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CLINICAL AUDIT AND REFORM OF THE UK RESEARCH ETHICS REVIEW SYSTEM

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ABSTRACT. There is an international consensus that medical research involving humans should only be undertaken in accordance with ethical principles. Paradoxically though, there is no consensus over the kinds of activities that constitute research and should be subject to review. In the UK and elsewhere, research requiring review is distinguished from clinical audit. Unfortunately the two activities are not always easy to differentiate from one another. Moreover, as the volume of audit increases and becomes more formal in response to the demand for evidence-based practice in medicine, the overlap between research and audit grows more acute. Arguably, similar ethical standards and systems for ensuring that those standards are met should be applied regardless of whether or not a project is classified as research or audit. At a time when the research ethics review system in the UK is undergoing significant reform it is important that the opportunity is not missed to address the longstanding research-audit problem. We discuss suggestions for further reform that addresses this issue.

INTRODUCTION

Which activities should be subject to ethical review by research ethics committees (RECs)? The obvious and traditional answer is that if the activity qualifies as research then it falls within the remit of RECs.¹ Unfortunately, research is notoriously difficult to define. The purpose or objective of most research is new and generalizable knowledge. Clinical audit, on the other hand, is used to monitor the standard of care received by patients or outcomes of treatment. Audit is a cyclical activity designed to monitor service quality. Standards are defined, evidence is gathered about performance and the results are compared against standards. Actions are then taken, if necessary, to improve practice and the cycle begins again. But both research and audit may utilise similar methodologies or expose participants to risk of similar kinds of harm. We need to separate the problem of defining research from the problem of defining the limits of ethical review. Recent focus on quality and standards in health services means that interest in audit is increasing. Audits are becoming more formal, sophisticated and increasingly results are published in peer reviewed journals. Greater overlap between research and audit is problematic for investigators, research ethics committees, and journal editors as opinions differ over the requirement for ethical review. This can lead to delays in the commencement of audit and publication difficulties. In addition, the lack of both clear ethical guidelines for audit and a robust system of compliance puts participants at risk and potentially erodes public support.

Whilst ethical review of research is widely accepted, the REC system has come in for heavy criticism from researchers who find the

process overly burdensome and slow.² Therefore, any expansion of ethical review to encompass audit must be carefully balanced so that it does not disproportionately impede good quality studies. In Australia, these issues were at the heart of reform of the ethical review system. We consider whether lessons learned from the Australian example can be applied to the evolving UK NHS national research ethics service.

THE CHANGING NATURE OF CLINICAL AUDIT IN A POST-BRISTOL NHS
In 1999, scandal hit the National Health Service (NHS) when doctors carrying out complex heart surgery on children in Bristol were found to have done so despite higher death rates for such surgery than their colleagues. One of the outcomes of the Bristol Royal Infirmary Inquiry,³ chaired by Sir Ian Kennedy, was to reignite interest in clinical audit. Not only has this contributed to an increase in the volume of clinical audit, but the nature of audit has also changed. Greater formality and rigour in the audit process together with wider dissemination and interest in the results of audit has meant that the line distinguishing it from other kinds of research has become increasingly blurred.

Clinical quality was not a policy issue before the 1980s when public concern first arose over variations in practice and outcomes. Until that time the emphasis was firmly on professional autonomy and self-regulation.⁴ In 1985 the World Health Organisation called on member states to introduce quality systems,⁵ and in 1989 a formal structure was finally implemented.⁶ The US 'total quality management' model was favoured.⁷ Audit became a branch of quality assurance, along with other intelligence-gathering activities including review, evaluation, surveillance, appraisal and monitoring.⁸ Audit may be medical, clinical or organisational:

Clinical audit refers to audit covering all aspects of clinical care, including that provided by nursing and paramedical staff. Medical audit refers to audit of activities initiated directly by doctors. Organisational audit refers to investigation of aspects of practice such as appointments systems which are regarded as primarily administrative.⁹

Here we concentrate on clinical audit where the grey area between research and audit is most apparent. From 1989, the responsibility of the NHS to monitor quality extended to cover clinical audit. Clinical audit was traditionally the exclusive domain of clinicians. It was seen largely as an ad hoc teaching aid which formed part of the system of professional self-regulation. Critics pointed out the difficulties of achieving good clinical audit,¹⁰ and the ethical issues that some audit raises.¹¹

One of the effects of the Bristol Royal Infirmary (BRI) debacle was to renew the demand for monitoring and accountability of doctors.¹² The Bristol Royal Infirmary Inquiry recommended that clinical audit should be at the core of a system of local monitoring of performance; that it should be fully supported by the local NHS Trusts which commission services for hospitals and General Practitioners' practices; and should be compulsory for all healthcare professionals

providing clinical care.¹³ More rigorous standards in terms of study design and data analysis now apply to audit and the results of audits are much more likely to be published than in the past, making the distinction between audit and research much more difficult to draw.

PURPOSIVE DEFINITIONS OF RESEARCH AND AUDIT: NO LONGER FIT FOR PURPOSE?

Audit is a species of quality improvement / quality assurance, which has its roots in management. In contrast, research has its roots in science and academia. There have been numerous attempts to provide simple definitions differentiating research from audit:

Research is concerned with discovering the right thing to do; audit with ensuring that it is done right.¹⁴

Research...helps to answer the question 'what is best practice?' Clinical audit answers the question 'are we following best practice?'¹⁵

Perhaps the most helpful distinction [between research and audit] is about motivation and the objectives of the project: audit has the objective of directly improving services against a standard; research may include the objective of defining best practice.¹⁶

In the majority of cases research and audit can adequately be distinguished on the basis of their different objectives or purposes. However, this approach is limited as it fails to deal with activities that are multifunctional. Some studies exhibit features of both research and audit. This has left investigators and research ethics committee members in a sea of confusion.

