Why do research ethics committees disagree with each other?

ABSTRACT—Research ethics committees have to ensure that research projects are asking sensible questions and are designed so that the questions will be answered, that the research subjects who are involved will not come to unnecessary harm, and that the autonomy of the research subjects will be respected. Where research proposals cannot fulfil all these criteria, research ethics committees have to perform a delicate balancing act amongst competing moral claims. These arise when, for example, the research is non-therapeutic or the research subjects are incompetent to give consent. Given that the balance of conclusions is so sensitive, it is hardly surprising that different committees sometimes disagree with each other.

Local research ethics committees are being widely criticised at present, not least for their diversity of practice [1–4]. Some of their inconsistencies and administrative delays should be resolved as soon as possible. However, there are some very good reasons for local research ethics committees disagreeing with each other. In this article I shall show how the ethical acceptability of many research proposals is established only by resorting to a careful balancing act between conflicting moral claims, and this can lead to research ethics committees coming to different conclusions. If we change the system of ethical review in this country for the sake of expediency, we must take care not to lose the sensitivity that sound and reasonable ethical review demands.

Moral outlook of research ethics committees

When research ethics committees evaluate research projects they have three basic questions to ask:

- Does the project ask an important question?
- Are the risks to the research subjects acceptable?
- Will the research subjects' autonomy be respected by obtaining consent?

These three questions loosely reflect three moral approaches to making decisions:

- My action is good if its outcome is good (goal-based)
- My action is good if it obeys my moral code, eg not to harm anyone (duty-based)
- My action is good if the person affected wants me to do it (rights-based).

Often people favour one approach over another when making moral decisions. Research ethics committees are supposed to balance all three by ensuring that the science is good and the research subjects' interests are protected. A well balanced committee which understands its function should be capable of this delicate balancing act [5].

Let us assume that we have three local research ethics committees which are slanted in favour of one each of these moral approaches, and a fourth which rightly tries to balance them all, and we make Pemberside a predominantly goal-based committee, Watermere a predominantly duty-based committee and Palton a rights-based committee. Falkwyche, by contrast, is a good balance between all three. Now, before anyone cries that Pemberside, Watermere and Palton are unrealistic examples, consider for a moment the effect on this kind of lay/professional/public service committee of one or two members who have strong feelings about research, or about welfare, or about human rights. In our example, Pemberside committee has on it two doctors who conduct a lot of research in their own fields and know the benefits of research; they are intelligent and articulate people who can put their case well. How easy is it for, say, the nurse, or one of the lay members, to argue against them? By contrast, Watermere committee has some concerned members from the Community Health Council who are most anxious that patients are not exploited for medical gain, and who are suspicious of doctors in general. Palton, again different, has some younger members, a nurse, say, and a junior doctor, as well as active lay members, who are keen to defend the rights of people to determine what happens to them, especially in such a dependent environment as a hospital or general practice surgery. Falkwyche, however, contains all these views, but each member is willing to listen to the others and is also capable of seeing the validity of different points of view. Falkwyche represents the ideal committee, but even it, as I will show, will not always come to conclusions that every reasonable committee would share.

We will take different kinds of research projects in turn and see how each committee would respond to them.

Therapeutic research on competent people [6]

A multi-centre trial was proposed to evaluate a new form of chemotherapy for patients with a particular form of cancer. The trial was a randomised double-blind comparison of treatment A (the standard treat-
ment) with treatment B (the new treatment). The potential research subjects were all legally competent adults.

Pemberside committee passed the trial; the trial was asking a sensible research question and was properly designed so that a statistically significant answer would be obtained. Watermere also passed the trial; it was therapeutic, and there was equipoise, ie the researchers were genuinely uncertain whether B was better than A, so the research subjects would not be exposed to any greater risk by being in the trial than by not being in the trial; the drugs were toxic, but these patients would be receiving toxic drugs anyway as part of their ordinary treatment; in any case, any patient who did not go into the trial would receive treatment A, because that was the standard treatment. Palton also passed the trial because the patients were to receive appropriate information, including an excellent explanation of randomisation, and would be given plenty of time to think about whether or not they wanted to join. Falkwych, for all three reasons described, also passed the trial.

Now, some local researchers in the trial asked their own research ethics committees to consider whether or not they might be allowed to waive the consent requirement. The researchers argued that the difficulties in obtaining consent, even from competent adults, have jeopardised much research by decreasing recruitment levels to the point where the research is no longer viable [7,8,9]. No additional harm would come to the patients by being in the trial. Doctors who are not conducting research are not expected to meet research ethics committees’ demands for detailed consent procedures. These patients, had they gone to a doctor not involved in the trial, would have been asked to consent to treatment based on far less information than that which would have to be provided to them as potential subjects in a trial—yet they would not have been better protected from harm.

