RESEARCH ETHICS

"Fair's fair argument" and voluntarism in clinical research: But, is it fair?

M A Perna

J Med Ethics 2006;32:478–482. doi: 10.1136/jme.2005.013763

This article sets out to counteract HM Evans's "fair's fair argument" in support of abolishing veto to research participation. Evans's argument attempts to assimilate ordinary clinical practice to clinical research. I shall refer to this attempt as "assimilation claim". I shall attempt to show that this assimilation, as it is carried out in Evans's argument, is misleading and, ultimately, logically undermines the conclusion. I shall then proceed to show that when the fair's fair argument is proposed independently of the assimilation claim, Evans's conclusion is not unavoidable and possible alternatives are equally open within the terms of the argument itself.

designed that everyone enrolled in it will receive some active treatment or other whose relative merits are genuinely unknown and thus sincerely assumed to be equivalent when you enter the trial THEN I think is your duty as a beneficiary of the pooled cost, pooled benefit NHS system to do for future patients exactly what past patients have done for you – that is, you must receive the treatment within the parameters of the clinical trial in question.¹

COMPONENTS OF EVANS'S ARGUMENT

I am going to examine specific points of Evans's argument in relation to a few relevant features of the answers he offers to objections moved against it.

Evans's argument lies on two claims:

The first claim is that no substantial difference exists between experimental and ordinary treatment in terms of risks and expectations of benefit. In addition, some specific features of ordinary clinical conduct may be overlooked and the conduct itself assimilated to the practice of enrolment and participation in clinical research, if certain contingent circumstances are present—that is, points (1)–(5) of Evans's argument described earlier. I refer to this claim as an assimilation claim

The second claim is a "fair's fair argument", which Evans presents as follows: "don't take it if you can't hand it out." In particular,

in taking advantage of publicly funded healthcare...I am receiving treatments that have been brought to their present state of perfection by having been tried out by other people first. In effect, I stand on the shoulders of patients who took part in past research. Do I not therefore have an obligation to bear the feet of future patients, by allowing my treatment to be included in systematic research?

I think both claims taken singly are neither necessary nor sufficient, but they are meant to be jointly sufficient to establish the obligation to enrol as a research participant. In particular, Evans's argument may be stated as follows: the obligation to participate in research is morally justified if (a) the "fair's fair principle" applies to the case in point, and (b) the claim that no substantial difference exists between experimental and ordinary treatment in terms of risks and expectation of benefit holds.

This paper is a response to HM Evans's argument in support of a duty to participate in clinical research.¹ This duty in Evans's interpretation means abolishing the right we enjoy to say "no" to being a research participant. In other words, it is morally obligatory for a person, given a number of provisos that I shall list shortly, to be a research participant, but this is only a first step towards justifying the legal enforcement of the abolition of voluntary participation in research. The present intervention is an attempt to reject this conclusion by offering a criticism of Evans's argument, which will take into consideration his answers to some of the objections already moved against his position. I am glad to point out that both Evans and I share some reluctance at the conclusion of his argument. Evans's view and mine, however, diverge in so far as Evans considers such conclusion as being logically inescapable, whereas I do not. Much hinges on how the premises of the argument are interpreted.

EVANS'S ARGUMENT

A summary of Evan's argument is as follows:

If (1) you go to your doctor in search of treatment, and if (2) you are prescribed a type of treatment, which your doctor competently judges that you need or from which you could benefit, and if (3) that type of treatment happens to be the subject of ongoing clinical research in a context of genuine equipoise (clinical uncertainty about which is the best available treatment), and if (4) you meet the inclusion and exclusion criteria for entry into the relevant trial, and if (5) that trial is so

Correspondence to:
Dr Maria Antonietta
Perna, Public Health Policy
Unit, School of Public
Policy, University College
London, Research &
Development Directorate –
NHS Foundation Trust
UCLH, 17 Westall Close,
West Street, Herts,
Hertford SG13 8EY, UK;
m.perna@ucl.ac.uk