The United Bristol Healthcare Trust (UBHT) has recently issued two simple guides attempting to define first clinical audit¹⁷ and second the ethical issues contained therein.¹⁸ The former document seeks to differentiate between the two on the basis of purpose, a line followed in the Central Office for NHS Research Ethics Committee's (COREC's) recent guidance.¹⁹ The latter document examines potential ethical issues arising in audit, concentrating in particular on confidentiality issues. It concludes that audit does not require independent ethical review except in two situations:

1) if the study is research and not audit. The document points out that audit never involves 'experimentation on patients, placebo or new treatments, allocation of subjects to control groups or randomisation or any disturbance to the patient beyond that required for routine clinical management'.²⁰ The guide recognises that a 'purposive' approach will not always work and the grey areas must be resolved with dialogue between the Research and Effectiveness Department, the Clinical Audit Team and the relevant NHS REC. In those cases where the project contains elements of both audit and research, the document recommends that ethics approval be obtained.

2) if the study involves a patient survey.²¹ The advice, again, is to look to purpose to determine whether the survey is research or audit. If it is audit, then ethical approval will not be required though 'there are still a number of questions you should address which have an ethical dimension'.²² Some such questions are listed.

This guidance is as clear as an approach based on definitions of research and audit can be, but borderline cases are not easily resolved, and some audit will raise ethical issues that will not be subjected to independent ethical review. The UBHT advises that

research ethics committees are consulted in cases of doubt. The Royal College of Physicians gives similar advice,²³ but then ethics committees are faced with the same difficulty.

Although there are differences between audit and research, there are also significant similarities, the most relevant being the involvement of patients and the use of their personal information. Ethical review does not exist because research is concerned with generalizable knowledge. Rather ethical review exists to protect research participants from risks of research. This level of paternalism is justified because of the imbalance in power and knowledge that is manifest in the doctor-patient relationship, which gives rise to the potential for undue influence. The same doctor-patient relationship and the associated risk of undue influence are potentially as prevalent in clinical audit as they are in some types of clinical research.

The burdens and risks involved in research are justified on the basis that research contributes to the public good. Yet the public good of research lies not in the contribution it makes to generalisable knowledge per se, but in the subsequent improvement in the treatment and care of future patients that results from the application of that knowledge. Thus in terms of the relevant ethical considerations, the purpose of research is more appropriately expressed as the improvement of healthcare for future patients. Exactly the same can be said of the purpose of clinical audit.

In summary, both the benefits and the burdens of clinical audit and other types of clinical research are similar in kind. Both involve methods that potentially expose participants to burdens and risks of psychosocial harm and undue influence. Both activities are ethically justified if the public benefit in terms of the contribution made to further improvements in healthcare for future patients outweighs the burden and risk to the participant. Ethically, clinical audit and other research differ only in degree, not in kind. As a result, there can be no clear dividing line between the two activities. UK regulations which attempt to drive a wedge between research and clinical audit are flawed.

THE CONSEQUENCES OF DRAWING INAPPROPRIATE DISTINCTIONS BETWEEN RESEARCH AND AUDIT

The difficulty distinguishing between clinical audit and research is not merely semantic. This uncertainty has important consequences because of the different ways in which audit and research are regulated. Whilst all research protocols must receive prior approval by a REC, audit is exempt from this requirement. Given that the REC system has been strongly criticised for being too cumbersome and bureaucratic,²⁴ any opportunity to circumvent the system must be tempting. Additionally, the arrangements for ensuring that audit conforms to appropriate ethical standards are fragmented and lack clarity. Where audit poses risks to participants or overlaps with research there is a

case for greater consistency in ethical standards, including the requirement for prior ethical review.²⁵ Participants in clinical audit may be recruited to projects that would not have been approved by an ethics committee had they been labelled as research. There are problems too for the investigator. He may encounter difficulties in the case of a multi-site investigation if some authorities classify it as audit and others as research.

For example, a national audit of screening for diabetic retinopathy reported by Wilson et al. in the British Medical Journal (BMJ) involved collecting data from every health authority in England and Wales.²⁶ While some health authorities saw the study as audit, others were unsure and passed it on to the relevant NHS local research ethics committee, with inconsistent results. Some ethics committees viewed the study as audit and outside their remit, some saw it as research, and others did not define it as either but felt that the use of patient questionnaires, access to NHS patients, or the use of an outside researcher warranted ethical approval. Some ethics committees were applying the (vague) definitions supported by the NHS. Arguably others were ignoring them completely and reviewing projects according to the risks posed to participants. Some of the problems experienced by Wilson et al. were resolved by the introduction of multi-centre research ethics committees in 1997. However the crux of the problem remains: audit is not within the remit of research ethics committees, which are subject to the same (lack of) guidance when it comes to differentiating between research and audit as investigators. Relying on them to define which borderline studies should be subjected to review potentially leads to inconsistency, delay and substandard protection of participants.

