Fair play for "researchers": Can editors and regulators develop a common approach to the need (or lack of need) for ethical review?

There are a number of legitimate and valuable tools for gaining information and evidence for scientific advance and improving health care. These include research, evaluation, audit, and others. There is a real danger that UK "researchers" using tools other than "research", duly following guidance in UK research regulation stating a lack of need for ethical review, find that journal editors will not consider their manuscript for publication because editors dispute the definition of what needs or does not need ethical review.

Many of these issues, of course, also apply to animal ethics approval.

Questions for discussion

1. What current guidance do journal editors use to determine if Research Ethics Committee review is mandatory for publication?
2. Can we develop a shared process (using current decision tools) that doesn't unfairly disadvantage "researchers" (and hinder research based care)?
3. Recognising that in inevitable grey areas, judgement is needed and will vary, can we develop a process to resolve differences between regulators and editors, that doesn't burden the researcher to start with?
4. Is this a problem beyond the UK and part of what Greg Koski has defined as the creeping "hyper-regulation" of research?

BACKGROUND

The remit of Research Ethics Committees (RECs) is the consideration of research, and the Health Research Authority (HRA) holds firmly to the view that health research should undergo independent ethical review. Audit, service evaluation and public health surveillance, usually of minimal risk, are excluded under official policy (GAfREC 2.3.12 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213753/dh_133993.pdf). Their scrutiny lies elsewhere. While this is contended by some, it can be robustly defended and is current UK policy. Hence "researchers" need to categorise their work at an early stage to determine appropriate review. With its partners, the National Research Ethics Service (now part of HRA) collected the literature in 2009 and devised categorisation (http://www.hra.nhs.uk/documents/2013/09/defining-research.pdf) to help and set up a queries line to arbitrate in case of difficulty. In these it was recognised that there could be no clear, unambiguous answer. Judgement is needed and has to be given if the work is to proceed. In 2013 this guidance was further refined and a decision tool developed (http://www.hra-decisiontools.org.uk/research/).

By and large the distinction is clear (if it looks like a duck, then it is a duck) but difficulties in categorisation can arise and there is the risk that, in following guidance, "researchers" can then be disadvantaged if regulators, reviewers and editors either don't recognise due regulations or don't share common guidance. It is a concern that has been voiced on several occasions through our queries line. In such a case there is the possibility that REC review is deemed unnecessary within UK regulation at the beginning but later publication is jeopardised if a journal editor disagrees.

The HRA approached COPE and together it was agreed to put this discussion paper on the COPE website for discussion at the COPE Forum, to seek views and, if possible, establish a common approach which would not disadvantage "researchers" (and would expedite health care work).

The topic was discussed at the COPE Forum on 8 July 2014.

COMMENTS FROM THE FORUM (8 July 2014) – NOTE, Comments do not imply formal COPE advice, or consensus.

- Editors receive papers from around the world, and if details of ethics review have been documented by authors, this provides some assurance to editors that the data have not been fabricated.

