Manual for Research Ethics Committees

6th edition

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The ethics of clinical research

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History is unfortunately peppered with stories of abuse carried out in the context of medical research. No one can remain unaware of the dreadful medical atrocities of the Nazi period, some of which were carried out by doctors motivated as much by scientific curiosity as by Nazi ideology.[1] In the late 1990s, the US President, Bill Clinton, offered an apology to the families of those men involved in the infamous Tuskegee project,[2] and in the opening years of the new millennium there has been international concern over the conduct of clinical trials in the developing world. In an attempt to protect individuals from abuse, international and national guidelines now govern this area of science, and in the United Kingdom research is carefully monitored through the work of funding bodies, peer review systems, Local Research Ethics Committees (LRECs) and Multi-Centre Research Ethics Committees (MRECs). However, at ground level, the moral responsibilities primarily lie with those who design and carry out the research, and then publicise the findings. It is therefore crucially important that these individuals understand the ethical issues that arise when human beings come under the scientific gaze.

The benefits of good medical research speak for themselves. In our own lifetime, killer diseases have been eradicated, death sentences have been lifted from a number of diseases, and incredible advances have been made in such areas as reproductive technology and transplant surgery. However, there are still important battles to be won, and discoveries we yearn to make. If research is to continue to bring about the benefits we hope for, we have to accept that there will be costs involved. The moral question is what type of benefits ought we to pursue and at what cost to individuals and society?

Research passes through various phases, so over time one individual might be involved in different types of research intervention, be it as a researcher or volunteer participant. In the past, researchers have been keen to make the distinction between therapeutic and non-therapeutic research, where therapeutic research permits the hope of a direct health-related benefit to the participant, whilst non-therapeutic research means that the participant might be a healthy volunteer, or a patient who is asked to contribute to some work unrelated to their particular problem, or to participate in very early research which will not be at a stage to benefit them. In these cases the potential benefits are of a different type, possibly financial. Whilst the specific issues raised may differ, the fundamental questions remain the same: ought we to do this research, and if so how ought we to do it? The distinction between therapeutic and non-therapeutic is thus becoming increasingly blurred. It is tempting to think that the clear presence of quantifiable costs and benefits means that the ethical status of medical research could, and should, be judged through consequentialist means. However, this assumption needs to be explored.

Consequentialism

In the simplest terms a consequentialist believes that the morality of an action should be judged in terms of the consequences that follow from it. If the consequences are on balance good, then so is the action; if the consequences are bad, then the action must be seen in the same way. This means that a proposed course of action need not be seen as intrinsically good or bad, but rather must be judged

[1] Annas, G. and Grodin, M. (eds.) (1992). *The Nazi Doctors and the Nuremberg Code*. New York: Oxford University Press.

[2] Jones J.H. (1981). *Bad Blood: The Tuskegee Syphilis Experiment*. New York: The Free Press.

in terms of what is predicted to follow on from it. To coin a cliché, for the consequentialist, the ends justify the means.[3]

The most famous variant of consequentialism is utilitarianism, the theory developed by Jeremy Bentham in the mid-nineteenth century.[4] Bentham had a reductionist view of human nature in which he claimed that all human beings were fundamentally concerned primarily with the pursuit of pleasure and the avoidance of pain. He believed that a moral theory should acknowledge this fact, and thus to be moral is to be concerned with the maximisation of pleasure and the minimisation of pain. Human nature inclines one to be concerned about one's personal pain and pleasure; morality requires that we be equally concerned with the pain and pleasure of all sentient beings.

Should we be doing this?

In the context of clinical research we can see that a consequentialist could support a piece of research as morally acceptable if we minimised the harms and maximised the benefits resulting from the intervention, and on balance created more good than harm. This sounds intuitively appealing and certainly offers a starting point for ethical analysis. However, clinical experimentation also highlights the problems with the consequentialist approach when applied to real life.

First, we have to ascertain what counts as a benefit in this context, and how the value of different types of benefit compare. Defining and calculating happiness was a difficult problem for Bentham and his followers; defining and calculating benefits in this context is also challenging. How do we compare the benefit of curing a disease with the benefits of preventing it in the first place? How do you compare the benefits of palliating symptoms with increasing patient satisfaction through other means? Is reducing the cost of health care a significant benefit compared with improving treatment? How does one weight 'hope' and 'worth' as benefits of involvement? All these questions might be relevant when deciding how to allocate a pool of money between different types of research, but they might also have an impact on the types of risks (if any) you would allow people to run in pursuit of the types of benefits on offer.

