

## Summary points

Antiretroviral therapy is becoming more affordable for developing countries

Infrastructure is also essential to deliver the complex and sensitive drug regimen

DOTS has been suggested as a method for delivering antiretroviral therapy, although it has limited success for tuberculosis in much of Africa

Suboptimal adherence to antiretroviral therapy is likely to result in the transmission of drug resistant virus strains within the community

Other methods for ensuring adherence need to be developed and evaluated

Competing interests: None declared.

prescribing practices and poor monitoring of therapy and adherence.

A rational approach is required in which systematic delivery and proved methods for maximising adherence are as important as procuring the drugs themselves. This should be led by a respected international organisation that has the objectives of overcoming short term suffering as well as preventing a similar disaster in the long run, by insisting that antiretroviral policies incorporate a phase of piloting systems that seek to maximise adherence.

Contributors and sources: WS has worked with the World Bank in predicting the effect of HIV in West Africa, and with the Department for International Development and the London School of Hygiene and Tropical Medicine on the economics of tuberculosis control programmes. SK has worked on monitoring HIV drug resistance in trials of antiretroviral therapy conducted in the United Kingdom and Europe. TC has been in charge of the clinical services provided by the MRC unit in the Gambia since 1986 and has specialised in the care and treatment of patients infected with HIV and tuberculosis.

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## Evaluating the health effects of social interventions

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Is no evidence better than any evidence when controlled studies are unethical?

Rigorous evidence on the health effects of social interventions is scarce<sup>1 2</sup> despite calls for more evidence from randomised studies.<sup>3</sup> One reason for the lack of such experimental research on social interventions may be the perception among researchers, policymakers, and others that randomised designs belong to the biomedical world and that their application to social interventions is both unethical and simplistic.<sup>4</sup> Applying experimental designs to social interventions may be problematic but is not always impossible and is a desirable alternative to uncontrolled experimentation.<sup>3</sup> However, even when randomised designs have

been used to evaluate social interventions, opportunities to incorporate health measures have often been missed.<sup>5</sup> For example, income supplementation is thought to be a key part of reducing health inequalities,<sup>6</sup> but rigorous evidence to support this is lacking because most randomised controlled trials of income supplementation have not included health measures.<sup>5</sup> Current moves to increase uptake of benefits offer new opportunities to establish the effects of income supplements on health. In attempting to design such a study, however, we found that randomised or other controlled trials were

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BMJ 2004;328:282-5

**Box 1 Attendance allowance**

- Attendance allowance is payable to people aged 65 or older who need frequent help or supervision and whose need has existed for at least six months
- The rate payable depends on whether they need help at home or only when going out and whether they need help during the day or the evening, or both

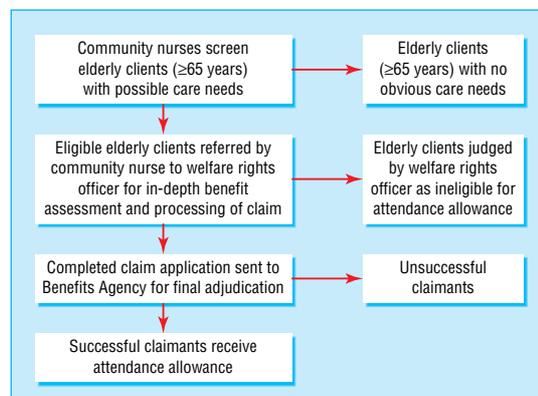
difficult to justify ethically, and our eventual design was rejected by funders.

**Aims of study**

A pilot study carried out by one of us (RH) showed substantial health gains among elderly people after receipt of attendance allowance. We therefore decided to pursue a full scale study of the health effects of income supplementation. The research team comprised a multidisciplinary group of academics and a representative from the Benefits Agency (TQ). Our aim was to construct a robust experimental or quasi-experimental design (in which a control group is included but not randomly allocated) that would be sensitive enough to measure the health and social effects of an attendance allowance award on frail, elderly recipients.

**The intervention**

The intervention involved a primary care based programme that aimed to increase uptake of benefits. In 2001, community nurses, attached to a general practice serving the unhealthiest parliamentary constituency in the United Kingdom,<sup>7</sup> screened their frail elderly clients for unclaimed attendance allowance (box 1). Potential underclaimants were then visited by a welfare rights officer, who carried out a benefit assessment, and the claim was then forwarded to the Benefits Agency (part of the Department of Social Security) for the final adjudication of applications (figure). This resulted in 41 clients receiving additional benefit totalling £112 892 (£160 307; \$200 302), with monthly incomes increasing by £163-£243.<sup>8</sup>



Process of screening to promote uptake of attendance allowance. The groups represented by the boxes on the right would be unsuitable as controls because they would be systematically different from benefit recipients in terms of care needs and health status



Health effects of social intervention can be hard to study

**Outcomes**

We chose change in health status measured by the SF-36 questionnaire as the main outcome variable. Explanatory variables, which recipients had linked to increased income in pilot interviews, were also incorporated. These included diet, stress levels, levels of social participation, and access to services. We intended to assess health status before receipt of the benefit and at six and 12 months afterwards. An economic evaluation was also planned.