Another problem is this: investigators who genuinely believe that they are conducting an audit may encounter resistance from journal editors if they decide to publish their findings and the editor views the study as research. Journal editors are subject to their own ethical code and will be reluctant to publish the results of what they perceive to be human research, without prior ethical review. A UK study published by the Lancet in 1998 demonstrates the problem well.²⁷ The study was labelled an 'audit of results from a clinical service' and as such no ethical review was sought. It compared the prevalent method of detecting women at a high risk of carrying a foetus with trisomy 21 (Down's Syndrome) which involved a combination of the maternal age and a second-trimester maternal serum biochemistry with an emerging method, which combined maternal age with a nuchaltranslucency thickness ultrasound scan at the end of the first trimester.

In 306 centres across the country, women attending routine antenatal care were offered the option of having their risk of trisomy 21 assessed by measurement of the nuchal-translucency thickness at an ultrasound scan performed between 10 and 14 weeks gestation. They were given an information leaflet, told of the risks and given a request form to complete about the outcome of pregnancy. Many of

these women would not have otherwise had a first trimester scan, which is performed transabdominally or, in cases of poor visualisation, transvaginally. The latter method is clearly invasive. Consent was obtained and an information sheet produced, but no independent ethics committee vetted the procedure. Pregnancy outcomes were obtained from maternity units, general practitioners or from the participating women; methods which raise data protection and confidentiality issues. The project also posed risks and benefits to the participants personally, directly affecting the care of the patients and their foetuses. The Lancet published the study but followed it with an editorial outlining the difficulties inherent in borderline studies.²⁸ The review system attempts to ensure adequate protection before the research begins; internal quality assurance or, in the case of clinical trials of investigational medicinal products, statutory regulation by the Medicines and Healthcare Products Regulatory Agency attempts to ensure that the recommendations are indeed being carried out; increasingly, journal editors are seen as a final barrier to unethical research. Where research is (intentionally or unintentionally) mislabelled as audit, the review system is bypassed altogether and the role of editors becomes especially important. Increasing numbers of audit studies are now published, but editors have no magic solution to the definition quandary.

The Council of Science Editors,²⁹ UK Committee on Publication Ethics (COPE),³⁰ and the World Association of Medical Editors (WAME)³¹ all advise that the editor requires evidence of ethical review before publishing 'research'.³² In borderline cases, journals might simply insist on prior ethical approval or a statement from the relevant ethics committee that review was not required. In this way they might abdicate responsibility. Yet a statement from an ethics committee that no review is required is not always the end of the matter. Given the current lack of certainty and resulting inconsistency editors arguably have a moral duty to consider the matter more deeply. In theory a journal editor might disagree with an ethics committee decision to classify a project as audit. Or a project may begin as audit but raise unexpected findings, which render a definition of research more appropriate. For articles submitted to the BMJ, its own ethics committee can be called upon to advise the editor in such cases. The BMJ's submission guidance states that:

Many people consider that studies referred to as audit do not need any consideration of ethics, whereas all research must be approved by a formally constituted research ethics committee or, in the USA, an institutional review board. But the distinction between audit and research is unclear, and the assumption that audit or analysing previously collected data is never unethical may not be justified. Furthermore, review by an ethics committee cannot necessarily guarantee that work is morally sound. For these reasons journals have a duty to consider the ethical aspects of both submitted and published work.³³

Members of COPE are advised to ensure that their journals have in place 'a mechanism to ensure correct ethics committee or institutional review board approval',³⁴ which assumes some determination as to whether the study is correctly labelled as research or something else. The International Society of Medical Journal Editors³⁵ insist

that editors review the protocol to the extent that:

If doubt exists whether the research was conducted in accordance with the Helsinki Declaration, the authors must explain the rationale for their approach and demonstrate that the institutional review body explicitly approved the doubtful aspects of the study.³⁶

But there are problems with editors subjecting studies to ethical scrutiny. The review is not independent and may not conform to national standards. It might conceivably undermine the decision of a NHS REC.

An alternative is to refuse to publish borderline studies. The UBHT³⁷ advises that the results of audit may be published without prior ethical approval, but journal editors may refuse to publish articles if there are ethical concerns and REC ethical approval has not been granted'. Given that audit is not currently within the remit of NHS RECs, whatever the ethical issues it might raise, this leaves authors in an unenviable position. It is also likely to allow valuable studies in the grey area between research and audit, to go unpublished. A third option is to demand that the study is given retrospective ethical approval. However this practice is barred in the UK. Retrospective review is occasionally utilised in Australia, but a clinical study published in the Medical Journal of Australia in 2001³⁸ led to debate about whether the practice was acceptable. Guidance followed in 2003³⁹ aimed at preventing the necessity for retrospective review. We will examine that guidance later.

In the UK, the definitional problem is passed around from investigator, to ethics committee, to editor. No one has a definitive answer. One recent report in the BMJ lamented the continuing difficulties of getting quality improvement studies published:

Journals treat quality improvement as research and wonder why there's no ethics committee approval...And many, perhaps most, ethics committees are still unclear what to do with quality improvement proposals.⁴⁰

In consequence, despite efforts to create publishing avenues for clinical audit and other types of quality improvement (such as the Quality Improvement Report format in Quality and Safety in Health Care), the results of clinical audit are under reported in the literature, hampering efforts to establish national standards of best practice.