Having looked at the type of benefits available, we also have to identify to whom the benefits attach and ask whether this further weights their significance. Utilitarianism demands that we treat each individual as one and no more than one. However, when there are a wide range of potential beneficiaries as in the case of clinical trials – participants in the trials (healthy or unhealthy), other sufferers of the same condition, future sufferers (some as yet unborn), researchers and student researchers, society as a whole, health-care professionals, and drug companies – there are still complex calculations to be made. Knowing to whom benefits attach might help us to decide how to allocate resources to research, and it could also help us decide what costs it would be acceptable to attach to whom.

One might assume that the consequentialist ideal would be to conduct a piece of research which imposed minimum costs upon the smallest possible number of people, but secured substantial benefits for a significantly higher number of people (particularly those who participated). However, this ideal type model is not always possible, nor indeed is the consequentialist necessarily committed to it above all else. As we shall see, the consequentialist can justify some rather different outcomes, some of which are less intuitively appealing. Furthermore, what the consequentialist would see as morally desirable might not fit comfortably with the realities of a commercially driven pharmaceutical industry, or western dominated models of health-care delivery. Furthermore, the globalism inherent in consequentialism might sometimes be at odds with the localised concerns of those deliberating upon research protocols, a dilemma reflected in the sometimes difficult relationship between Local Research Ethics Committees (LRECs) and Multi-Centre Research Ethics Committees (MRECs).

Some examples

- One can see that research that is directed at the alleviation of widespread and significant suffering should easily pass the consequentialist test, even if quite significant risks are posed to a relatively small amount of research participants. It is worth bearing in mind that allowing the costs to be too high might undermine public support for clinical research with dire consequences, and the consequentialist would wish to avoid this risk. On this basis, research to alleviate the HIV epidemic in Africa should gain significant support because of the scale of the problem and the consequent degree of suffering entailed. However, we know that, in the past, such work was not given high

[3] For a more detailed examination of consequentialist positions see the following: Glover, J. (ed.) (1990). *Utilitarianism and Its Critics*. Macmillan.

Samual, S. (ed.) (1988). *Consequentialism and its Critics*. Oxford: Oxford Readings in Philosophy.

Smart J.J.C. and Williams B. (1973). *Utilitarianism: For and Against*. Cambridge: Cambridge University Press.

[4] Bentham, J. (1970). *Introduction to the Theory of Morals and Legislation*. Ed. J.H. Burns and H.L.A. Hart. London: Athlone Press.

priority due to the financial realities of the regions involved, which meant that the benefits would not be purchasable at the prices dictated by market forces. In consequentialist terms the sums worked out; in commercial terms they did not.

- At a local level one sometimes encounters proposals advocating trivial but commercially motivated research; for example, post-licensing drug comparisons that have more to do with marketing than with useful clinical comparison. The benefits to drug companies of usurping a market leader might be great, but the benefits to patients will be negligible if the treatment is already known to have nothing new to offer. Here, the consequentialist sums do not add up, but the commercial ones do.
- A difficult problem is posed by student research. The benefits to the particular student and the benefits to society and future patients of having well-trained professionals will speak in favour of supporting student research. However, the costs borne by the participants in student research projects might be higher and the benefits to be gained by the research itself may be small or non-existent. Here, the benefits and costs might, to some extent, appear incommensurate.

Distinguishing between types of benefit and looking at the potential quantity of benefits on offer, and assessing who gains the benefits as opposed to bearing the costs of research can offer the basis for a searing critique of current practice. By evaluating the moral costs and benefits, one can decide what ought to be done, but it is often the case that other types of accounting are shown to determine what is done.

How should we do research?

A key to proceeding appropriately in consequentialist terms must be the provision of adequate information to facilitate the evaluation of costs and benefits and allow for a rational decision to be made. An initial problem arises from the fact that the ideal starting point for a piece of clinical research is a position of equipoise.[5] This is a scientific or methodological as well as an ethical issue. Put simply, being in equipoise means that, when attempting to compare two approaches, be it a new drug with an established drug, or the use of a new procedure where none was previously attempted, the researcher should not proceed if he or she has any fixed assumptions about how the new option will be better. Only the results of the comparison will show which is the more beneficial approach. Until the results are available, the researcher cannot promise any benefits to those who enrol in the trial, she or he can only explain what is hoped for. Admittedly, all consequentialist calculations are based on potentially unreliable calculations about future benefits, but one could argue that in this case the problem is heightened by the fact that the trial is only going ahead because the benefits are as yet unknown. This must be highlighted when providing a potential participant with the information upon which they will base their own consequentialist calculation when deciding whether or not to participate.

