmj.com

Scenario A

A cardiac surgery department with three surgeons receives a complaint from a patient that his surgeon had used an inferior technique such that he was left with continuing angina. The patient's friend, who was operated on by another surgeon in the same hospital using a more expensive technique, did well. The chief executive was worried about the death rate of the second surgeon and was also concerned that the technique used by the second surgeon costs 20% more. The third surgeon used both techniques, according to ill defined criteria. The chief executive proposed an audit, suggesting that every patient should be recalled at six months for angiography and stress testing for angina to determine whether the expensive technique led to a higher rate of arterial patency in the long term, and whether this was associated with less angina. Before this audit, the routine follow up was for patients to see a specialist nurse at three months: 80% were seen and 46% completed the SF-36 questionnaire. One hundred of 109 surviving patients returned for follow up, and all had angiography and exercise testing. Patients of the surgeon who always used the cheaper technique had more patent arteries and less angina than patients of the surgeon who always used the expensive method ($P < 0.01$); the third surgeon treated only 20 patients, and no statistical differences emerged. The results were written up because the chief executive felt that the findings would influence practice. There was no scrutiny by an ethics committee "because it was audit" and ethical considerations were not discussed in the paper.

Questions:

1. Should the study have taken place?
2. Should an ethical review have taken place before starting?
3. Should the journal publish the paper (a covering letter was received confirming that the local ethics committee had explicitly decided it was audit and did not need review)?

Scenario B

A letter from a clinic in Sweden suggests that melanoma is caused by viral infection with a specific parvovirus, previously not known but easily identified with monoclonal antibodies. A dermatology unit with slides from 100 melanomas excised over the past five years applies the antibody to the slides and finds evidence of virus in 40% of cases, whereas no slides of similar skin biopsies in other diseases showed infection. This is submitted as research, but without ethics committee approval and without consent from all patients (not least because 15 had died). The authors provide

evidence that they had considered the matter, and indeed include a paragraph on the arguments. They specifically find that all 15 who died had evidence of infection, and conclude that there is a causal link.

Questions:

1. Should the researchers have sought external ethical review?
2. Should the journal publish the paper (peer review suggesting that the finding is novel and important, and that the methodology is sound)?

Scenario C

A registrar in a psychiatric hospital thinks that when a fire alarm goes off schizophrenic patients taking risperidone leave fast and congregate in the correct place, depressed patients leave slowly and congregate in the right place, and schizophrenic patients taking chlorpromazine do not bother to move unless asked, and then go to the wrong place. He has a theory that this relates to dopamine and serotonin concentrations affecting drive and ability to locate self in space. Fire alarms are quite frequent. He therefore structures observations over six months (eight fire alarms), and also notes the diagnoses and drugs taken. He finds that patients taking risperidone leave in half the time, and that patients taking drugs that affect serotonin usually get lost. This is submitted as research, but without any ethics committee approval "because there was no experimentation" (the fire alarms were all real).

Questions:

1. Should the registrar have sought external ethical review (he discussed it with the senior ward nurse)?
2. Should the journal publish it (assuming that they decide that it is of interest)?

Scenario D

A UK study in 2002 randomised patients with stroke to general medical wards or to a stroke unit. The study had approval from an ethics committee and was submitted for publication. The editor knows that patients were randomised to known inferior care (in general medical wards), which is generally considered unethical. However, in the UK many patients are still unable to receive stroke unit care. Should the study be published?

Questions:

1. Was it ethical to randomise patients to a known inferior treatment in the circumstances?
2. Should the journal publish it, and if so should they insist on an ethical commentary?

scrutiny. One obvious mechanism is for a properly constituted, independent ethics committee to scrutinise the study. However, the conclusions of an ethics committee should not be accepted without question because the variation in decisions is well documented.^{16 17} This variation may be permissible,¹⁸ but any third party should always make its own judgment.

However, the external review does not need to be the same for all studies or situations. Current UK and European practice needs urgent review to encourage proportionate review focused on the ethical issues.¹⁹ Proportionality should also apply to obtaining consent from the participant, just as it already applies to all other clinical encounters that, in principle, require consent. If the burdens or risks are small, then implicit consent is adequate, but if the burdens or risks are larger then a more formal procedure is used with its rigour varying according to circumstances.

Ethical scrutiny should continue after the study is complete, especially when it is submitted for publica-

tion. Journals generally consider that all research must be approved by an ethics committee and that audit does not need such approval. They devolve responsibility for ethical scrutiny to ethics committees. This approach is inadequate because research and audit cannot be distinguished and because ethical judgments vary. Journals should consider the moral aspects of any study submitted. They can discharge their duty in several ways: accepting the opinion of an ethics committee, obtaining their own external ethical review, considering the ethical position themselves, or asking the author to discuss the ethical dilemmas within the paper and allowing readers to decide morality for themselves.

Lead investigators: one way forward?

The problems generated by the false categorical distinction between research and audit, especially but not only in relation to ethical considerations, mirror

other problems faced in all services—namely, the lack of trust and the futile and wasteful attempt to monitor every practice.²⁰ The solution is to return to the better aspects of professional practice. Professional lead investigators could take responsibility for research and audit.²¹ Their professional responsibilities would include upholding good ethical practice (already integral to professional standards for many professional groups).

Ethics committees could then exist to answer specific ethical concerns. They would not need to distinguish between audit and research, or indeed other areas of clinical practice. They would consider the ethical aspects of any study or situation needing it and help the investigator or clinician reach a reasonable decision. They would be expected to explain and justify their reasoning and decision, but this would be tailored to the question concerned.

Responsibility for the more bureaucratic aspects of current work of ethics committees, such as ensuring clear communication with patients and documenting participant agreement, would remain with the principal investigator (with appropriate guidance and standards). This approach should reduce the burden on ethics committees by removing the bulk of minor research projects with little ethical challenge and leaving more time to review more challenging proposals, both research and audit.

Contributors: DTW is a member of the BMJ ethics committee and edits a clinical journal (which does not have an ethics committee). He is involved in many research projects and advises other researchers. Information was sought from searching Medline and EMBASE using words such as audit, research, and ethics but it was not a systematic search. The ideas came from discussions held with many people, including the BMJ ethics committee. Liz Wager gave some specific advice and Peter Halligan stimulated some changes.

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Summary points

Distinctions between audit and research may affect a study's funding, insurance, and need for external review

Audit and research cannot be distinguished in a reliable or valid way

Ethical (moral) aspects should be considered for every action within health systems

Any direct patient contact is the responsibility of the clinician involved; other ethical aspects should be the responsibility of a named investigator

External ethical review should be sought according to the nature and extent of moral conflict

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Commentary: patients may be less risk averse than committees

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Ethical considerations should apply to all medical practice and interventions that affect patients. This should include social caregiving, which at present is not seen as being in need of moral or ethical consideration. And if audit is potentially more likely to lead to change than research, as Wade claims,¹ clearly it should be given equal consideration and outcomes followed up.

Sometimes, however, it feels as though ethics committees are putting up barriers to much needed research. As a former carer for my husband, a general practitioner who developed Alzheimer's disease in his

50s, I know that some people with dementia and their carers perceive acceptable risk differently from ethics committees and are more willing to take risks, feeling there is little to lose. Indeed, research has shown that carers and people with dementia are particularly altruistic in their desire to be included in research.²

Affected patients should be given a voice on what constitutes "adverse effects" in ethical decisions on research and treatment interventions. Being included in a clinical research project has considerable placebo effect on the wellbeing of both patient (and carer), and

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