REFORM OF THE UK RESEARCH ETHICS SYSTEM

In 2005, Lord Warner commissioned a review of the UK NHS research ethics committee system and subsequently recommended that:

The remit of NHS RECs should not include surveys or other non-research activity if they present no material ethical issues for human participants. COREC should develop guidelines to aid researchers and committees in deciding what is appropriate or inappropriate for submission to RECs.⁴¹

This implies two things. First, it implies counter-intuitively that survey-based studies are not research. This might be problematic in the rare cases where such surveys raise ethical issues. Second, it might imply that the remit of research ethics committees ought to include non-research activities if they involve significant ethical issues. The National Patient Safety Agency took on responsibility of COREC in

2005. Together with COREC, it proposed an alternative interpretation of the CMO's recommendation in 2006.⁴² The definition-based approach will be retained. Audit will remain outside the remit of RECs. The National Research Ethics Service was launched in April 2007. A team of National Research Ethics Advisors (NREAs) will screen applications in order to identify studies which:

1. fall outside the remit of NHS RECs;
2. are patently of poor scientific quality or are poorly presented;
3. apparently present no material ethical issues;
4. are complex...[whereupon] the research ethics service will arrange for experts to provide...advice.⁴³

Low risk research will be considered by the NREAs, provided they contain 'no material ethical issues'.⁴⁴ Research of higher risk, and research containing material ethical issues, will go before a full research ethics committee. The service will operate on a continuous full-time basis so that straightforward studies can be approved without undue delay. This will also free up time so that ethics committees can concentrate on applications that require closer ethical scrutiny. There will therefore be advantages to investigators in terms of increased throughput and efficiency. At the same time the interests of potential research participants will also be protected by retaining independent ethical review of the majority of research in the NHS. A pilot screening process was launched in May 2007.

Improved efficiency and greater proportionality promised by the reforms should be welcomed by investigators. Moreover, the incentive to circumvent the ethical review process by mislabelling audit as research should also be weaker under the proposed system, thereby strengthening the degree of protection afforded to potential research participants. However, uncertainty will still reign in the case of studies that fall on the borderline between research and audit. It remains the case that an NREA ought to reject such a proposal on the basis that it is outside the REC's remit because it is judged to be an audit, regardless of the ethical issues inherent in the protocol. Guidance produced by the NPSA/COREC in 2006 does not shy away from the problem. It states:

Although any of these [i.e. research, clinical audit and service evaluation] may raise ethical issues, under current guidance, research requires REC review, audit does not require REC review, service evaluation does not require REC review.⁴⁵

The proposed system will reduce delay and bureaucracy for researchers. It may even clarify the situation for ethics committees. It adds nothing of benefit to participants of audit projects that raise ethical issues and will result in confusion whenever a project does not fit neatly into the definition of research.

ALTERNATIVE MODELS

Rather than the definition of research taking centre stage in setting the limits of the remit of research ethics committees one could specify

which activities require prior ethical review. This approach has been adopted in several European countries. In France, for example, prior ethical approval is only required for studies that involve medical intervention, medication, or physical risk.⁴⁶ Elsewhere, in Denmark and The Netherlands for example, surveys and questionnaire-based studies are excluded from the requirement for prior ethical review. In the UK, the issue of whether or not to exclude surveys from the remit of RECs is still under consideration.⁴⁷

Currently in the UK, it is claimed that the research / audit distinction is an adequate proxy for risk. Likewise, the inclusion or exclusion of certain kinds of activities is justified on the basis that they generally involve greater or lesser risk. There is therefore a consensus that ethical review is warranted for studies which exceed or potentially exceed a certain threshold of risk. That threshold is usually referred to as 'minimal risk'. Many definitions exist, but there is no universally accepted standard.⁴⁸ There are many kinds of risk that are relevant in determining whether or not a project is ethical and opinions differ over which kinds of risk are the more important. Thus, the French ethical review system acknowledges risk of physical harm as the primary concern, whereas in the UK the risk of social and psychological harms is expressly recognised. Other less paternalistic approaches are possible. The moral philosopher John Harris, for example, emphasises the risk of undue influence.⁴⁹

A system which defines the requirement for independent ethical review by reference to a definition of research or of a certain activity will inevitably result in substandard review for those studies that fall on the borderlines of the definition or outside it altogether. As we have seen, this has potential to result in substandard protection for the participant, and also as a barrier to the publication of borderline studies. But what are the alternatives, and, equally important, are they proportionate?

EXPEDITED REVIEW FOR RESEARCH AND AUDIT

Another possibility would be to subject all biomedical research, including audit where that involves patients, participants, or their personal information, to independent ethical review. Historically in the UK, this would have led to unacceptable delays in the approval of important studies. However, the screening system that is being introduced by the National Research Ethics Service may relieve such problems. It could be extended to apply to types of clinical audit. But would this constitute a proportionate use of time and resources? Arguably such outlay cannot be justified to protect participants in the few cases where research is mislabelled or audit raises ethical concerns. And there is another difficulty. Whilst there is an area of overlap between the two activities there are also instances when research and audit clearly differ. As currently constituted, research ethics committees may lack the required knowledge and expertise to evaluate some kinds of audit. The distinction between audit and research runs deep within the NHS. Auditors may feel uneasy about having their applications reviewed by a service that has

little experience of reviewing audits.