A consequentialist approach will necessarily impact upon who are recruited as participants in research projects. This will, in part, be determined by the preceding question of what research should be done, but once that has been decided recruitment will be effected by the requirement to secure 'the greatest good of the greatest number'. As a maximising theory, consequentialism is more concerned with the total quantity of benefits and costs than with their distribution. This can cause problems when considering how to evaluate the moral acceptability of the distribution of costs and benefits in a particular case. In some cases we might allow that a small number of participants might risk a very severe harm in the interests of securing a benefit for a much larger number of people, but in other cases this might be deemed unacceptable. Those charged with the ethical monitoring of research ought surely to be troubled if they discover over time that the same type of people are always bearing the costs and different types of people are deriving the benefits. An example of this is where research is carried out in the developing world in order to create products that will realistically only be available in richer countries.

Theoretically, a consequentialist could consider any distribution of costs and benefits, subject to the greatest happiness of the greatest number being secured. Certainly, early versions of utilitarianism were criticised in this regard despite the pragmatic constraints that would usually operate. However, it should be possible for consequentialism to tackle the problem of distribution by allowing multiple criteria for evaluating consequences, including distributive ones. A consequentialist could thereby address not only how much benefit would follow a proposed intervention, but also how those benefits are to be distributed – the sort of questions that need to be raised in cases such as these:

- A small number of people are paid a large amount of money to risk significant harm in the interests of a very large number of people enjoying a small increase in their quality of life.

[5] Freedman, B. (1987). Equipoise and the ethics of clinical research. *New England Journal of Medicine*, **317**, 141–5.

- A large number of people suffer a minor inconvenience in the interests of a very small number of people benefiting significantly
- One person loses his/her life in the course of a trial that will benefit other sufferers of a rare disease
- No money is given to fund research into rare diseases affecting small numbers of people

In some cases such decisions might be challenged by others as morally unacceptable on grounds of justice and fairness. The fear is that consequentialism leaves little room for judging the impact of research upon the individual participant due to its focus upon the group as a whole. As a maximising theory, it does not pay due regard as to how costs and benefits are distributed.

Consequentialist goals might also impact upon the preference that scientists show for particular methodologies. Clinical research is a form of scientific endeavour, and one could argue that the first step towards ensuring the ethical validity of a piece of research is to ensure the scientific validity of the proposed project. Thus the means must be fitting to the ends. If there are to be any benefits gained (which there must be for the consequentialist), then the scientific approach must be suitable to the task, the methodology must be appropriate, and the investigator should have the ability and resources necessary for the task. Consequentialism therefore requires scientists to make a valid assessment of their ability to attain the potential benefits by the means proposed before proceeding. This can only be of benefit to society, and to those whose time would otherwise be wasted in the course of badly designed or under-resourced research.

However, the consequentialist will also want to know that research will have a beneficial impact (it is not enough to establish a truth; one needs to persuade others of it in order to secure the benefits), and, on occasion, this goal could conflict with the interests of participants. Different scientific questions will demand different approaches, but in this age of evidence-based medicine the fact is that, in terms of impact, the most benefits will probably be derived from the research that produces the most widely accepted form of evidence that something works. In practice, this means that a large randomised controlled trial (be it with or without placebo, blinded or not) will usually be seen as the gold standard, and the benefits to be derived from other forms of research might immediately be assumed inferior. This is, in part, due to the inherent power of the results acquired through such means, but might also be due in part to lingering prejudices against other forms of methodology, notably small-scale qualitative studies. Thus the consequentialist might have to commit wherever possible to a form of experimentation that is acknowledged to entail specific costs for participants and complex ethical problems. It could therefore be argued that the maximising nature of consequentialism immediately increases the potential for a large number of participants being involved in what has been seen as ethically challenging research.

In some contexts, for example where patient numbers will always be small, where drug companies are not interested in funding large-scale trials, or where the ethical problems posed by this particular approach are considered insurmountable, other research approaches will have to be adopted. It is possible, therefore, that on occasion ethics will dictate that maximum benefits in terms of impact are forfeited because of the costs entailed for individual participants by using the most effective means of pursuing them. There is always the need to balance the value of scientific knowledge and proof against the costs of acquiring it, and it is no coincidence that research has proceeded more slowly in the contexts where potential research participants are viewed as particularly vulnerable.

