Rationing, randomising, and researching in health care provision

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In this paper the need for valid evidence of the cost-effectiveness of treatments that have not been properly evaluated, yet are already available, albeit in short supply, are examined. Such treatments cannot be withdrawn, pending proper evaluation, nor can they be made more widely available until they have been shown to be cost-effective. As a solution to this impasse the argument put forward recently by Toroyan *et al* is discussed. They say that randomised controlled trials of such resources could be done but only if resources are randomly allocated independently of a research context. Relevant outcome data could then be collected for research, given this opportunity. (There are already a few investigators who have turned limited resources, mostly health service provision, to their advantage in this way.) We agree. We disagree with Toroyan *et al* on a number of points. First, they claim that no ethical issue relating to equipoise arises. We disagree and this disagreement depends on our showing that equipoise should be maintained in a relationship that they do not consider. Secondly, they say that consent to data collection is always needed. Again we disagree. Thirdly, they claim that the previous two issues are the only possible ethical issues that could arise. We argue, instead, that there is a further conflict of interests that has ethical import.

There is now a pressing need to research some health care provisions, particularly health services, that have not been properly evaluated, but are still too expensive to make widely available without favourable data on their relative cost-effectiveness. Yet many are already available on a limited basis. Such health care provision cannot be withdrawn, pending proper evaluation, because of political and ethical pressure to continue providing a level of access, nor can it be made more widely available, because of lack of funds, until it has been shown to be cost-effective.

As a solution to this impasse, we discuss the argument, put forward by Toroyan *et al*, that valid research data can be sought from randomised controlled trials of such resources.¹ The way to turn the perceived problem of limited resources to the advantage of researchers and future patients may be to use randomisation as a fair method of distributing scarce resources *independently* of the research context. By “independent” we mean that the reasons for distributing the scarce resources (for example, for reasons of social justice) are different from the reasons for doing good science. Once randomisation has occurred it may then be prudent to collect data on outcomes for research analysis. The practice has already been used in the context of evaluating the effectiveness of supplying day care for children in the London area on the child's health and the family's welfare.¹ The ethical question is whether the opportunity to do valid research should be “exploited” under these circumstances. We will examine three ethical issues in relation to this proposal.

The first is a potential conflict of interests between benefiting the current population, as a whole, by distributing resources fairly among its individual members, and benefiting future populations by doing good science. For this reason, it is important to establish that the decision to do research is really independent of the decision to randomise. We will examine the implications of this for designing and sponsoring studies in such cases.

The second is the requirement for scientific uncertainty or, more exactly, doctor-patient equipoise. An informed and perfectly rational patient would agree to be randomised only if the expected utility of the trial was at least as good as the

available alternatives. When a potential recruit could choose either trial arm outside the trial, then he/she would have to be in a state of equipoise, meaning his/her expected utility of either trial treatment would have to be the same, before agreeing to be randomised. In this way, individuals are not expected to lose out for the sake of future patients and the medical profession can rest easy in the knowledge that it has not broken its promise to do the best it can for each individual in its care. When trial treatments are already available, many individuals prefer to select the intervention rather than accept randomisation. Toroyan *et al* claim that doctor and patient—when discussing the trial together—need not be in a mutual state of equipoise when their preferred treatment is available only on a limited basis outside a trial. (We explain this relationship below.) We will examine this argument in more detail and discuss under what conditions randomisation would be used as a way of allocating scarce resources. We agree that the doctor and the patient need not be in a mutual state of equipoise. We think, however, that the person making the rationing decisions should be in a state of equipoise between who out of a given set of individuals should get the treatment before random allocation of that treatment is ethical.

The third is the requirement for consent from those who participate. Adequate information needs to be provided to competent individuals without undue pressure from anyone to decide either way. In the present circumstances, individuals could consent to data collection, although it is arguably not morally necessary. Yet, individuals cannot consent to the initial randomisation process because that would already have been decided at a population level for rationing purposes.