- In the UK there are online decision tools (together with a queries facility) on the Health Research Authority (HRA) website, and researchers are informed, based on answering a set of questions, that they may not need ethics review because their study is an audit or service evaluation, or the participants have been recruited from members of the NHS. This decision can be printed out by researchers and submitted to editors, along with their paper, as evidence that their study does not require ethics approval. However, editors would find it easier if there was a letter from the chair of an ethics committee or ethics coordinator from the HRA, stating that this study does not require ethics review in the UK, and stating the reason why. This could be submitted to the editor at the same time as the manuscript.
- If there are any ethical concerns with a paper, these concerns should be followed-up, regardless of whether or not the study has ethical approval.
- It can be difficult for editors to determine if authors have complied with national regulations and laws, as requirements for ethics approval vary greatly from country to country. Editors could keep a database of links to national guidelines in different countries, which could be useful to check against if a paper is submitted and the author claims ethics approval was not required. Editors can ask for proof, in the form of details of national guidelines or a letter from their ethics committee. It would be good if authors could submit this proof when they submit their manuscript. Editors can also contact the ethics committee for clarification in they have concerns.
- What is the difference between (interventional) research and audit (or more observational type research)? Ethics approval extends beyond the health sciences. In the UK, the HRA uses the definition of research from the Research Governance Framework, which defines research as "an attempt to derive generalisable new knowledge by addressing clearly defined questions with systematic and rigorous methods". But it is difficult to define exactly what research is, but generalisable is often used as the key, although audits can also be generalisable, to other hospitals for example. The HRA are likely to gain responsibility for re-drafting a document to replace the Research Governance Framework's definition of research in the UK, and they hope to add more definitions around these terms and to explain research more clearly. The HRA also provide definitions of clinical audit and service evaluations on their website. However, there is no definitive definition of research, and there will always be variations in opinion as well as different standards around the world.
- In some developing countries there are institutions where ethics committees do not exist. In these situations, it can be difficult for authors. Is retrospective review acceptable? Some journals may consider retrospective ethics approval if no ethics committee exists in a particular country.
- In general, retrospective ethics approval should be discouraged. Researchers need to address these issues in advance and they need to seek some kind of process that they can then present to the journal to give some reassurance to the editor that some form of process has been followed. We need to encourage a global culture whereby researchers are aware of their obligations and that they need to find some form of process that they can then present to the journal. It is then up to the editor to review these processes and decide if they are acceptable.
- Editors should engage with ethics committees, but they need to be aware that the existence and standards of ethics committees is highly variable and in some areas of the world there is no ethics review process available. Should there be an international or global ethics review service?
- Transparency is key for editors who decide to publish research where there is some ambiguity about the ethics approval and whether ethics approval is required. Editors should consider publishing the details of the review process if necessary, and correspondence between them and the authors, so that readers can have confidence that due process has been followed and that the issues have been considered.

- There should be some form of ethical framework against which to evaluate research design, and authors and researchers should make this clear when they submit their paper. If there is no framework, some editors are not prepared to consider publication.
- COPE could have a role in reminding researchers and editors to ensure they have informed consent from patients, particularly in the absence of formal ethics approval.
- If researchers in developing countries collaborate on research with researchers in developed countries, they should use the institutional review boards in the developed countries, and not use the lack of ethics approval in the developing country as a excuse.
- In some instances institutional review boards are not properly constituted, and authors may sit on these boards or even chair them. In these cases, conflicts of interest should be declared.
- As a minimum, researchers should follow institutional regulations as well as local legislation. Editors need to ensure that authors have followed the standard regulations for their country.

In summary, the editor's position, when presented with a research paper, is to make sure that by the best standards that are available, or best relevant standards, that the work has been proven to be ethical. It is hard to define when formal ethics approval is required for some types of research, and defining what is research is tricky. The key is demonstrating to the editor that due process has been followed, and there should be transparency, including reference to the guidance and standards that the authors have followed, and proof, where required, that those standards or processes have been followed. We need to empower and support those research communities that do not have an ethical review infrastructure in a sensitive manner, and in accordance with their cultures. There should be transparency around the constitution of ethics committees. The minimum standards that could be applied should be institutional regulations as well as local legislation, and due process needs to be demonstrated and proved to the editor by the researcher so that the editor can be satisfied that the relevant standards have been applied.

COMMENTS POSTED ON THE WEBSITE

Posted by Foppe van Mil, 6/6/2014
As editor of a biomedical journal, I find this confusing myself. We now have the mandatory header 'Ethical approval' for all research papers, to be inserted directly before the Method. We accept the option for the authors to write that no ethical approval was needed for the study, plus the arguments. Thus the reader can decide for him/herself.

As editor guidance I usually check if individual patient or health care provider data have been used; in such cases I think ethical approval is definitely needed. When the researchers use large properly anonymised database then ethical approval, in my view, is not necessary.

Nowadays I notice that our reviewers also increasingly pay attention to the ethical approval issue.

Posted by Hugh Davies 6/6/2014
Thanks for replying.
You say
"As Editor guidance I usually check if individual patient or health care provider data have been used; in such cases I think ethical approval is definitely needed"

Is this based on definite guidance (legal or ethical) anywhere?

For example, would you think ethical review is needed if data are handled or first anonymised by the clinical team?

Posted by Dr Maggie Watson 6/6/2014

As an Editor in the biomedical area a simple rule applies; if a journal publishes papers involving human subjects ethical committee approval is required. The Helsinki Declaration requires ethical approval of studies with human participants.