Clinical experimentation can provide numerous examples where the utility calculation could still work in favour of proceeding, but the moral problems should be apparent. The problem with such cases is that, in the interests of an undeniably significant good, certain individuals are required to bear an unusually high risk of significant harm. In the early stages of research (Phase One and Phase Two trials) they are asked to do so with no hope of direct personal benefit in terms of cure or improved health. The fact that we accept the need for such trials suggests that, in part at least, we adopt a consequentialist approach to our evaluation of clinical trials.

Consequentialism

- Seeks to maximise benefits and minimise harms
- Pays less attention to the way in which harms and benefits are distributed than to how they balance out
- Need not place limits on the level of acceptable harm if it is outweighed by a significant benefit
- Allows that beneficial ends might be pursued by potentially harmful means.

Consequentialism provides us with the means to critique the allocation of funds, researchers' time and participants' time/commitment to medical research on a global level, but offers us little scope to concentrate upon the impact of research upon individual participants once that individual has been counted in as one part of the whole picture. One is left with the sense that one needs to temper the potential excesses that could result from a purely consequentialist approach. It is not enough to know that, at the end of the exercise, the benefits will substantially outweigh the harms, we need to monitor how those costs and benefits

are distributed, and where necessary we need to ensure that they are limited. It is therefore prudent to look to another type of ethical theory for guidance.

Deontological approaches

Unlike consequentialism which is forward looking, deontological theories judge the morality of a choice or action by looking back at the intentions or motivations behind it, and the duties or obligations it seeks to fulfil or honour.[6] Whilst one might hope for good consequences to follow, this is irrelevant to the moral judgement of the action. *Logically I can do the right thing with disastrous consequences, or bring about a good outcome by immoral (and therefore unacceptable) means.* The deontologist will not allow the ends to justify the means and must therefore be concerned with the details of how research is conducted and what is done to whom, irrespective of the benefits on offer.

Whereas Bentham has come to epitomise the consequentialist approach, the figurehead of deontology is the eighteenth century German philosopher Immanuel Kant. Whilst one must be careful not to oversimplify Kant's elegant theorising, his most useful idea in this context is that no one should treat another person merely as a means to an end but rather as an end in themselves.[7] Thus we should acknowledge our duties towards others, and seek only to do unto them as we would have done unto us. The individual research participant is thus protected from having his or her own rights or interests overlooked in the interests of pursuing a substantial communal good. Deontological theories and theorists tend to vary much more than those who follow the consequentialist model; thus it is somewhat misleading to make general claims about 'deontology'. However, for the sake of simplicity one can make some claims about how such theories differ from consequentialist approaches.

Consequentialism and good medical science could be seen as having similar goals and being in step when the science in question seeks to alleviate suffering and promote well being. Moral concerns of a deontological type might well work in opposition to scientific goals, and will undoubtedly increase some of the costs of clinical research in the interests of minimising the toll on those involved as participants. Thus there is always the potential for conflict. Deontological theories are restrictive by nature, in contrast to the permissiveness of consequentialism. It is sometimes claimed that Kant was much better at telling people what not to do, as opposed to helping them decide what they ought to do when faced with a number of options. There is a risk of this happening when deontological considerations are brought to bear in the context of clinical research. It is therefore important to remember that it is possible to prescribe as well as prohibit, to require as well as disallow. It is also important to acknowledge that, on occasion, it might be impossible to reconcile the competing rights and duties that can be shown to be relevant in a particular case. The important thing is to explore how both the basic and particular rights people can claim, and the fundamental duties we have towards others, translate within the research setting. As reflected in the later sections of this book, the deontologist can appeal to law and to professional guidance, but ultimately the individual researcher might be left to decide which are the most important moral rights and duties in a particular case.

The deontological approach:

- Concentrates attention upon the individual researcher or participant
- Outlines the duties and rights of the respective parties
- Seeks to prioritise particular moral duties or rights as appropriate to the situation
- Permits or prohibits actions on the basis of their relationship to the relevant moral responsibilities
- Can pronounce some rights and duties absolute and non-negotiable whilst giving others only *prima facie* status.