We will refer to the recently revised Declaration of Helsinki throughout.²

RATIONING SCARCE RESOURCES

It is increasingly being recognised that demand for health care is outstripping supply. This leads inevitably to a need to prioritise or to ration interventions, even if they are considered or known to be effective.

There may be circumstances under which randomisation could be used as a fair way to allocate scarce resources, but

these circumstances may arise only after more morally relevant considerations do not prove decisive. In the UK, the National Health Service (NHS) tries to distribute its resources according to individual need or the cost of treating an individual so as to cater for his capacity to benefit.^{1,3} Need is sometimes defined as having an immediate threat to life, which avoids conflating need with expected utility.³ Comparative judgments about the relative degree of individual need could thus be made and limited resources could be distributed accordingly. In the USA, on the other hand, the influence of a person's ability to pay bears heavily on his provision of health care. So, where does randomisation fit in?

A particularly important idea for the present discussion comes from John Harris, who suggests using a second principle in cases where the first moral principle does not give definitive answers.⁴ His first principle states that we should help those who are under an immediate threat to their life. While one might want to argue with this, the idea of having a principle to fall back on when the first is indecisive (for example, when two people are equally placed in terms of having an immediate threat to their lives) remains important. Harris's fall back principle is that we should allocate resources by lot if all other morally relevant factors are equal and resources are too scarce to provide treatment for everyone. In other words, individuals may be considered equal in all relevant respects but they must be treated unequally due to limited resources. In this case, a decision to randomise or allocate in an apparently more arbitrary way avoids actively discriminating against any one individual unfairly. Randomisation is famously the way to avoid "selection bias". But randomly allocating individuals to what treatment is available should not be undertaken lightly and only as a secondary measure. And, other things being equal, randomisation may be at least permissible or even obligatory as it may be the only rational and "fair" way to decide such cases. There seems to be nothing about the decision to randomise as such that would make it inherently unacceptable or in need of more stringent review than other rationing decisions.⁵ The more explicit all rationing decisions become the more able the public will be to elect people democratically or voice their opinions of specific practices through polls or even referenda in extreme cases. The idea of a health care lottery may be viewed pejoratively, and there may be political objections to it, but this is an empirical question.

RESEARCH WITH LIMITED RESOURCES

When interventions have not been properly evaluated, yet are already in the public domain, even if in limited supply, the usual way of gaining some research data is to rely on observational study. The best way to make valid observations is to design the perfect cohort study and to compare outcomes of those already getting the treatment of interest with those not getting it. In our case, the treatment would already have been distributed randomly. This makes a controlled trial a particularly reliable form of observational study as the respective cohorts would be free of selection bias. The juxtaposition of rationing and researching thus appears to be a winning combination. It is important to stress this research would *not* be experimental as such.

We have examined the case for randomising as a way of distributing scarce resources and we have shown that, without adequate data on a treatment's cost-effectiveness, the NHS may have little choice but to randomise limited, yet available, resources because it cannot tell who is likely to benefit the most. While the following arguments make research permissible in such cases, there is a question of whether research is obligatory (assuming one has the opportunity). Yet, since this question is raised by any form of research and not just research in these circumstances, we will not discuss it further in this paper. We will now examine the implications of having

a potential conflict of interests that could affect the decision to randomise and we will then discuss popular ideas of equipoise and informed consent.

1. The decision to do research is independent of rationing decisions

It is important not to forget the rationale for doing randomised controlled trials where there are limited, yet available, resources. It hinges on the prudential assumption that the resources, which would be too expensive to implement more widely without adequate data on their cost-effectiveness, are sometimes distributed randomly for reasons to do with distributive justice that are independent of reasons to do good scientific research. The question again is *whether* the opportunity should be exploited. There is a potential conflict of interests between serving the best interests of the current population by distributing resources fairly among its individual members, and serving those of a future society by doing good science. In other words, the interests of the current population and the rights of its individual members lie in the fair distribution of resources, while the interests of a future population lie in getting valid research data on the cost-effectiveness of health care, *however that health care is distributed*. If the methods for doing good science were allowed to affect the way health care was distributed among the current population, then individuals within that population might be treated unfairly. In short, science and distributive justice might conflict.