ABANDONING THE QUEST FOR A DEFINITION OF RESEARCH

Australia's National Statement on Ethical Conduct in Research Involving Humans⁵⁰ implements a radical alternative. It does not attempt to define research,⁵¹ recognising that the meaning is dependant on context. Instead the emphasis is on defining the remit of Human Research Ethics Committees (HRECs).⁵² Consequently a broad view of research is taken and it is left to the investigator and the HREC to determine whether or not it is research and so subject to ethical review.⁵³ It is risk to the participant that is the all-important factor in the Australian ethical review system. The Statement makes it explicit that, where participant involvement has potential for infringing basic ethical principles, review is warranted.⁵⁴

The Statement recognises the evolving research environment and the resulting need for flexibility in approach. On this basis, audit will not normally be included, but those rare cases of audit that have potential to infringe ethical principles can legitimately be incorporated within the remit of the HREC. This procedure, however, merely passes on the definition problem to the research ethics committees. Indeed the Statement recognises that:

Researchers, regulators, funding bodies, institutions, organisations and HRECs will need to address these issues...and arrive at provisional descriptions of what constitutes research that merits ethical review. ⁵⁵

Accordingly the National Health and Medical Research Council published guidance in 2003.⁵⁶ In Australia, the term 'quality assurance' (QA) is used. QA is wider than clinical audit. It can encompass types of health services research and a variety of quality improvement studies. The Australian guidance aims to protect participants, but also to facilitate QA, to help investigators determine when ethical review is necessary and to assist journal editors assessing articles for publication. The report notes that no authority has been able to adequately separate the definitions of QA and clinical research and consequently focuses on central features of any QA proposal that must be considered in deciding whether or not the proposal requires independent ethical review.

Attempts to clearly separate quality assurance from research are difficult, and can be artificial and unhelpful. What really matters is that:

- (a) quality assurance is undertaken for a valid purpose and its outcomes are used to improve health care; and
- (b) those who undertake quality assurance adhere to relevant ethical principles and...legislation; and
- (c) where quality assurance proposals could infringe ethical principles that guide human research, independent ethical scrutiny of such proposals should be sought.⁵⁷

According to the guidance, QA can proceed without ethical review

if either the participant gives informed consent or the results are fully and appropriately anonymised and participants are unlikely to suffer burden or harm.⁵⁸ Section 5 breaks these issues down into a helpful list of questions. Only if all are answered in the negative can the investigator proceed without the advice of an independent ethics committee. Even when some answers are positive, however, the report advises that a detailed application or review by a full HREC will rarely prove necessary and sets down suggested means by which delegates of the HREC can swiftly deal with proposals involving minimal risk.⁵⁹

A system of expedited review operates in Australia. There are three levels of review in the Australian system: no independent review of minimal-risk quality assurance; expedited review of low-risk quality assurance and other research; full ethics committee review of higher risk research. The application process for expedited review is less onerous than an application for full review. Applications are screened and, if accepted for expedited review, will be evaluated by two HREC members; the investigator will be notified within two weeks whether or not the application has been approved. Alternatively, if an application for expedited review is not accepted, notice will be sent to the investigator that an application for full ethics committee review is required.

The strengths of the Australian system are flexibility and sensitivity to the ethical significance of audit. There is however a danger that the system could fail to protect participants by relying on investigators to identify when ethics review may be required. Whilst the guidance is helpful, some investigators might try to avoid ethical scrutiny. However this risk can be overstated. Provided the system of expedited review ensures that minimal-risk studies are swiftly processed, investigators have little to gain by mislabelling their study and much to lose if they intend to publish the results. More problematic is the fact that opinions are likely to differ on a case by case basis as to what exactly constitutes more than minimal risk. This could lead to uncertainty and difficulties publishing audit that has not been subject to prior ethical review. In this respect, one troublesome definition (research) is replaced by another (minimal risk). For example, Maxwell and Kaye reported that their planned multi-site audit was severely delayed because the participating health authorities came to different conclusions over whether or not full ethics review was required.⁶⁰ So, despite extensive guidelines, practical difficulties in allocating projects to the correct ethics review track are still evident.

THE WAY FORWARD

COREC defines the remit of ethics committees in paragraph 3.1 of its Governance Arrangements for NHS RECs (GAfREC). A second edition of GAfREC is expected in 2007. It is likely to develop an approach based on defining the activities which require prior ethical review. Audit will be excluded, possibly alongside NHS surveys.⁶¹ The aim is to achieve proportionality: few studies which raise ethical issues will bypass review. Some inevitably will. We have explored a

number of alternative approaches. All clinical audit involving patients, participants or their personal information could be required to come under the ethical review umbrella. A system of expedited review would ensure that the vast majority of projects would be quickly turned around. Nevertheless, the cost in terms of time and resources would be prohibitive. Another option would be to follow the Australian model and abandon the quest for a definition of research.

Instead, risk to the participant would be key. The investigator would bear the responsibility for deciding whether or not his study posed sufficient risk to the participant for ethical review to be warranted, and ethics committees would be given the authority to review any NHS project, research, audit, or service evaluation that raises ethical issues. There is much to recommend this system. But one problem with both alternatives is this: research ethics committees are not audit ethics committees. As we have seen there is a significant area of overlap between audit and research that can on occasion make the two activities difficult to distinguish, yet it is also true that there are significant differences between the two activities. Moreover, those differences are entrenched within the NHS. Arguably, even if the resources could be found to extend review to all studies raising ethical issues, the multiple differences between most research and most clinical audit would make the National Research Ethics Service an unsuitable reviewing body. Given the expenditure invested in the new research ethics system, the radical change required to implement a system based on the Australian model is unlikely to be embraced. We propose a fourth option. First, COREC would formally recognise that in borderline studies which contain ethical issues, RECs should err on the side of caution and submit the protocol to ethical review. This is probably what happens in many borderline cases in any event. At present, however, studies that are obviously audit but raise ethical issues, are not subject to review: there are incentives to mislabel research as audit, and investigators are unsure whether to publish studies raising ethical issues without prior ethical review. Additional measures are necessary.