Researchers as moral agents

Those conducting health-related research often have to combine the roles of scientist and carer, roles which, though related, might entail different types of duty that might at times conflict. The situation might be further complicated by the perception of the research subject as to which role should, or does, take primacy, and the assumptions they make on the basis of this. If someone has been in the long-term care of a physician, he or she might assume that the physician would have the same attitude towards them when acting as a research scientist as when offering care on an ordinary basis. However, scientific demands might, at times, require the scientist/physician to pursue the interests of the project as opposed to that of an individual patient who might, for example, be randomised into a placebo group where their preference was for the new drug. There

[6] Davis, N. (1991). Contemporary deontology. In *A Companion to Ethics*, ed. P. Singer, pp. 205–218. Oxford: Blackwell.

O'Neill, O. (1991). Kantian ethics. In *A Companion to Ethics*, ed. P. Singer, pp. 175–185. Oxford: Blackwell.

[7] Kant, E. (1949). *The Critique of Practical Reason and Other Writings in Moral Philosophy* trans. L.W. Beck. Chicago: University of Chicago Press.

Foundations of the Metaphysics of Morals (1959). trans. L.W. Beck, Indianapolis: Bobbs-Merrill. 1959.

would therefore appear to be a fundamental duty for potential researchers to consider the extent to which they can combine the roles of carer and scientist without compromising either.

The right to be included vs. the right to be protected

Traditionally, a significant moral duty in the context of clinical research has been the duty to protect the vulnerable from inappropriate inclusion in trials. We commonly refer to 'vulnerable groups' and the expectation is that they will be spared the risks and costs involved with being a research participant whatever the benefits on offer.[8] However, we now realise that members of these groups might actually want to participate and that they should have the right to do so. We might also feel that having lost out on the benefits of research in the past, we need to find more sophisticated ways of protecting their interests rather than simply excluding them from the practice. The challenge facing committee members is to decide when the right to be included trumps the very real concern with protecting the individual from the costs of doing so. Furthermore, the committee needs to decide what additional duties might attach to those wishing to engage members of vulnerable groups in their research.[9]

Recruitment

It is easy to see why clinical research needs to rely on the participation of volunteers as opposed to conscripts. It is important to ensure that those who become involved in research understand themselves as having done so voluntarily. Indeed, one could take this further and say that it is important for researchers to prioritise voluntariness, even when a level of false consciousness prevents potential participants from realising the extent to which they are subject to coercive elements.

[8] Jonas, H. (1972). Philosophical reflections on experimenting with human subjects. In *Experiments with Human Subjects*, ed. P. Freund, pp. 1–31. Allen Unwin, **and in** *Daedalus* 1969 98:219–247.

[9] Alderson, P. and Montgomery J. (1996). *Health Care Choices: making decisions with children*, London: Institute for Public Policy Research.

Fulford, K.W.M. and Howse, K. (1993). Ethics of research with psychiatric patients: principles, problems and the primary responsibility of researchers. *Journal of Medical Ethics*, **19**, 85–91.

Nicholson, R.H. (1986). *Medical Research with Children: Ethics Law and Practice,* Oxford: Oxford University Press. Mental Health Act Commission (1997). *Research Involving Detained Patients.* Position Paper 1 Nottingham: Mental Health Act Commission.

The primary moral duties when recruiting to research are:

(i) to ensure that the participation is voluntary and uncoerced
(ii) to recruit a sample appropriate to the research question/hypothesis and scientific methodology
(iii) to ensure that recruits are chosen in a non-discriminatory manner.

The first point relates to the process of recruitment. Whilst few, if any, practitioners could be accused of forcing their patients to become research participants, it is important to recognise the forces that work against voluntariness in this context. The fact of being a patient is often enough to make an individual feel disempowered, dependent and certainly apprehensive. Practical realities, such as long waiting times for appointments or procedures, might make a patient unwilling to rock the boat, once they have been seen. Despite several high profile cases of misconduct in the late 1990s, doctors still command respect in our society, and individual patients might take the fact that an invitation has come from their doctor as an endorsement. This might be particularly true in the context of a long-term caring relationship where the patient might assume that anything the doctor proposes is bound to be in the patient's interest.

In the context of non-therapeutic research, the issue of payment sometimes arises and with it the potential for inducement or manipulation. This subject reappears in its own right below, but suffice to say that, in terms of permitting the appropriate recruitment of volunteers, it is important to ensure that the level of financial reward available is not so high as to lead people to unreasonably discount the risks they might run by participating.