Pemberside and Watermere research ethics committees, which respectively think that it is most important to conduct good research, and not to do harm, might both have listened with sympathy to the researcher who did not want to obtain consent even from his competent patients (leaving aside the question of whether it would be legal or not). However, Palton committee would be of the view that obtaining consent was paramount because respecting autonomy is so important, and the committee would have no sympathy with the researcher’s request. Palton committee would be of the opinion that it is up to each individual to decide whether or not to take part. His or her decision may be based on considerations other than those which the researcher thinks are important, which could not be measured by anyone but the individual himself. Not seeking consent would prevent such unseen considerations from being weighed in the balance of whether or not an individual should take part. Rights-based moralists like Palton committee would argue that it is for other doctors to bring their standards of consent-seeking up to those demanded by research ethics committees, not for research doctors to lower theirs to the standards of others.

Once again, the balance of approach on each committee would determine whether or not such requests as this one, itself seen as positively ethical by the researcher, would be acceptable. A well balanced committee such as Falkwych, having considered the merits of such a moral demand in the context in which it was set, and having weighed it in the balance along with other moral demands, like that of respecting autonomy, might conclude either way.

Research on incompetent subjects

A multi-centre, randomised, double-blind trial was proposed which would test a new drug for people with well progressed Alzheimer’s disease. There is no standard drug treatment against which to compare the new drug, so the patients would be randomised to receive placebo or the new drug. All other treatments would continue to be administered for both groups.

Pemberside committee passed the trial; in its view the new drug represented an exciting development in the treatment of Alzheimer’s disease from which so many people suffer; the research promised to yield rich findings. Watermere committee also passed the trial. It spent a considerable time ensuring that there really was equipoise; but the committee was finally satisfied on this point since, although there were good indications that the new drug would benefit Alzheimer’s sufferers, the fact was not proven, and there was some evidence of side effects. This put the placebo alternative on a level with the new drug, as far as could be known at the time. Of course, the patients not in the trial would be receiving ‘placebo’ (ie no treatment) anyway.

Palton committee had a terrible time with this proposal. The committee interviewed the researcher, asking whether he could use only subjects whose Alzheimer’s was less developed, so that they would be able to understand the trial for themselves and give their consent to participate. The researcher explained that the drug was specifically intended for Alzheimer’s patients who had deteriorated significantly. Palton knew very well that the law does not recognise any other persons’ consent as valid for an adult, no matter what their state [10]. In any case, the committee was more concerned with the infringement of the Alzheimer’s sufferers’ rights than about whether their carers would want them to take part or not. The committee sensed that the research was important and probably should be done, but it really believed that the people who should be the judges of this were the research subjects, since they were the ones most committed (like the hen who asked the pig if he knew the difference between commitment and involvement; the pig said he did not, and the hen explained that, when
the farmer has bacon and eggs for breakfast, the pig is committed and the hen is involved). Caught in a quandary, because it could not honour the one ethical principle it held as paramount, the committee took so long arguing about the project that the researcher finally decided not to conduct the research in Palton. (After all, he could run the trial in Pemberise and Watermere.)

Falkwych committee also investigated the possibility of using as research subjects Alzheimer patients who were still competent. The committee obtained the same answer as Palton. It too understood that no one can consent on behalf of the patients. On balance, however, the committee took the view that, since the research was important, was therapeutic and the balance of equipoise was established, it should therefore be allowed to go ahead. The committee requested that carers of the potential subjects be consulted, however, before each patient was recruited. It discovered an excellent information sheet about treatment and research for Alzheimer patients [11], and asked the researcher to consider using this sheet when consulting the carers. It should be noted that one of the reasons why Falkwych finally allowed the research to go ahead was that it was satisfied, having interviewed him, that the researcher had integrity and would act in his patients’ best interests. This favourable impression weighed in the balance of the committee’s debate on the merits of the competing moral claims.

Non-therapeutic research on competent subjects [12]

A junior doctor, working as a registrar in a rehabilitation department with paraplegics, wished to conduct a research project looking at ventilatory responses to electrical stimulation of leg muscles. Stimulation of muscles causes breathlessness, and the junior doctor wanted to discover whether this was because of a nervous reaction or because of chemical changes in the blood. If his paraplegic patients became breathless when their leg muscles were stimulated, it must be because of a chemical change in the blood, since paraplegics have no nervous connection to their leg muscles. He proposed to ask 10 long-term paraplegic patients to be his research subjects. They would have to sit with a screen hiding their legs (in case the sight of the electrical stimulator made them breathless with worry), and have their legs stimulated while at the same time having their inspired and expired breath measured. Although the research was non-therapeutic, the researcher felt it would still be acceptable because the risk associated with stimulating muscles electrically was so small.

Pemberise committee did not pass the study. It felt that the study was not designed to answer the question properly, and indeed one doctor on the committee was of the view that we already knew the answer to the question [13,14]. The committee was well aware that the junior doctor needed to undertake research projects for his MD thesis, but the committee believed that if he wanted to move on in his career he should be running useful and necessary trials, not playing around with a few paraplegics’ legs.