We therefore suggest that, second, Audit Committees in NHS organisations conducting clinical audit should be formalised. At present, no coherent system is in place to ensure that principles of good medical practice in audit are applied. Each healthcare organisation needs latitude in setting its own priorities for audit, and whilst guidance recommends a structured audit programme, including a committee structure and regular meetings, there is little guidance as to the constitution and remit of the committees and little to help them reach a decision as to the suitability of the particular study.⁶² Arguably, greater formality is needed in the internal review of audit. Audit committees might even be required to include lay representatives who would be ideally placed to call attention to issues relating to participant protection. Audit committees would come under the inspection of the Healthcare Commission, enhancing confidence in their deliberations. Formal guidance would not only help ensure that

audit is ethical, it might also raise the standard of audit. A number of articles have drawn attention to a quality gap, both in terms of ethics and scientific rigour between research and audit.⁶³ The introduction of formal review of audit could help to close the quality gap, save resources from being wasted on ineffective audit and protect the rights and dignity of participants. But would the internal Audit Committee be suitably placed to review projects that do raise ethical issues?

We think not and argue that, third, a clear pathway should be developed by which internal Audit Committees could pass those studies which raise ethical issues to an ethics committee. If the audit is conducted in a Trust which has a clinical ethics committee, then that committee may be suited to the task. Ideally, however, a National NHS Audit Ethics Committee would be set up. Low risk audit containing ethical issues could be dealt with by expedited review. Studies posing greater risk could be reviewed by the full committee. Just as we propose for RECs, the Audit Ethics Committee could be given the authority to review studies on the borderline between research and audit. This solution would protect research participants. It would also give confidence to investigators, ethics committees and journal editors. More audit would be published. And what is published would have been subjected to a consistent level of prior scientific and ethical review.

There is a price to pay, and that price is delay. Recent reforms of the research ethical review process have aimed to ensure that internal NHS Research and Development (R&D) review occurs alongside independent ethical review in order to reduce duplication and delay. The method we propose involves the project going first to the internal Audit Committee and subsequently, if necessary, to the National Audit Ethics Committee. However the crucial difference is this: all NHS research must receive both R&D review and ethical review. In our case, only audit/borderline audit studies raising ethical issues would need to go before National Audit Ethics Committee. Cases are likely to be few: hence the need for only a single, national committee. The National Audit Ethics Committee would require detailed operational guidance. Currently the Principles of Best Practice in Clinical Audit recognises only that health service professionals 'should be aware of the ethical implications of audit'.⁶⁴ The UBHT gives more substantive guidance⁶⁵ which could be developed, alongside a consideration of the Australian guidance, into a suitable format for ethics committee use.

The introduction of independent ethical review of audit has been suggested many times—sometimes by investigators themselves frustrated by the problematic distinction between audit and research.⁶⁶ Ethical review systems must strike an appropriate balance between the duty to protect participants and the duty to facilitate research and promote continued improvements in healthcare for the benefit of the wider public.⁶⁷ There is a strong duty to facilitate clinical audit as the

results are likely to have a direct impact on the quality of patient care. Thus, any changes to the regulation of clinical audit must be carefully considered so that they do not disproportionately impede studies of good quality. Such a system ought to be possible. Independent ethical review of audit would be reserved for those cases identified by internal audit committees. Even when ethical review is required, a triage system could reserve full review for studies involving more than minimal risk to participants. Review would be undertaken by people with the appropriate experience so that investigators could have confidence that reviewers understand the purpose and methodology of their study. The development of such a system is not necessarily antithetic to the duty to facilitate good quality audit.

CONCLUSIONS

Lack of clarity over the remit of research ethics committees and overreliance on confused definitions fail to serve the interests of investigators, research participants, and journal editors alike. Resources are wasted, progress is impeded, and participants are put at risk. A straightforward and transparent system of ethical review is needed, one that facilitates research and audit of good quality whilst ensuring that the rights and dignity of participants are respected. Current proposals for reform of the research ethics system should help to alleviate the concerns of researchers. However, further reforms are needed to ensure that participants are not put at risk or research impeded as a result of artificial distinctions between research and audit. Greater flexibility in the remit of research ethics committees combined with greater formality in the remit of Audit Committees within NHS organisations and the establishment of an independent National Audit Ethics Committee would achieve that goal. The cost, we argue, would be justified by the increased scientific and ethical quality of audit in the NHS.

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¹See Central Office for Research Ethics Committees (COREC), Governance Arrangements for RECs, (London: Department of Health, 2001): para. 3.1. A revised version is expected early in 2007.

²See special edition of *BMJ* 329 (2004): 241-282. See also M. Hayry, J. Takala, P. Jallinoja, S. Lotjonen, and T. Takala, "Ethicalization in Bioscience - A Pilot Study in Finland" *Cambridge Quarterly of Healthcare Ethics* 15 (2006): 282-284.

³Secretary of State for Health, *Learning from Bristol: The Report of the Public Inquiry Into Children's Heart Surgery at the Bristol Royal Infirmary 1984 -1995*, Command Paper: CM 5207 (London: HMSO, 2001).

⁴As eschewed by the Medical Act 1858, which established the General Medical Council to regulate the medical profession.