The second requirement – a demand for appropriate sampling – is generated by the pre-existing duty to produce scientifically valid work that has a chance of producing valuable results. Sometimes the inclusion criteria are determined by the subject under study and the methodology employed. So, an interview-based study looking at pregnant women's views on, or experience of, midwifery care would justifiably exclude all men and non-pregnant women. However, the same study might seek to exclude non-English speaking women. The reason given might be the lack of resources for translation. In another case there might be an age limit or an exclusion of women of childbearing age. In all cases the important issue is the reason given and whether or not it should be seen as scientifically and morally relevant. In practice, many exclusions are based on financial or pragmatic considerations and there would be a much better scientific result if a wider group were recruited. In some cases the result of excluding people

on the basis of race, class or gender is plainly discriminatory and should be challenged.

The third point relates to the inclusion and exclusion criteria that might be morally acceptable or unacceptable in clinical research. In the past we have largely accepted the idea that one protects vulnerable groups by excluding them from research. However, we now realise that this can lead to those groups becoming even more vulnerable because they are rendered therapeutic orphans due to the lack of research involving people like them. The obvious cases are children, the elderly, and people with cognitive impairment. A right to equal treatment means that the members of vulnerable groups should be able to access treatments that have been appropriately tested, and this must involve the recruitment of members of the group to clinical trials. However, where their extra vulnerability is proven (rather than wrongly assumed), steps must be taken to offer them appropriate protections.

In evaluating a research protocol one needs to address:

(i) the suitability of the inclusion/exclusion criteria given the scientific methodology
(ii) in the absence of valid scientific reasons, the moral reasons for excluding potential participants
(iii) the manner in which recruitment is managed and the context within which it occurs.

Participants not subjects

One of the most significant implications of a deontological approach is that the person involved in research can, and should, be characterised as something other than a mere subject or object of scientific curiosity. One way of underlining this is to use the term, research participant, as opposed to research subject. By adopting the title participant one highlights the importance of avoiding the use of people as means to ends, and instead acknowledges their independent status, their rights, and the duties we have towards them. Furthermore, by incorporating the idea of participation, one suggests the scope for active involvement in research design, conduct and dissemination which many see to be of both scientific and moral value. Admittedly, in some contexts full participation is not possible, and the term might seem inappropriate. In other situations individuals might be happier with the passive role of subject. Even so, the symbolic value of the term is significant, and should be preferred in the majority of cases. One of the potential advantages of engaging people as participants rather than subjects is that they might more easily recognise and embrace some of the duties that they need to acknowledge in order to secure a valid and ethical outcome from the research.

Whilst the deontologists will not wish to unquestioningly sacrifice the interests of research participants to a greater good such as significant scientific advance, they must reconcile the duties of researchers and the rights of participants in such a way as to ensure maximum protection and scientific viability. A participant will be given significant rights, which enable them to withdraw from any trial should they wish to do so, but whilst participating they will be bound by certain duties which are seen as necessary for the scientific validity of the trial and the ethical protection of participants. So, whilst consent remains valid, the participant is bound to a duty of concordance with the requirements of the protocol being followed; this might in turn entail a duty of openness and veracity in the reporting of experiences relevant to the trial.

Consent

One of the most fundamental ways in which we demonstrate our respect for others is by gaining their consent to actions that will impact upon them. In medical treatment generally and in clinical research specifically there is a moral and legal duty upon health-care professionals to acquire the consent of participants. Raanon Gillon tells us that consent in a health-care setting entails:

> . . . a voluntary un-coerced decision made by a sufficiently autonomous person on the basis of adequate information to accept or reject some proposed course of action that will affect him or her.[10]

It is important to stress that consent is a process, not a single event, and that the ethical standards which must be met to ensure the validity of the consent might be far more stringent than the legal ones. A signature on a consent form means very little in the absence of a full account of how it was acquired. This subject could fill a book in its own right,[11] but it is possible to sketch in the major issues that arise in relation to acquiring a research participant's consent.

- Concerns about voluntariness and coercion re-emerge, as outlined above in relation to recruitment. It is important not to approach those whose autonomy is known to be too compromised to allow them to consent, but it is

[10] Gillon, R. (1986). *Philosophical Medical Ethics*, p. 113. Chichester: John Wiley.

[11] Doyal, L. and Tobias, J.S. (eds.) (2001). *Informed Consent in Medical Research*, London: BMJ Books.

also important to support those who might be vulnerable to coercion despite their competence and autonomy in other contexts.

