

influence subject consent at the point of entry to the trial, thereby distorting recruitment and potentially compromising the interpretation of results.

Emily Finch, Michael Gossop, Louise Hankinson, Co/in Taylor, Michael Farrell, John Strang

National Addiction Centre, 4 Windsor Walk, London SE5 8AF, UK

- 1 **Zelen M. Randomised consent designs for clinical trials: an update.** *Stats Med* 1990; 9: 645-56.
- 2 **Gossop M, Johns A, Green L. Opiate withdrawal: inpatient versus outpatient programmes and preferred versus random assignment to treatment.** *BMJ* 1986; 293: 103-04.

SIR—Silverman discusses alternative trial designs and the design and conduct of trials recently discussed at a workshop at the Cochrane Centre in Oxford that explored the expression of patients' preferences in trials. A common factor in all the presentations at this workshop was that the expression of patients' preferences was confined to an examination of choices within the system as it now operates, or modified as, for example, in Brewin and Bradley's method,¹ in which the profession have devised the protocols.

Widder's² notion that: "before even monitoring a study, the patients must be asked and helped to find out for themselves why they want to be treated and what their own aims are ... If, and only if, a patient's aim about treatment is identical with the aim implied by the study, can consent to participation be regarded as reasonable choice" was not brought forward as new and different. The obvious but difficult solution is that patients should be allowed to state their preference for aims at the planning of the protocol. As Widder states "this topic becomes even more important when life-prolonging and life-quality enhancing intentions merge as treatment intentions".

Surely Silverman's concluding suggestion that "we should explore study designs that take into account patients' preferences" is the way forward? We may then see trials that are more acceptable to patients, thus improving accrual and hastening our determination of interventions that are "efficient and effective".³ Cochrane would surely have applauded this support of his principles.

Hazel Thornton

Saionara, 31 Regent Street, Rowhedge, Colchester CO5 7EA, UK

- 1 **Brewin CR, Bradley C. Patient preferences and randomised clinical trials.** *BMJ* 1989; 299: 3 13-1 5.
- 2 **Widder J. Randomising means, not aims in clinical trials.** *Lancet* 1994; 343: 359.
- 3 **Cochrane AL. Effectiveness and efficiency: random reflections on health services.** London: Nuffield Provincial Hospitals Trust, 1972.

Sterilisation by quinacrine

SIR—In your April 23 editorial you unjustly accused WHO of failing to expose clearly its criticism of the clinical use of quinacrine for tubal sterilisation. In our response (June 4, p 1425) we mentioned that WHO would undertake formal review of the use of quinacrine. This review was undertaken in July at a consultation in which 22 experts took part from Australia, Chile, China, the Dominican Republic, Hungary, India, New Zealand, Turkey, Uganda, UK, USA, and Vietnam. The group noted that there had been several technological advances since the last WHO review in 1983 and felt it timely to identify promising approaches for use in developed countries, and to set priorities for research. The participants' conclusions and recommendations were as follows.

A safe, effective, non-surgical method of sterilisation is needed and should be developed. There are two constraints to early success in this development: the chemicals available are limited, as are the methods whereby they may be delivered reliably and consistently to the fallopian tubes. Standardised testing of all compounds with known or potential use as tubal occlusive agents should precede clinical studies, which should be conducted in a stepwise fashion. Methylcyanoacrylate (MCA) for transcervical sterilisation has passed all toxicology testing, and phase I and phase II clinical studies have been completed. A balloon-pump device for the instillation of MCA has been developed but concern remains about the consistent delivery of the material to one or both tubes. After the development of a stable solution of elemental iodine, appropriate animal studies should be undertaken to determine the efficacy of this substance in producing tubal closure.

Although an estimated 70 000 women in several developing countries have been treated with one or more instillations of quinacrine pellets, the protocols used for these studies, the method of instillation, and the dose of quinacrine used have varied among centres. The toxicology testing of locally applied quinacrine completed more than a decade ago is inadequate. Further use of quinacrine requires that the necessary toxicology testing, including the full range of genotoxicity studies, be completed and, if needed, long-term animal carcinogenicity testing. Other animal tests, including tests for teratogenicity, should be done if these initial results are satisfactory. If initial toxicology tests are satisfactory, phase I and phase II clinical studies of intrauterine quinacrine following properly designed and peer-reviewed protocols should be initiated. Irrespective of the results of toxicology testing, retrospective studies of women already treated with quinacrine should be continued and completed. Quinacrine studies might lead to the identification of other chemicals with similar action. Other research should establish a standard method of use and investigate the role of pre-treatment with progestogens or other drugs, the effects of age and parity on efficacy, and the effect of quinacrine treatment on ascending genital infections. Consensus is needed on whether the high level of efficacy already established for surgical methods should be required of non-surgical methods or whether less efficacy would be acceptable.

The outcome of this consultation substantiates our statement that WHO's position is that further clinical research is not justified until various toxicological issues have been resolved. The high standards of safety demanded in the testing and use of contraceptives should apply whether the subjects recruited to the studies are from the developed or developing world.

Giuseppe Benagiano

Special Programme of Research, Development and Research Training in Human Reproduction, World Health Organization, Geneva 1211, Switzerland

Health-care reform in the USA

SIR—I was surprised to read in Greenberg's June 25 Washington Perspective that "as originally envisaged by the Clintons, the big insurers were to have a limited role, and perhaps even no role, in the health-care revolution planned by the new administration". In fact, the centrepiece of the Clinton proposal—so-called managed competition—was designed by the Jackson Hole Group, an informal association of health-care industry executives that included representatives of the nation's largest insurance companies, and it is much to their liking (see, for example, Hillary Clinton's potent brain-trust on health reform, *New York*