Received 28 July 2005
In revised form
16 September 2005
Accepted for publication
25 September 2005

Evans's position can be interpreted in either of the following manners. As some of my fellow citizens, or patients in this particular case, have previously freely undertaken some kinds of action from which I somehow presently happen to benefit, then I have a duty towards other fellow citizens or patients to undertake the same kinds of action. Alternatively, patients in the past did act within the parameters of a social obligation to undertake actions of that sort. Consequently, as beneficiary of a public healthcare system, I am in turn obligated to do the same. It is not clear from the text, however, which one of these readings may be appropriately attributed to Evans. As I think that no free choice someone made in the past from which I happen to benefit puts me under an obligation to make the same choice with regard to others, I shall take the second reading as constituting the core of the fair's fair argument. Consequently, I shall mainly attempt to examine the grounds for an obligation to be a research participant on the basis of this understanding of the argument.

I shall discuss the first claim and show that, if true, it undermines the claim to the duty that it is intended to support. Then, I shall go on to the core of the fair's fair argument by examining the second claim, which, I shall argue, is not plausibly tenable considered either by itself or in conjunction with the first claim; better still, in conjunction with the first claim its acceptability is in an inverse ratio relationship to the conflation between clinical research and ordinary medical practice held in the first claim. The logical incompatibility of both claims in support of the conclusion is sufficient to undermine the argument, and the second claim by itself does not suffice to ground an obligation to participate in clinical research.

THE ASSIMILATION CLAIM

The assimilation claim is particularly relevant in responding to the second and third objections in Evans's article under discussion. Were we to object that "research carries the sort of uncertainties, or put more unsympathetically the risk of harms, which are unacceptable within the normal expectations of a clinical encounter", Evans would be quick to point out that "this objection is naïve. It completely ignores the facts of life about the clinical encounter. It ignores the uncomfortable truth that, from the moment you step into the consulting room, you have already entered the research context in at least two counts." Before proceeding to the specification of the two counts Evans has in mind here, it would be worth pointing out, firstly, that by "research", Evans refers to randomised clinical trials; secondly, that the assimilation claim is noticeable in the manner Evans articulates his argument, namely, in the first three points. The first two points present the term "treatment" in the context of the clinical encounter with the physician, the same term is then in third point embedded in a different context—that is, research—but the meaning remains unchanged throughout the argument: rather than arguing for the assimilation claim, Evans inadvertently builds it into the flow of his argument. This is likely to lead to the misguided conclusion that asking for treatment in the first context is the same as asking for treatment in the second context—that is, asking for an experimental drug.

Considering the article as a whole, the conflation seems to be brought about through the following steps:

- The norms governing the ordinary clinical encounter are disregarded, as I shall show later. Everyday clinical practice comes to be referred to as "hurly burly of routine clinical practice", and comes through as being a somewhat shoddy business, highly risky, subject to the physician's "hunch".
- Ordinary clinical practice is then assimilated to research practice, given the five conditions of Evans's argument described earlier. Some of those features of ordinary clinical practice, which are recalcitrant to such assimilation, are considered by Evans to have no considerable negative effect on the well-being of patients (objections 4 and 5 in Evans's original article).

That said, I shall move on to the two counts with respect to which Evans claims that entering the consulting room and entering a clinical trial do amount to the same thing:

First, you are inevitably a beneficiary of previous research – which is being *applied* to you, courtesy of those patients who were your predecessors. Second, all clinical interventions are also experiments upon a study population of $n=1$, simply because your actual response to a treatment is unknowable in advance of trying it out. The minute you invite your doctor to treat you then you have volunteered for an experiment, and you must accept the risks this involves even in the ordinary clinical context.¹