- Information giving is key to the successful consent process, just as it is crucial to a valid consequentialist evaluation of pros and cons. Information must be sufficiently detailed to allow for an informed choice between the various options; it must be appropriately aligned to what the patient already knows about their condition and their prognosis.[12] It must be provided in clear and non-patronising language, and, where necessary, in the language of the non-English speaking participant. The way in which information is given should be appropriate to the context and to the individuals involved, wherever possible combining verbal and written information and, if necessary, as in the case of children or cognitively impaired adults, visual aids. As experienced committee members will know, there is an art to producing a good patient information sheet, and sometimes practitioners find themselves on a steep learning curve.
- Ideally, a participant should be given time to deliberate upon the information they have been given before deciding whether or not to consent. This should usually be possible through the appropriate timing of information giving and through the careful staging of the consent process. However, in some contexts an immediate decision is required,[13] and we are well aware that these are the contexts in which issues of consent can become very problematic. Where there is no time for measured deliberation, it is particularly important that information is given as clearly and as fully as possible and that those giving consent (sometimes on behalf of children or incompetent adults) are encouraged to ask as many questions as they want.
- Consent should be seen as an on-going requirement rather than as a one-off event at the start of a project. This raises questions about how informed a participant should be kept, given that information collected in the course of the trial might, if known, affect their willingness to continue. Good scientific practice might require that a participant continues in a trial until definitive results can be produced, even if early results suggest that a trial drug shows promising results. This would be the case if the drug was being compared to an acceptable, though possibly slightly inferior, alternative, and in such a case it might be acceptable to keep participants in the dark until the trial is complete. However, where information relating to significant harms becomes available, there would be a moral duty to ensure that consent was re-negotiated in the knowledge of this. In some extreme cases a practitioner could decide to withdraw patients from a trial, despite their willingness to continue, if she thought that the risks had become too high. Thus there might be a duty to revisit consent in the face of reported adverse events, but if there is a suggestion in the data that a trial drug is significantly better than a standard treatment, this information could be withheld until the data is sufficiently robust. (The situation would probably look different if one was looking at a new treatment for a life-threatening disease for which there was no effective treatment at present.)
- All LREC and MREC committee members will be familiar with the need to reassure participants of their right to withdraw at any time without needing to provide reasons for doing so, and in the knowledge that their care will not suffer as a result. This is an important right which must be underlined given the worries about coercion and non-voluntariness outlined above. Without the right to refuse or withdraw, the right to consent is meaningless, a difficult issue in English law as it relates to consent of minors.

Confidentiality and anonymity

Medical data is highly sensitive, and health-care professionals have always acknowledged an explicit duty of confidentiality to their patients. More so than ever with the growth of genetics, we have an interest in keeping tight control over information about our bodies. Other changes are also having an impact, with the growth of multi-agency involvement in patient care; research problems can arise in the context of multi-disciplinary research if the professional groups involved do not share the same attitude and commitment to preserving the confidentiality of patients. The growing importance of qualitative research heightens the need to address the ethical issues relating to the collection, storage and analysis of potentially sensitive data. Particularly where samples, data or records are going to be stored over a long period of time, or where there is the potential for their being used for multiple purposes, the initial assurance of confidentiality and anonymity must be honoured.[14]

[12] Tobias, J.S. and Souhami, R.L. (1993). Fully informed consent may be needlessly cruel. BMJ **307**, *British Medical Journal*, 199–201.

[13] Biros, M.H., Lewis, R.J., Olson, C.M., Runge, J.W., Cummins, R.O. and Fost, N. (1995). Informed consent in emergency research: consensus statement from the coalition conference on acute resuscitation and critical care researchers. *Journal of the American Medical Association*, **272**, 1283–7.

[14] Gostin, L. (1991). Ethical principles for the conduct of human subject research: population based research and ethics, *Law Medicine and Health Care*, **19**, 191–202.

This is an area in which duties of research participants might also need to be made explicit. For example, in the context of qualitative research involving group discussions, participants need to understand that they also have a duty of confidentiality towards their fellow participants. Or, where participants have been brought together in a common location for treatment or testing, they should understand that any other people attending have the right for this to remain confidential.

Dissemination

At the beginning of this piece, it was argued that the scientific integrity of a piece of research is a necessary component of its ethical value. This issue extends beyond the design and the management of the research to its completion and dissemination. It is increasingly stressed that there is strong duty to publish and publicise research findings. One can see that there would be consequentialist support for this idea where the results would clearly benefit society, but the consequentialist could theoretically decide that publication of some research finding would not be in the public interest. Publication of results needs to be handled delicately in order to preserve anonymity and confidentiality but also to minimise the harms associated with publication.