⁵World Health Organisation, "The Principles of Quality Assurance- Report on Working Group Meeting Convened by Regional Office for Europe (Copenhagen) in Barcelona, 1983," *European Reports and Studies* (Copenhagen: WHO, 1985): 94.

⁶Secretaries of State for Social Services, Wales, Northern Ireland and Scotland,

Working for Patients, Cm. 555, (London: HMSO, 1989), defining medical audit as 'a systematic critical analysis of the quality of medical care, including the procedures used for diagnosis and treatment, the use of resources, and the resulting outcome for the patient'.

⁷BRI Inquiry Secretariat, BRI Inquiry Paper on Medical and Clinical Audit in the NHS, (1999): para. 1.1. Total quality management is defined at p. 24 as: 'An approach to quality assurance first developed in industry and subsequently widely adopted by management in the public sector. Main components of TQM approach are that: the aim is not simply to maintain standards but to increase organisational success through continuously seeking out ways to do things better; expert criteria for quality are eschewed in favour of customers' definitions of their own needs; quality assurance is seen as a generic internal activity whereby all participants in the organisation take responsibility for their own areas of work; problems are assumed to derive from weaknesses in the system rather than individual failings.'

⁸Ibid., 1.3.4.i. quoting a taxonomy by D.H. Stone, "Proposed Taxonomy of Audit and Related Activities" Journal of the Royal College of Physicians of London 24 (1990):30-1. 'Review is the process of critical reflection used by clinicians wishing to assess their (or their peers) performance; audit is the activity of review when conducted on a continuous and routine basis; evaluation is one-off assessment of the impact of a service on indices of health; surveillance is routinely repeated evaluation; appraisal is ad hoc data collection and analysis by management in relation to health care delivery; monitoring is ongoing appraisal'. ... 'Stone summarises audit, surveillance and monitoring as routine processes which share a common objective of continuous quality assessment by are distinguished by the nature of their feedback loops to clinical, public health and administrative action respectively'.

⁹Ibid., p. 24.

¹⁰For example, M.J. Buxton, "Achievements of Audit in the NHS" Quality in Health Care 3 (Supplement) (1994): S31-S34. 'Scientific audit is a complex and not easily replicable technology. It is not a technology embodied in hardware and software or purchasable "off the shelf" but instead has to be created locally. Audit needs to follow a relatively complex sequence of procedures to be effective, and it entails a difficult set of organisational processes ... The limited evidence available [suggests] very clearly that the process necessary for good audit is difficult and not easily replicated and maintained over time without appropriate skills or enthusiasm.'

¹¹BRI Inquiry Secretariat, 2.2.1.iii.

¹²See for example, Department of Health, A First Class Service: Quality in the New NHS, HSC 1999/033 (London: Department of Health, 1999).

¹³Secretary of State for Health, Learning, p. 143-145.

¹⁴R. Smith, "Audit and Research" BMJ 315 (1992): 905-6.

¹⁵United Bristol Healthcare Trust Clinical Audit Central Office (UBHT), What is Clinical Audit? v.2.2 (Bristol: UBHT, 2005): 4.

¹⁶A. Wilson, G. Grimshaw, R. Baker, and J. Thompson, "Differentiating Between Audit and Research: Postal Survey of Health Authorities' Views" BMJ 319 (1999):1235.

¹⁷UBHT, Clinical Audit.

¹⁸United Bristol Healthcare Trust Clinical Audit Central Office (UBHT), How to Apply Ethics to Clinical Audit v 2.2 (Bristol: UBHT, 2005).

¹⁹See NPSA and COREC, Differentiating Audit, Service Evaluation and Research (London: Department of Health, 2006).

²⁰UBHT, How to Apply Ethics, p. 4.

²¹Note that the Department of Health, Report of the Ad Hoc Group on the Operation of NHS Research Ethics Committees, (DH, June 2005):13 recommends that "Much research, such as surveys, service evaluation, and research on NHS staff does not require ethical review". This matter is still under consultation.

²²UBHT, How to Apply Ethics, p. 4.

²³Royal College of Physicians of London, Guidelines on the Practice of Ethics Committees in Medical Research Involving Human Subjects 3rd ed. (London: RCP, 1996).

²⁴BMJ 329 (2004): 241-282; T. Takala, et. al., Ethicalization, p. 282.

²⁵G. Rix and K. Cutting, "Clinical Audit, The Case For Ethical Scrutiny?" International Journal of Health Care Quality Assurance 9 (1996): 8-20.

²⁶A. Wilson, et al., Differentiation, p. 1235.

²⁷R.J.M. Snijders, P. Noble, N. Sebire, A. Souka, and K.H. Nicolaides, for the Fetal

Medicine Foundation First Trimester Screening Group, "UK Multicentre Project on Assessment of Risk Trisomy 21 By Maternal Age and Fetal Nuchal-Translucency Thickness at 10-14 Weeks of Gestation" *The Lancet* 352 (1998): 343-46.

²⁸ V. Choo, "Thin Line Between Research and Audit" *The Lancet* 351 (1998): 337-338: 338 'The decision to publish the Snijders paper today reflects a quandary about where the line should be drawn between research and audit, about the line between research and best standard of care, about whether the need for IRB approval varies between studies (eg, between interventional and observational studies, between main study and subset of study already given approval), and about when audit should undergo IRB approval.'

²⁹ <http://www.councilscienceeditors.org/> Accessed on June 8 2007.

³⁰ <http://www.publicationethics.org.uk/> COPE, formed in 1997, is a voluntary body providing a sounding board for editors attempting to deal with breaches in research and publication ethics. Accessed on June 8 2007.