The only exception is reviews which use secondary data.

The aim is to protect patients and human participants.

This an important responsibility for those journals publishing in the biomedical/psychosocial research arena.

Posted by Hugh Davies 10/6/2014 3.41pm
Thanks Maggie,
You refer to "papers" or "studies". Do you mean research? Some journals may print "audit" or "service evaluations". Do you feel REC review is needed for these?

When you say "secondary data", do you include tissue? For example, how might we review use of tissue from a tissue bank?

Posted by Maggie Watson 20/6/2014
Hugh, the journal I edit doesn't take audit papers. Service evaluation papers that include data collected directly from patients would—for our journal—require REC approval. I use "secondary" data to refer to reviews or epidemiological/national databases.

We also don't publish any papers on the use of human tissue , so I have no comments to offer.

Posted by Phillipa Hay 20/6/2014
I think that editors should be aware of the Helsinki declaration and ethical principles, and be expected to competently use their judgement/discretion in applying these principals and not rely solely on a statement of clearance from an external committee. Research that has a committee approval may not be ethical when subsequently submitted for publication. Some guidelines (eg, in Australia) indicated that de-identified data that is used for clinical audit as part of quality assurance does not require 'clearance' from a duly constituted research ethics committee. Sometimes it is appropriate to publish this —and in the interests of patient care to do so, provided ethical principals are met. Similarly, in case reports provided there is evidence of full and voluntary informed consent. Also, when the work of ethics committees is taken up with a lot of low risk audit and similar, there is less time (and expertise) available for assessment of primary research and high risk studies, which itself has risk. So I'm supporting some discretion and flexibility for editors I think.

Posted by Roger Rawbone 20/6/2014
It is surely time that regulators, editors and "researchers" themselves stopped equating 'ethical review' with 'independent ethical review'. All parties want to see 'good work', and 'good work', whatever it's categorisation, has to be, by any definition, ethical. The onus should therefore be for the "researcher" to demonstrate to editors and readers that the work presented has had ethical consideration and has been conducted to accepted ethical standards. Independent ethical review is (arguably) one way authors can do this but if independent review is not available, for whatever reason, a couple of short sentences in the methodology section will usually demonstrate and give confidence that the work has been conducted taking into account ethical principles (and by this I don't just mean by referencing 'high level' ethics guidelines). If I see a paper containing the sentence 'this work was considered audit and did not require ethical review' then I advise that it be returned to the authors for revision.

Posted by Ken Stein 20/6/2014
Although I don't think we make as much use of audit/evaluation data as we might, and I agree that resources can be wasted in unnecessary pursuit of ethical approval, I think the problem here is when data are collected for one purpose —for example, clinical service improvement within a particular service context, hopefully with appropriate consent—but then submitted for publication, which could be construed

as a different purpose for which consent was not given. That different purpose may well be what would make the paper more interesting to a journal, but if the subjects haven't consented to the use of data for that purpose, would that not be unethical? I wouldn't include the use of data routinely collected as a consequence of service contact —that is, "administrative activity data"— which would usually (though perhaps not always, in the context of small area geographical analysis) be sufficiently anonymised.

Posted by Hugh Davies 23/6/2014
Thanks, agree about discretion and RECS bogged down with work of no risk or consequence.

I suppose one of our problems is whether the WMA Declaration really applies to the types of work we are now seeing? What did the original authors have in mind when they first drafted this document? Did they foresee the changing nature of "research"?

I agree editors have a role in deciding if REC review is needed but our reason for starting this was to see how we can prevent researchers being caught in this "gap" not of their own making? Can we develop a procedure where we resolve these issues between ourselves (regulators and editors) rather than disadvantage researchers who have followed advice given at the initiation of their study (and now find themselves stuck)?

Posted by Charon Pierson 28/6/2014
I have struggled with this issue several times over the past few years as papers have become more varied and creative in approaches to answering questions of interest to clinical practice and health service management.

One arena that seems to confuse not only researchers but IRBs (in the US) is audit/evaluation. Some institutions have taken the approach that anything going to publication beyond the institution where the audit was conducted must have an IRB review. Another area of concern is educational research, often really only an audit or evaluation process, where university students are involved as subjects. I expect IRB review of these projects even if data are anonymised because to me, students are a vulnerable population so their participation must be voluntary and they must be guarded from undue pressure to participate in their faculty's project—a project that will progress to publication. As an editor, I can't guarantee that; that should be the responsibility of the university's IRB.