CRITIQUE OF THE ASSIMILATION CLAIM

Are the first and the second points above compatible? Surely, the sense in which the "predecessor patient" is an "experimental subject" cannot be equivalent to the sense in which a patient in an ordinary clinical encounter can be so regarded: how can I be a beneficiary of previous research if the moment I use a medical treatment, I am an experimental subject, hence it makes no material difference whether the treatment has been or has not been previously tested on other patients? Evans does not raise the point explicitly, but he is careful to use the term research in the first point, but not in the second; this, I suppose, may be because, although an intervention on a particular patient may be characterised as experimental in certain circumstances, this is not extensionally equivalent with research. There may perhaps be a rationale underlying Evans's claim according to which a patient would be under an obligation towards research participants, but the same rationale could not support the same obligation towards patients who undergo "experimental" treatment within an ordinary clinical encounter; briefly put, the rationale would presumably be that the results obtained by means of research are supposed to be generalisable at the population level, thus potentially benefiting you, me and everyone else in society. But this is not so as far as ordinary clinical practice applying an experimental treatment is concerned. Although Evans's position in the quotation given earlier may be so reconstructed, the fact that he refers to "all clinical interventions" as "experiments" throws some doubts on such reading. Rejecting the latter would only lead to an unqualified conflation of clinical research and ordinary clinical encounter.

In conclusion, as a way of supporting a claim for the recognition of what research participants do for society in view of grounding an obligation to participate in clinical research, failure to distinguish between clinical research and ordinary medical practice can be only detrimental.

But, is it tenable to claim that the uncertainties regarding harms and benefits are not substantially different in the two

- The normative criteria, both epistemological and ethical, governing experimental conduct, are regarded as being fully satisfied in practice, so that assurance of minimal risk of harm and of optimal expectation of benefit becomes an intrinsic, unproblematic, de facto rather than a hypothetical, feature of a clinical trial.

contexts? If this were the case, then Evans would not be advocating research in terms such as the following:

...medicine can do so much for you now, but preferably would be able to do far more for you in the future given the necessary research. (As proof of this, look at how much less medicine was able to do for comparable patients in the past.)¹

I shall offer two counterclaims: (a) the first claim is a factual claim regarding the concept of minimal risk in research and (b) the second is a conceptual claim regarding research.

The factual claim

Some ambiguity exists in the interpretation of the term “risk” as it is used in medicine. As Resnik² aptly points out, risk in the sense of both probability and magnitude of the harm is classified according to two different standards:

- The daily life risks standard, which is modelled around what are taken to be the risks ordinarily run by the average subject
- The routine test standard, which is modelled around the risks of the patient during what are taken to be routine medical examinations and tests.

Although it may be convincingly argued that the routine test standard is more appropriate for the protection of the research subject, it is the daily life risks standard that is adopted for risk assessment in research. One central reason why this is so is that it would be both logically and practically problematic to assess risks in testing new treatments and complex studies according to a standard of risk that is derived from, or based on, the risks assessed in relation to ordinary routine clinical treatments and tests. Independently of the validity of Resnik’s claim regarding the preference of the routine test standard over the daily life risks standard, the point of his claim that is relevant to my argument is the following: how can we equate, as Evans seems to do, clinical practice and research with regard to risks, if the concept of risk worked out in terms of ordinary routine examination and tests cannot even be unproblematically applied to risk assessment in research?

The conceptual claim

The clinician confronts an enormous wealth of information, trial results being an important part, and the professional ability of the clinician is required to incorporate the information into a more comprehensive judgement on what is best for each patient.³ In the case of the clinical trial, it is exactly this information that is being sought, and for this reason alone it is not already part of the data which in the clinical context further aids clinicians to make their judgements for the patient’s benefit. One thing is to tell the patient that accepting a treatment which has had a high percentage of success in trials still brings with it a percentage of risk for that patient, and quite another to tell the patient that the treatment has never been tried before. In the case of the treatment that has never been tried before, that percentage of risk is of a different kind with respect to the one, which has had a high percentage of success in trials. In particular, we have no information as to the percentage of risks it involves at the population level. Despite his reliance on equipoise, Evans implicitly concedes this point as he writes, “For the expectations that drive any ethically acceptable research are, standardly, that the subjects entering the trial will receive treatment that is—for all we know [italics in the original] – at least as good as the standard treatment.”⁴