³¹ <http://www.wame.org>. WAME is the leading professional organisation for a broad range of biomedical communicators. Accessed on June 8 2007.

³² For example, the "Notice to Contributors" *Anaesthesia* 52 (1997): inside back cover, states; 'Prospective ethical approval should be acquired for papers based on clinical audit data.' This was subsequently removed having been viewed as excessively onerous by contributors: P. Scott, "Clinical Audit is Research" *BMJ* 320 (2000): 713.

³³ <http://resources.bmj.com/bmj/authors/editorial-policies/guidelines> Accessed on June 8 2007.

³⁴ COPE, Code of Conduct for Editors: Checklist and Survey. Emphasis added. <http://www.publicationethics.org.uk/guidelines/checklist2.doc> Accessed on June 8 2007.

³⁵ <http://www.icmje.org/> Accessed on June 8 2007.

³⁶ International Committee of Medical Journal Editors, Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication (1994) at II.F <http://www.icmje.org/index.html#privacy>

³⁷ UBHT, How to Apply Ethics, p. 6.

³⁸ S.R. Grover, R. Morley, "Vitamin D deficiency in Veiled or Dark-Skinned Pregnant Women" *Medical Journal of Australia* 175(5) (1991): 251-2.

³⁹ National Health and Medical Research Council (NHMRC), When Does Quality Assurance in Health Care Require Independent Ethical Review? Advice to Institutions, Human Research Ethics Committees and Health Care Professionals (Canberra, February 2003): section 7 page 9.

⁴⁰ F. Godlee, "Improving On Improvement" *BMJ* 332 (2006):7549.

⁴¹ Department of Health, Report on Ad Hoc Group, recommendation 1.

⁴² NPSA and COREC, Building on Improvement: Implementing the Recommendations of the Ad Hoc Advisory Group on the Operation of NHS RECs, (2006).

⁴³ *Ibid.*, para. 2.1.5.

⁴⁴ *Ibid.*, para. 2.1.8.

⁴⁵ NPSA and COREC, Differentiating Audit, p. 1.

⁴⁶ H. Hearnshaw, "Comparison of Requirements of Research Ethics Committees in 11 European Countries for a Non-Invasive Interventional Study" *BMJ* 328 (2004): 140-141.

⁴⁷ NPSA and COREC, Improvement, p. 4.

⁴⁸ L.M. Kopelman, "Minimal Risk as an International Ethical Standard in Research", *Journal of Medicine and Philosophy* 29 (2004): 351-378.

⁴⁹ J. Harris, "Scientific Research Is a Moral Duty," *Journal of Medical Ethics* 31 (2005): 242-248.

⁵⁰ National Health and Medical Research Council (NHMRC), (Canberra, 1999).

⁵¹ *Ibid.*, p. 6.

⁵² *Ibid.*, p. 7.

⁵³ *Ibid.*, p. 7. 'Where activity involves human participation of definable human involvement and has a purpose of establishing facts, principles or knowledge or of obtaining or confirming knowledge, the features of human involvement will be the focus of deciding whether it is research and so subject to review by an HREC.'

⁵⁴ *Ibid.*, p. 8. 'Such a potential arises: where that involvement could cause harm to the well-being of participants, whether physically, psychologically, spiritually or emotionally; or in the exploitation of cultural knowledge and /or property, where their involvement, or the use of their personal or community-based information, has

a potential for infringement of their privacy or of the confidentiality or ownership that attaches to that information; or where their involvement imposes burdens with little benefit.'

⁵⁵ Ibid.

⁵⁶ NHMRC, *When Does Quality Assurance*.

⁵⁷ Ibid., section 2 page 3.

⁵⁸ Ibid., section 4 page 5.

⁵⁹ Ibid., section 6 page 8.

⁶⁰ D.J. Maxwell and K.I. Kaye, "Multicentre Research: Negotiating the Ethics Approval Obstacle Course" *Medical Journal of Australia* 181 (2004): 460.

⁶¹ NPSA / COREC, Report of Ad Hoc Group, p. 4.

⁶² See *Principles of Best Practice in Clinical Audit* (Radcliffe Medical Press, 2002): 14. Endorsed by the National Institute for Health and Clinical Excellence and the Healthcare Commission.

⁶³ See H.M. Hearnshaw, R.M. Harker, F.M. Cheater, R.H. Baker, and G.M. Grimshaw, "Are Audits Wasting Resources by Measuring the Wrong Things? A Survey of Methods Used to Select Audit Review Criteria" *Quality and Safety in Health Care* 12 (2003): 24-28 and J.E. Ibrahim, "Translating Quality Into Research: Do we Need More Research into Quality or Should Quality Activities be Conducted Using the Principles and Methodological Rigour of Scientific Research?" *Journal of Quality in Clinical Practice* 20 (2000): 63-64.

⁶⁴ Maxwell, *Multicenter Research*, p. 107.

⁶⁵ UBHT, *How to Apply Ethics*.

⁶⁶ A. Wilson, et al., *Differentiating*, p. 1235

⁶⁷ J. Harris, "Scientific Research is a Moral Duty," *Journal of Medical Ethics* 31 (2005): 242-248; E. Cave, C. Nichols, "Reforming the Ethical Review System: Balancing the Rights and Interests of Research Subjects with the Duty to Facilitate Good Research," *Clinical Ethics* 2(1) 2007: forthcoming.

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