Watermere committee rejected the proposal. It felt that the paraplegics were a vulnerable group, who would not in any way benefit from the research, which was only being done to satisfy the curiosity of the researcher (and further his career). However slight the risks, they were nevertheless directly related to the research which was of no benefit to the paraplegics themselves.

Palton committee asked the researcher to write to some disabled persons’ organisations to find out their view of whether it was right to use disabled people in this way. The response was that, of course, disabled people could take part in research. They were perfectly capable of making up their own minds and should not be protected by paternalistic do-gooders. Palton therefore passed the research but remained concerned that the patients would all want to please their long-term doctor on whom they were dependent, and would agree to take part in the trial for the wrong reasons. They therefore asked that the researcher find another person, who was not responsible for the care of the patients, to seek their consent before recruitment into the trial. The committee also changed the information sheet that was to be given to the patients.

Although Falkwych committee did not always turn down research which had no evidently useful outcome, on the grounds that knowledge gained for its own sake can be of benefit in some as yet unknown way, it remained unconvinced in this case. Furthermore, the committee was unhappy about the level of risk to which the subjects were to be exposed, and had the same concerns as Palton that the subjects’ relationship with the researcher might render their consent invalid by being involuntary. The committee discussed all these points fully with the researcher but could not come to any agreement with him. Obliged to seek an independent view, the committee was informed that the risk to which the subjects would be exposed was considerably higher than they had been led to believe, because of the danger inherent in stimulating muscles which have long been unused. Moreover, the independent assessor felt that the answer was already known. In the light of these responses, Falkwych committee decided to reject the proposal, giving its reasons in writing, and enclosing the report from their independent source.

Non-therapeutic research on incompetent subjects

A consultant cardiologist wished to evaluate a new technique for measuring lung blood flow in neonates and young children on ventilators. In order properly to do this he wished to use the new technique as well as the standard technique on each child in the study, so that each participant acted as its own control. This
meant that as far as each child in the study was concerned, the additional measurements were extra to normal care and nontherapeutic. Hence the study was a non-therapeutic research project involving very sick children who could not consent for themselves. The extra procedure involved adding tiny amounts of freon and argon gas (which are both inert harmless gases) to the air the child was breathing through his or her ventilator for about 30 seconds. Four blood samples would also be taken for oxygen measurement.

Pemberside committee was really excited at the prospect of developing a new way of measuring lung blood flow in babies on ventilators. The standard method was very much more invasive, involving inserting a pulmonary artery catheter after heart surgery was completed. Watermere committee turned the trial down point-blank. There was no benefit to the patients who could not speak for themselves. The risk, albeit a theoretical one, was high. Nothing could justify exposing such vulnerable people to such risk, no matter what the predicted benefits to future patients. As one committee member put it, ‘You would not kill someone just in order to use his organs to help five others, even if it meant five benefited and only one was harmed, would you?’

Palton spent a long time trying to work out whether, if we could ask them what they thought, the babies would agree to being used in this way. Some of the committee thought they would want to be used because it was a way of making meaningful a life that would almost certainly end soon. Others, however, said that we can make sacrifices of ourselves but we cannot make sacrifices of others without asking them first. Once more the committee was stumped and did not know what conclusion to come to. In the end it rejected the proposal because it felt that it was better to be safe than sorry.

Falkwych committee finally passed the research project, having considered each of the arguments outlined above. It passed the trial knowing that, of the three criteria it was supposed to fulfil, two had been subsumed in favour of the third, and the third was the scientific importance of the trial. It was very uncomfortable with its decision, and months later its members were still arguing amongst themselves about the proposal, though the trial had already started. The committee felt that, while it could not say that it had been completely wrong in its decision, and indeed that it might come to a similar conclusion faced with another non-therapeutic research project on incompetent subjects, it had nevertheless in some way been untrue to its function. Research ethics committees were created to stand as a guard against the kind of utilitarian, goal-based thinking which would justify a trial such as this one, by taking the other two moral concerns equally seriously. After all, researchers themselves are capable of judging their research on utilitarian grounds. The research ethics committee which finds non-therapeutic research on incompetent patients ethical has done so by reasoning in the same way as the researcher. It is a utilitarian calculus that counts up the number of people who will benefit and the number of people who will be harmed, and if more will benefit then the research is considered ethical.

In each of the trials described above, different responses were evoked from each of the committees because of the way they thought about moral decision making. Pemberside, Watermere and Palton research ethics committees were all unbalanced and could have done with some training in ethical analysis. But notice that Falkwych, which was well balanced, did not always come to an easy conclusion, and that another, equally well balanced committee might have come to different conclusions, having conducted the same sound and reasonable analysis of the same trials. When a research project cannot fulfil all these criteria of scientific merit, protection of subjects from harm, and respecting their autonomy, we cannot expect local research ethics committees to agree with each other, nor must we assume that differing conclusions are a proof of incompetence. Ethics is just not like that. Whatever solution to the multi-centre problem we arrive at, it is essential that the delicate and sensitive balance that research ethics committees have to achieve when considering research projects is not lost in the drive for speedy ethical review.

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