**Study design**

We initially considered a randomised controlled trial. However, we encountered problems with the key elements of this design. The study designs considered and the issues raised are outlined below.

**Design 1: randomisation of the intervention**

Under a randomised controlled design successful claimants would be randomised immediately after the adjudication decision by the benefits agency. Those in the control group would have their benefit delayed by one year, and those in the intervention group would receive the benefit immediately. This design would ensure that the health status and benefit eligibility of both groups were comparable at baseline. However, the research group considered this design unethical because of the deliberate withholding of an economic benefit, which would also be unacceptable to participants. This design was therefore abandoned.

**Design 2: randomising to waiting list**

The introduction of a three month waiting list between initial assessment by a nurse and assessment by the welfare rights officer provided an opportunity for random allocation to the control and intervention group. We obtained approval to randomise the clients to a waiting list of a maximum of three months from the Benefits Agency, which provides the welfare rights officer. Thus, elderly clients referred by the nurse to the welfare rights officer could have been randomised to receive the visit either immediately (the intervention group) or after three months (the control group).

This design would have allowed us to compare the groups at the desired time points and provided a directly comparable control group in terms of health

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status and benefit eligibility. However, it randomises the benefit assessment and not the intervention of interest (receipt of the benefit), and a delay of three months would probably not be long enough to detect important health differences between the two groups. More importantly, it is unlikely to be ethically acceptable to request that study participants, already assessed to be in need of an economic benefit, accept a 50% chance of delaying the application process for three months in the interests of research. We therefore rejected this design.

### Design 3: non-randomised controlled trial

A third potential design entailed identifying a non-randomised control group from a nearby area with a similar sociodemographic composition but with no welfare rights officers. In this design, community nurses would have screened potential underclaimants in the control area, who would then have been offered a standard leaflet on how to apply for attendance allowance (a nominal intervention corresponding to "usual care"). This design would have eliminated some of the ethical concerns associated with randomisation and delaying the receipt of benefit, and would have achieved an intermediate level of internal validity by retaining a comparison with a control group. However, recruitment and retention of this control group raises problems.

The success of this design depends on participants in the control group delaying their claim for the duration of the study. Although the effectiveness of the "usual care" intervention, the leaflet, is normally poor, we considered it unlikely that this would be the case after assessment for the study as participants are made aware of their potential eligibility for the benefit. We thought it unacceptable to request that participants delay claiming the additional benefit after drawing attention to their eligibility.

### Design 4: uncontrolled study

A before and after study of a group of benefit recipients would be more ethically acceptable, but it would be more difficult to attribute any observed change in health status to the intervention alone. We applied for research funding for a study based on this design, citing the practical and ethical difficulties in designing a randomised controlled trial, but the application was rejected mainly because of the lack of a control group. We presume that the underlying assumption was that such an uncontrolled study would be so biased as to provide no useful information.

## Discussion

Our initial aim was to design a randomised or controlled study to detect the health effects of income supplementation. Our failure to design such a study and to get funding for a less rigorous study poses the question of what sort of evidence is acceptable in such situations. Social interventions differ from clinical and most complex public health interventions in that changes in health are often an indirect effect rather than a primary aim of the intervention. Investigation of indirect health effects often requires choices to be made between competing values, usually health and social justice, creating a moral problem. When, as in our study, the tangible social and economic gains generated by the social interven-

## Summary points

The health effects of social interventions have rarely been assessed and are poorly understood

Studies are required to identify the possible positive or negative health impacts and the mechanisms for these health impacts

The assessment of indirect health effects of social interventions draws attention to competing values of health and social justice

Randomisation of a social intervention may be possible using natural delays, but adding delays for the sole purpose of health research is often unethical

When randomised or other controlled studies are not ethically possible, uncontrolled studies may have to be regarded as good enough

tions outweigh the theoretical possibility of marginal health effects, the moral issues are clear.

### Randomisation

Although judgments about equipoise have recently been challenged,<sup>9</sup> equipoise around the primary clinical outcome has been the ethical justification for randomising clinical interventions.<sup>10 11</sup> Equipoise implies uncertainty around the distribution of costs and benefits between two interventions. Designing a randomised study may be simple in theory, but in cases where the equipoise is around uncertain indirect health impacts, and the primary economic or social impacts seem certain, true equipoise is unlikely and randomisation may be unethical.

Randomising a control group need not always present ethical hurdles. There may be inherent delays in rolling out a new or reformed programme across an area, or an intervention may require rationing or be subject to long waiting lists. These delays may provide ethical and pragmatic opportunities for randomisation<sup>12</sup>; indeed, randomisation may be the fairest means of rationing an intervention.<sup>13</sup> However, delaying access to a tangible benefit for individuals who are assessed as "in need" may not be justifiable on research grounds.