In particular, sponsorship for research may influence the way in which health care is distributed among the current population. Funds may be available for doing research perhaps only from an external source and would not otherwise be available for routine service delivery. Even within the NHS, funding for doing research may not be easily transferred to delivering routine care, since the two budgets are usually kept entirely separate. Because the resources available come from a research sponsor, there would probably be scientific and pragmatic stipulations on how they were to be used. The researchers could select a study population which might not be the population most in need of the resources. And, even if it were, the scientifically chosen sample size and ratio of randomisation might influence how the resources were distributed. These scientific considerations may run counter to an ethical concern for distributive justice among the current population. The money on offer from research sponsors may be so attractive as to make it possible for more people to receive the intervention and reap the net benefits of it than would otherwise be the case. The decision to allocate by lot may thus be heavily influenced by, or even taken after, the decision to accept the sponsorship on offer and to do a trial. In this case, however, a trade-off would have to be made. On the one hand, the sheer number of people getting the resources would be greater and so arguably the current population as a whole would expect to benefit. On the other hand, the resources might not be distributed among current patients quite fairly and so the primary principle of individual need would not have been satisfied. Some more "needy" individuals might not get the resources while many others who were less "needy" might get it instead.

To make sure that science does not trump distributive justice in the way described above, one must somehow make sure that the current population does not expect to lose out for being in the trial relative to the status quo. The population would expect to lose out if the way in which its resources were distributed were determined by the requirements of the proposed research. Independent review by an ethics committee, perhaps jointly by a clinical and a research ethics committee, of collective rationing and research decisions, may prevent this potential conflict of interests becoming actual. In addition, there may be a "guardian" who is in a position to look after the best interests of a particular population as a

whole or a “cluster”. A cluster is a group of people and is sometimes randomised en bloc to receive one or other treatment in a trial. This situation is analogous to randomisation by cluster where independent guardians could become involved in the recruitment of clusters.⁶ When reviewing such proposals, the requirement of independence between the primary rationing and secondary researching decisions has implications for the chosen study population, the sample size of the protocol, and the ratio in which the intervention is allocated randomly among that sample population. The research population should be the population in need of the intervention. On the face of it, the chosen sample size should mean that all the resources available are used up in a just way. In other words, the available resources should not be withheld from individuals just to make the numbers of people getting the intervention the same as those getting the best available alternative care. If the resources available could be offered to two thirds of the population in need of it, then it should still be allocated in this way irrespective of scientific considerations favouring only half of the population getting it.⁷ This may, however, have implications for statistical power. It has been argued elsewhere that trials using unequal randomisation ratios can, in some contexts, serve justice more than those using equal ratios.⁸ If equal randomisation is needed for scientific reasons, then a random sample of the study (and hence patient) population could be identified and offered treatment *without withholding some resources* or distributing what resources are available in a partial way.

2. Decision maker equipoise

Equipoise is born of epistemological and scientific uncertainty and represents a state of indecision between two or more courses of action, as modelled by mathematical decision theory. The concept is usually used, and indeed is used by Toroyan *et al*, to describe the decision relating to which of two treatment options represents the best bet for a particular patient. The situation in conventional trials depends on whether the trial treatments are widely available. If they are, then the doctor and patient need to be in a state of equipoise.¹ If the trial treatments are only available within the trial, then the doctor and the patient must be in a state at least as good as equipoise, recognising that the trial could promise more utility than routine care.⁹ Toroyan *et al* claim that equipoise is never a moral requirement of trials in the first case where the trial treatments have been available routinely for some time. We disagree. We agree that doctor and patient need no longer be in equipoise between which out of two treatments is best and that a trial may be ethical nevertheless. Again, this assumes the treatment is not available outside what has already been allocated for rationing purposes. We suggest below, however, that a different person must now be in state of equipoise.