There is an increasing interest in online research and that is also a big grey area to me. Researchers who mine blog posts for data and quote participant comments need to be really mindful about whether or not participants in the online community see their postings as "confidential" because they used a login to access the site. Some of this is common sense, but within large organizations such as associations and publishing houses, the tendency will always be to err on the side of caution. The concerns may be legal rather than ethical, so I'm not sure that a universal guideline or procedure will work.

Posted by Margaret Rees 4/7/2014
Lack of evidence of ethical approval is a red flag to editors that participants have not been protected or that data have been fabricated or falsified. A few years ago, I asked a non-UK institution to investigate a submission where there was no evidence of ethical approval and the authors refused to provide it. The institution found that the study had never been conducted. Lack of ethical approval was one way in which extensive data fabrication by Fuiji and Boldt was discovered. It is unreasonable to expect editors of international journals to know local law for the various countries (eg, UK, US, Australia, Germany, France, India, etc) from which they receive manuscripts. Evidence of ethical approval or oversight by a local IRB not the author is reassuring that the study should have been conducted appropriately. Its lack means that otherwise sound papers and research may be rejected as editors err on the side of caution. This text from the BMJ is helpful. http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checkl...

Posted by Hugh Davies 4/7/2014
The underlying issue remains that we advise "researchers" before they start that some work falls outside our remit. We do this in an attempt to provide proportionate review and regulation (something researchers

and journals have been advocating for some while). If such advice is given and then publication is denied, have we unfairly penalised these people who have simply followed rules and guidance?

So can we develop a means of communication (a memorandum of understanding between regulators and journals that will at least allow us to discuss these situations when they arise (probably infrequently)) and avoid penalising the authors?

This discussion might include:
(i) a check that the authors DID consult us;
(ii) an assessment to see if the article actually reports the study that was presented to us as regulators; and
(iii) if necessary, an assessment as to its classification.
(Falsification and fraud is an issue but I wonder if the results can be fabricated, so can ethical review (unless this is closely scrutinised)).

Posted by Stephanie Harriman 7/7/2014
Thank you for bringing this issue to the forum. I think there are two main considerations for editors when it comes to ethics of the research we publish.

The first is whether we are satisfied the research was conducted ethically. Even a study that has been approved by an ethics committee may raise ethical concerns and may need to be investigated and potentially discussed with the authors' ethics committee or institution.

The second consideration is whether the authors complied with national regulations and law. This can be a minefield, as requirements for ethics approval vary from country to country. If authors did not obtain ethics approval because it was not required in the country where the research was carried out (eg, in the case of an audit) and there are no ethical concerns, then I would consider a manuscript without ethics approval. In such cases I may ask to see proof that it did not require approval (eg, national guidelines or a letter from their ethics committee). In rare cases, I have contacted the ethics committee for clarification.

I think that, as editors, we need to balance making sure that the work that we publish was conducted ethically without disadvantaging researchers who have conducted ethical research and followed local/national research regulation stating that their research did not require ethics approval.

Posted by Reynir Tomas7/7/2014
As a chief editor of a European international clinical journal, I frequently encounter problems with research having been done on material from one institution/hospital in an ´audit´ fashion or on large databases with just the comment that ethical approval was not needed or that data were anonymised. It may be stated that a data protection authority approved the use of the data, which is good but not the same as ethical consideration. Apart from the UK, Denmark and The Netherlands are examples. Such statements are no guarantee of proper conduct of a study and it is difficult to work with such submissions, partly because there is the risk that such studies may not be cited, even if good. We request reference to a clear official law or regulation granting exemption. The authors word for exemption is not sufficient—the appropriate committee or IRB has to have said so. Researchers cannot decide solely by themselves what is ethical information gathering, neither from patient case notes nor large databases. Studies involving biological material require almost everywhere permission, but when it comes to looking at personal details in case records or databases, should that be different? There is a need for international consensus, that without undue restrictions, guarantees correct handing of clinical as well as experimental or biological data gathering, and ensures that databases are used within proper ethical and safety confines.