The experiment is designed to find out that among other things, the treatment is at least as good. Thus, the difference in the meaning of “treatment” in the two contexts of ordinary clinical practice and research is conceptual, rather than simply empirical—that is, it can be held even if in practice the patients really end up confronting the same level of risks, in actual cases in which a patient treated in the ordinary clinical context and another treated in a trial fare in the same way, or in cases in which a trial participant fares even better than a patient outside the trial context. I suggest that if the difference in the knowledge of the harm–benefit ratio between the two contexts is thought of as being non-existent at the conceptual level, then there is a serious problem of translatability of trial results not only from the population to the individual level, which is the ordinary context within which clinicians form their judgements in the clinical encounter but also, and more importantly for the scientific status of trials, from the experimental, artificial conditions of the trial to the population level under ordinary, everyday conditions. So, although uncertainty as regards risk of harm and expectation of benefit are both conceptually and empirically present in both contexts, some conceptual differentiation between the two is worth making.

In this connection, it is perhaps interesting to point out that the Declaration of Helsinki further corroborates my conclusion, as it states: “When medical research is combined with medical care, *additional standards* apply to protect the patients who are research subjects [emphasis added].”⁵

THE ASSIMILATION CLAIM AND THE FAIR’S FAIR PRINCIPLE

I shall now pursue the argument from a different angle by assuming from the outset that the assimilation claim holds. So far, I have established that the more research and ordinary clinical treatment are assumed as being not substantially different, the less plausible it is for Evans to support his argument in favour of an obligation to enrol in clinical research. Furthermore, I have attempted to undermine Evans’s idea of the sameness of the kind of risk of harm and expectation of benefit (or lack of any noticeable ethical difference) involved in the two contexts.

Next, I shall take at face value Evans’s conflation of clinical treatment and research which is inbuilt in his first three points, and show that if this conflation is to be consistently maintained, then one feature which has a central role in the clinical encounter is to be brought to the fore. If preserved from the clinical to the research context, such a feature radically undermines Evans’s aim of establishing a duty of enrolment in research; if, on the other hand, it is eliminated, then the two contexts are changed in such a way as to render the assimilation claim untenable. As a consequence, the discourse regarding research participation would have to be rethought independently of the assimilation claim. As a preliminary point, the following is to be noted. Disregard of such a feature would imply disregard of an important aspect of the epistemological and ethical norms which more or less consensually govern today’s ordinary clinical practice. Consequently, the onus of justifying rejection of such a feature rests on those who undertake to challenge its validity.

I would like to draw attention to the final version of Evans’s argument which was quoted in the first section: in (1) I see the doctor; in (2) I am prescribed a type of treatment which my doctor competently judges that I need; in (3) that treatment happens to be the subject of ongoing clinical research. What seems to be missing here is my participation in the choice of treatment options. The fact that the treatment which is good for me happens to be tested in a clinical trial under the conditions specified by Evans—that is, under conditions of equipoise against an already proven

active treatment—indicates that there is at least one more treatment available, which would be both equally beneficial to me and available outside the trial context. Still, according to Evans, in such circumstances, I would be obligated, in the sense that I would not have any choice in the matter, to enrol, at least if I wished to be treated. Unless the ground for obligatory participation were already established, which by hypothesis it is not, as this is exactly the matter into which I am enquiring, the manner of managing the clinical encounter illustrated in Evans's scenario runs counter to ethically correct norms; for instance:

...we must always treat our patients as people, involving them in those significant decisions about their care that will affect their lives and well-being. That is why our conception of substantial benefit is and should remain patient-centred, and the patient should be able to regard the doctor as a partner and an experienced guide on the journey that is their illness. We must be particularly strict about any violation of this principle.⁵

The fact that respect for patients' involvement in treatment choice is disregarded by Evans is further corroborated by his attitude towards sharing clinical information with the patient. He voices this attitude as he answers objection (5) in his article, according to which both clinician and patient in a clinical trial, but not in an ordinary clinical encounter, are required to be ignorant regarding which treatment is to be given to which arm of the trial.¹ My point is quite different from this, as it concerns the exercise of patients' autonomy in treatment choice rather than clinicians' or even patients' mere knowledge of treatment, but Evans's response is equally relevant in terms of the attitude that I am attempting to bring to the fore:

In the usual clinical context the doctor chooses the treatment, and tells the patient what she is prescribing to him, and in an outpatient setting the patient may even go and obtain it himself at the pharmacy.¹

Obviously, the subject of the encounter is the doctor, and the patient would not even need to know what kind of treatment is being prescribed if it were not for the fact that he would eventually have to ask for it at the pharmacy. Evans further writes:

Well, what of it? Just what's in a name? Less, I think, than the mock affection noted by James Agate in his diary (9th April 1937) following a visit to Thorpe Bay without his antiasthma medication: "I just can't bear to run short of Acetylmethyldimethylamoxidiphenylhydrazine."⁶

Evans's point seems clear: there is no need to convey treatment information to the patient, as it would be meaningless to a layperson anyway. But this is exactly why medical staff are ethically required to inform the patient about treatment options by using clear, layperson language and to make sure the patient has understood and retained the information given so that an appropriate decision may be arrived at:

Autonomy, information, and respect all go together to form the crux of current ethical views of the professional-patient relationship as a partnership of intelligent equals.⁵

The paternalistic attitude seems prevalent in this instance of clinical encounter, although its presence is not openly

highlighted, and this move vitiates the form of the argument by using treatment ambiguously in his points (1)–(3): the context of its use shifts from one where it is prescribed after the clinical encounter to one where it is given as part of the conduct of a clinical trial, whereas its meaning, which ought to shift accordingly, instead remains the same throughout. Emphasising the aspect of autonomy with respect to the lack of patients' participation in treatment choice is not question-begging with regard to either Evans's disposal of objections (4) and (5) in his article or to Evans's overall argument, which aims at establishing the abolition of a different aspect of autonomy—namely, the voluntary consent to enrol in clinical research.

The dilemma confronted by Evans's argument is the following: either ordinary clinical encounter and clinical research are not differentiated, and in this case Evans must include patients' participation in treatment choice as an essential component of research, as this aspect of the relationship between clinician and patient is constitutive of the norms governing the clinical encounter; or the ordinary clinical encounter and research are essentially different practices. If they are considered not differentiated, then this logically rules out the possibility of establishing any kind of obligation for the patient to enrol in research, as the requirement of exercise of autonomy with respect to full information and involvement in decision making regarding treatment is logically incompatible with such an obligation, let alone with its enforcement. If, on the other hand, they are considered as different practices, then the requirement of patients' autonomy regarding treatment choice is not binding, and the possibility of an obligation to enrol in research opens up, although it is still in need of being established independently of the assimilation claim.

AN INDEPENDENT CASE FOR A DUTY TO ENROL IN CLINICAL RESEARCH

A non-question-begging manner of reconstructing Evans's thesis independently of the assimilation claim would be as follows: beneficiaries of a public health service have no right to veto their participation in research, or, in Evans's words, they have an obligation to put "aspects of [their] body's function temporarily at the service of the common good", given that they are also by the same token beneficiaries of the results obtained by means of clinical research on human participants. A preliminary point is that Evans does not place such a public service within an egalitarian socioeconomic system. Namely, he writes:

There are, in short, some things that you can veto and some things that you cannot veto. And [participation in research] is one of the things that – suggests my modest proposal – you cannot veto unless your income allows it.¹

For one thing, Evans admits the positive function of income tax as a social mechanism, as he refers to income tax as being an apt analogy for the research participation policy he proposes in the article under discussion. Given his endorsement of such practice, I begin by noticing that through income tax, all citizens, rich and poor, contribute to the public good according to what they can afford, including provision of a public healthcare system. But this does not seem to be enough in Evans's view: there is an extra fee to be paid, or something extra that is owed, which is either paid through research participation or through buying treatment, if we can afford to do so. In this case, it seems to me, the buyer of medical treatment is not paying the extra fee for the public health service as such, which by hypothesis is already being paid for through taxation by both richer and poorer

citizens, both public and private healthcare consumers, unless Evans wishes to claim otherwise, but specifically for research participation itself. This points to an alternative to Evans's obligatory participation—namely, payment offered for participation in research.

In my view, the alternatives to either buying our way out of participation or renouncing the power to veto our participation in research (at least if we wish to be treated) would be: abolition of the extra fee within a well-functioning public health service supported by the community as a whole, both financially and in terms of democratic decision-making processes. The democratic decision-making processes would aim at reaching consensus regarding, among other things, the risks that the members of the entire community would be prepared to take for health-related benefits. This would preserve voluntary participation.

Or, alternatively, preserve the extra fee whereby we understand the payment is offered for research participation itself rather than for medical treatment. This would counteract Evans's alleged justification for abolishing veto to research participation: if it is established that something is owed to the research participants beyond what every citizen contributes to a publicly funded healthcare system through taxation, and Evans seems to think that it does, the obligation could equally, or even more appropriately, be fulfilled by offering them payment. Consequently, their participation in clinical research would be neither obligatory

nor enforceable. Even if, for the sake of argument, this should prove to be a less efficient system than enforcing research participation, efficiency as such is not an ethically sufficient ground for enforcement of a social mechanism or practice. If "fair's fair", this much at least seems to be fair.

ACKNOWLEDGEMENTS

Many thanks are due to the Research and Development Department, NHS Foundation Trust and the School of Public Policy, UCL for financial support. Also, I am extremely grateful to Professor H M Evans, Professor R Ashcroft, Dr Neil Levy and one anonymous reviewer of the JME, Dr Piers Benn, Ms Karen Gui, Mr Daniel Sokol from Imperial College, London, and Dr Eunice Goes for the valuable comments on earlier drafts of this article.

REFERENCES

- 1 **Evans HM.** Should patients be allowed to veto their participation in clinical research? *J Med Ethics* 2004;**30**:198–203.
- 2 **Resnik DB.** Eliminating the daily life risks standard from the definition of minimal risk. *J Med Ethics* 2005;**31**:35–8.
- 3 **Jadad A.** *Randomised controlled trials*. London: BMJ Publishing Group Ltd, 1998.
- 4 **World Medical Assembly.** *Declaration of Helsinki: ethical principles for medical research involving human subjects*. Edinburgh: 52nd WMA General Assembly, 2000.
- 5 **Campbell A, Gillett G, Jones G.** *Medical ethics*, 3rd edn. Victoria, Australia: Oxford University Press, 2001.
- 6 **Sherrin N, ed.** *Oxford dictionary of humorous quotations*. Oxford: Oxford University Press, 1995.

bmjupdates+

bmjupdates+ is a unique and free alerting service, designed to keep you up to date with the medical literature that is truly important to your practice. bmjupdates+ will alert you to important new research and will provide you with the best new evidence concerning important advances in health care, tailored to your medical interests and time demands.

Where does the information come from?

bmjupdates+ applies an expert critical appraisal filter to over 100 top medical journals. A panel of over 2000 physicians find the few 'must read' studies for each area of clinical interest.

Sign up to receive your tailored email alerts, searching access and more...

www.bmjupdates.com