Recompense or compensation

As mentioned above, deontologists care about moral motivation and distinguish between good and bad motives. A consequentialist, on the other hand, believes that securing the appropriate outcome is the priority, and that we should motivate people to contribute towards good ends. This difference comes to the fore when discussing the possibility of offering financial reward to those who participate in research. The deontologist might face difficulties with this issue, wishing on the one hand to protect participants from exploitation, but also preferring that they participate for the 'right sort of reasons' for example, altruism as opposed to financial need. This preference is not simply born of a desire to promote the moral welfare of the participant, but might also be linked to worries about inducement and indirect coercion. Thus consent which is given when the only rewards are the rewards of being a good person might be seen as more robust than consent which is given on the promise of financial or other benefit. Having said this, the financial reality might be that the person conducting the research is being handsomely rewarded, and it could be seen as unfair not to pass some of the benefit on to the participants.

Conclusion: tempered consequentialism

Anyone who has studied moral philosophy will know how difficult it is to give a fair account of differing approaches to moral reasoning without devoting far more space than is available here. They will also know that there are other ways of thinking about moral questions that have not even been given a mention. It is rare these days for people not to be aware of the work of the American theorists, Beauchamp and Childress, who propose a form of moral principalism which has gained widespread support amongst health care professionals.[15] Similarly, much has been done in recent years to revive the tradition of virtue ethics which traces its roots back to the work of Aristotle.[16] Feminist ethics now has a rich and varied literature, which has contributed usefully to many debates. All these approaches have something to offer, but the priority here has been to present an introductory guide to two ways of thinking which intuitively appeal at some level to most people. A further aim has been to show some of the incompatibilities between these approaches, in the interests of de-personalising some of the disputes that might emerge during committee deliberations.

With this in mind, we invite you to use the many forms of guidance available in this manual to help decide whether a piece of work offers significant enough benefits to appropriate parties to justify the predicted costs involved. Having decided this, one then has to decide whether the participants upon whom the success of the venture depends can be safely and appropriately recruited and adequately protected during their participation. If that is possible, then practical mechanisms need to be put into place to secure these ends, and the research needs to be monitored to ensure that the safeguards remain in place. Thus a combination of approaches is required, borrowing the larger perspective from the consequentialist, and the specific detail from the deontologist. The goal of an ethics committee is to facilitate ethically sound practice, and to encourage researchers to honour their moral responsibilities towards participants. This is not an easy task, but society should be grateful to those who accept the responsibility and who give time and effort to ensuring that health-care practice is

[15] Beauchamp, T. and Childress, J. (2001). *Principles of Biomedical Ethics*. 5th edn. Oxford: Oxford University Press.

[16] Crisp, R. and Slote, M. (1997). *Virtue Ethics*. Oxford: Oxford Readings in Philosophy.

informed by evidence based on scientifically and ethically acceptable research.

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Smith, T. (1999). *Ethics in Medical Research: A Handbook of Good Practice*. Cambridge University Press.

USEFUL WEBSITES

Alder Hey (Royal Liverpool Children's Inquiry)
http://www.rlcinquiry.org.uk/download/index.htm

The American Journal of Bioethics
http://ajobonline.com/

The Bristol Royal Infirmary Inquiry
http://www.bristol-inquiry. org.uk/

British Medical Association
http://www.bma.org.uk/

Bulletin of Medical Ethics
http://www.bullmedeth.info/

Centre of Medical Law and Ethics
http://www.kcl.ac.uk/depsta/law/research/cmle/

Committee on Publication Ethics
http://www.publicationethics.org.uk

Ethical issues in research – bibliography
http://www.nlm.nih.gov/pubs/cbm/hum_exp.html

The Hastings Center
http://www.thehastingscenter.org/

Informed Consent in Medical Research
http://www.informedconsent.bmjbooks.com/

Journal of Medical Ethics
http://jme.bmjjournals.com/

Kant and Kantian ethics
http://ethics.acusd.edu/kant.html

Kennedy Institute of Ethics Journal
http://muse.jhu.edu/journals/kennedy_institute_of_ethics_journal/

Medical Research Council
http://www.mrc.ac.uk/index/public_interest/ethics_and_best_practice.htm

Royal College of Physicians of London
http://www.rcplondon.ac.uk

Stanford Encyclopaedia of Philosophy
http://plato.stanford.edu/contents.html

Utilitarian ethics
http://ethics.acusd.edu/utilitarianism.html