### Generating evidence for healthy public policy

An urgent need remains for studies of the indirect health effects of social interventions to improve our understanding of the mechanisms by which health effects can be achieved.<sup>14</sup> Attention has already been drawn to the need for careful design of evaluations of complex public health interventions,<sup>15-17</sup> but guidance for evaluating the indirect health impacts of social interventions may require further consideration in light of the issues outlined above. For example, when the direct effects are obvious, randomised controlled trials may be unnecessary and inappropriate.<sup>18</sup> In health technology assessment, other study designs have an important role in development<sup>15 19</sup> and in helping to detect secondary effects.<sup>18</sup> For example, new drugs with established pharmacological mechanisms

are investigated at increasing levels of internal and external validity before being tested in a population level randomised controlled trial. Phase I and II studies are often small and uncontrolled, but they help to establish positive and negative effects, clarify the dose-response relations, and provide the background for larger trials.<sup>15-19</sup> In addition, once approved, drugs are closely monitored at a population level to detect previously unidentified secondary adverse effects that may outweigh the primary positive effects.<sup>18</sup> Our pilot study was similar to a phase II study.

This matching of study designs to the level of development and knowledge of the effects of an intervention could be usefully applied to the study of social interventions. Non-randomised and uncontrolled studies could be used to shed light on the nature and possible size of health effects in practice, to illustrate mechanisms, and to establish plausible outcomes.<sup>18</sup> Such studies may serve as a precursor to experimental studies when these are ethically justifiable and appropriate. However, when randomised studies are not possible, we may have to accept data from uncontrolled studies as good enough, given the huge gaps in our knowledge.<sup>14</sup> We need to reconsider what sort of evidence is required, how this should be assembled and for what purpose, and the trade offs between bias and utility so that study designs that are acceptable to research participants, users, and funders can be agreed.

We thank Sally Macintyre and Graham Hart for comments on a previous draft of this article.

Contributors and sources: The initial idea for this study was developed by RH. All authors regularly attended and contributed to meetings of the study team, development of the research proposal, and writing the paper. HT, MP, and DO work on a research programme that evaluates the health impacts of social interventions. RH, GL, and TQ worked on initial pilot work investigating Attendance Allowance uptake and its health impacts. NC is a lecturer in health economics and has an active

research interest in designing economic evaluations of social welfare interventions.

Funding: HT and MP are employed by the Medical Research Council and funded by the Chief Scientist Office at the Scottish Executive Health Department. DO is funded by the Chief Scientist Office at the Scottish Executive Health Department.

Competing interests: None declared.

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(Accepted 25 November 2003)

## Two memorable patients

### Two nil

It is a dull wet Saturday afternoon in Goodison Park. The fans are filing in, and there is a tense excited atmosphere around the ground. It is nearing the end of the season, and everyone is hoping the seemingly inevitable relegation battle can be avoided this year. The Goodison faithful are buzzing with the prospect of taking three points from fellow strugglers. Behind the scenes, the usual band of St John Ambulance volunteers have gathered—doctors, nurses, firemen, policemen, dockers, students, and others from all walks of life.

As the match enters the last five minutes, the only thought echoing around the ground is how to put the ball into the goal. Until, that is, a simple radio message is received: "Code Blue, cardiac arrest in the Lower Bullens stand."

Our team jumps into action. We arrive to find an unresponsive, cyanotic, elderly man stretched out across four seats. Cardiopulmonary resuscitation is already being performed by a dockworker; he's an experienced first aider. Other members of our team and the club doctor arrive with oxygen and an automatic defibrillator. The casualty is in ventricular fibrillation, and the first three shocks are given immediately, but with no effect. We intubate and cannulate him, as slick as any hospital arrest team. A fourth shock is given, and we get a result—the rhythm change that everyone is looking for. A spontaneous circulation is returned.

Just as we all relax, lightning strikes twice: "Code Blue, cardiac arrest in the Gwladys Street stand." Half our team go tearing off to the second incident, with the match now in injury time. A second unresponsive man is found in cardiac arrest, but not for long. We are joined by an ambulance service team and soon once more have a spontaneous output.

The crowd are now filing out, blissfully unaware as two paramedic vehicles arrive. The first man has spat out his endotracheal tube and is conscious, asking what the score is. Two live casualties are taken to hospital. Our team of volunteers returns to the first aid point buzzing, but football and relegation are no longer important. The only score on everyone's mind now is St John 2—Undertakers 0.

Working in a state of the art hospital surrounded by machines that go beep and staff who have trained in their professions for many years can sometimes make us forget the basics. It is humbling to remember that the two lives saved that day weren't due to fancy new techniques or expensive modern technology. They were saved by a group of volunteers, the likes of whom may be found at every major sporting event and public gathering across the country.

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