There is a prior decision over how to allocate resources fairly among the current population. In the absence of empirical data on this subject, the indecision over how best to do this is, by definition, a state of equipoise. Randomisation, as a method of rationing, is thus based on indecision or agnosticism over who out of a given set of people should get the resources. The decision maker now is the health care trust which must act (and be seen to act) in the best interests of the population that it oversees. The indecision is not just a matter of indifference, as it is not yet known if an intervention is cost-effective. It is possible to be certain (or as much as one can be) that there is no difference with suitable data. Uncertainty over whether there is a difference provides the scientific rationale for collecting data on top of randomising simply to allocate resources. A piece of research would be a useful exercise only if there were still sufficient scientific uncertainty surrounding its effects on the population in which it is intended for routine use. Data collection under the pretext of research when the

intervention has already been shown to be effective may be more difficult to square with the revised Declaration of Helsinki, but this is a debate in its own right. Toroyan *et al* discuss the example of day care education for preschoolers and, although there is considerable evidence of cost-effectiveness from studies done in the USA, they still establish a scientific rationale for the trial by alluding to the following points. Firstly, they are interested in different, untested primary and secondary outcome measures; and secondly, there remains uncertainty as to whether the USA data could be applied directly in the UK without further study. The idea behind a trial is to establish that certain resources should be made more widely available. This is done on the basis of more research data showing that it is relatively more cost-effective than other interventions.

3. Consent to data collection

Toroyan *et al* state that for trials in such circumstances to be ethically acceptable individual patients who are eligible should be invited to participate actively in research and contribute their data.¹ Having recognised, however, that this form of research is now observational and not experimental in the strict sense, it is now debatable whether consent would always be needed. It is legally unclear how to interpret the Data Protection Act 1998 and researchers generally are not sure whether they should always ask for consent to use routine data, even if the data are made anonymous.¹⁰ In the past, research using routine data has not usually required the specific consent of individuals to whom the data relate. And the new MRC guidelines state that consent is required *wherever possible*, even if the data are to be made anonymous. The law in Iceland has taken this one step further and presumes patient consent for detailed routine data collection for all medical records, although there is an opt-out policy. However, a recent legal case in the UK questioned the practice.^{11 12} While this issue goes beyond the scope of this paper, the requirements on research in the circumstances described above should at least be consistent with requirements on observational research generally, whatever they are. In the UK, dissenting patients should still have the option of withholding their data wherever possible. Where patients are approached directly and personally, perhaps for follow up, and the data collection exceeds that which is considered routine, then specific consent from patients is usually appropriate. Ethics committee review is also seen as a necessary protective safeguard for observational research, as with all research, that involves patients, whether directly and personally or not. On top of these safeguards, the Council for International Organisations of Medical Sciences (CIOMS) guidelines urge investigators to take all possible steps to inform the affected community of the aims of the research and of the advantages and disadvantages expected from it.¹³

We should bear in mind that, by following the MRC guidelines, the results may become biased by always including only those who consent to data collection, although mathematical modelling may help in this respect. And where consent to data collection is sought, the chance to access the intervention should not be contingent on giving consent, since the threat of taking away the chance of receiving limited resources (that individuals would have got routinely by random allocation in spite of the trial) would be a form of coercion. This is in line with the revised Declaration of Helsinki, which states that patients offered entry into research should not feel bound to consent for fear of reprisal or getting inferior care if they refuse. The best routine care in this setting may be the randomly allocated intervention itself.

CONCLUSION

In this paper, we have examined the need for valid evidence of the effectiveness of available, yet limited, resources from randomised controlled trials despite the perceived problem of

limited funding. As a solution, randomisation could be used to distribute limited resources anyway and data could be collected for research purposes, given this opportunity. There are three important ethical considerations. First, the decision to ration should be independent of the decision to do research. Secondly, the person vested with the power to make rationing decisions must now be in a state of equipoise between who out of two or more individuals should get the limited resource. Thirdly, all those who are eligible for the intervention could be invited to participate in research actively and could consent to data collection simply for research without threat to the standard of care they would otherwise have got. The requirement for consent may exceed that for observational research generally, although the current situation on this is unclear.

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