endometrial cancer were detected many months after tamoxifen was stopped, but whether this reflects a persistent risk is unknown.

As in women with a uterus taking oestrogen replacement therapy, a balance with progestins may eliminate or protect against overstimulation by tamoxifen.[14,15] No data are available on this: polyps have been described in women taking combined treatment,[16] and tamoxifen remains in some ways a mystery drug with effects on the uterus never seen with oestrogen replacement therapy. The effect of progestins on serum lipoproteins and hence on cardiovascular disease and on the breast are of concern. Certainly some clinicians will argue that not every woman taking tamoxifen should be given a progestin.

Postmenopausal women taking tamoxifen who have not had a hysterectomy should be informed about potential endometrial hazards. Abnormal vaginal bleeding needs prompt endometrial assessment. Many questions remain about endometrial surveillance in healthy women taking the drug. Screening is feasible, and several approaches need evaluation. The benefits of screening and of other approaches to prevention have yet to be defined. Many of the questions may be answered if screening and preventive measures are included in trials of tamoxifen for the prevention of breast cancer.

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# Finding a way through the cost and benefit maze

## *Standardised instruments are needed*

See p1343

Two months ago the NHS Executive sent its letter "Improving the effectiveness of the NHS" to all district general managers, chief executives of trusts, and family health services authorities (for distribution to general practice fundholders).[1,2] Earlier letters had drawn their attention to the NHS research and development programme and existing evidence on clinical effectiveness[3] and asked them to purchase less during 1995-6 of two or more procedures known to be ineffective and more of at least two effective ones.[4] The most recent letter outlines the close links between this process and the new NHS research and development strategy. In its turn, the requirement to identify effective procedures should focus an intense spotlight on available research findings and have profound implications for future NHS research, especially since effectiveness covers "costs, outcomes, and acceptability to patients and society."[5]

It is salutary to examine the degree to which current research findings can provide this information for interventions used after myocardial infarctions. Coronary heart disease is the most common cause of death in Britain, consuming an estimated 2·5% of NHS resources and costing nearly £10 billion a year in lost production and hospital care. A comprehensive review of recent advances in cardiology shows the difficulties decision makers (in both purchaser and provider organisations) will encounter when interpreting research findings in this discipline (p 1343).[6]

Interventions after myocardial infarction are likely to interest decision makers because the number of options has increased greatly in recent years, especially with the development of thrombolytic treatment, and this technological explosion is set to continue. When streptokinase and tissue plasminogen activator are taken as examples of thrombolytic agents already evaluated, the literature shows that far greater effort has been expended in large clinical trials than in identifying which outcomes (other than death) should be measured and how different outcomes might be valued to measure overall benefit.[6] In the case of tissue plasminogen activator, for example, increases in adverse effects, such as stroke, have to be balanced against fewer deaths. Although these might be treated in an additive manner—for example, reduction in deaths minus increase in stroke[5]—quality of life should ideally also enter the equation. To date, extremely few trials have incorporated measures of the quality of life, perhaps because they cannot be obtained retrospectively from medical records.[7]

As defined above, effectiveness includes costs as well as outcomes.[5] This is particularly important in the case of streptokinase and tissue plasminogen activator, where costs differ substantially and measurable differences in benefit are small.[6] However, the literature contains few studies of cost effectiveness, and those that have been reported show little consistency in methods, costs mea-

sured, discounting of future costs and benefits, or how costs are related to outcomes.[8]

The simplest studies are those calculating cost per life saved. Two such studies have used modelling techniques applied retrospectively to trial results and produced different answers, at least partly because different perspectives on costs were used. One estimated the direct cost per life saved for a moderate infarct as $171 000 (1987 prices) for intravenous streptokinase and $158 000 for intravenous tissue plasminogen activator.[9] A similar study, but limited to Medicare costs, calculated a direct cost per life saved of $52 700 for streptokinase and $56 900 for tissue plasminogen activator.[10] Survival data can also be used for calculating cost per added life year. This has recently been reported for intravenous tissue plasminogen activator as a discounted cost per added life year of $29 000, which was based on the results at 30 days of follow up in the trial of global utilisation of streptokinase and tissue plasminogen activator for occluded coronary arteries (GUSTO).[11]

None of these reported studies, however, incorporate quality of life measures; such studies remain rare and vary in the instruments used to measure quality of life. Retrospective studies of intracoronary streptokinase have estimated a direct cost of $3300 (1993 prices) for each additional quality adjusted life year based on survival at one year[12]; a subsequent study using slightly different methods estimated a discounted value of $4000 (1993 prices) based on the results at three years of follow up in the same randomised clinical trial.[13] Finally, studies that measure costs and quality of life prospectively in parallel with clinical trials are extremely rare. One such study of tissue plasminogen activator estimated a cost per quality adjusted life year saved of $1000 (1993 prices) including indirect costs.[8]

The different methods used make existing research findings difficult to interpret and apply. Standardisation of instruments to measure both clinical and economic factors is obviously a critically important next step in the evolution of useful research based information. The fact that this is difficult should not be viewed as an adequate reason for failing to take this step. On the contrary, it indicates that more research effort is needed so that interventions after myocardial infarction can be systematically evaluated, something which the NHS Standing Group on Health Technology has identified as a top priority for the NHS.[5]

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# Need for rigorous assessment of palliative care

## *Although difficult, randomised controlled trials are mandatory*

See p 1340

By a strange coincidence, political and professional agendas simultaneously require evidence of effectiveness. This makes good sense with finite resources. Stop ineffective interventions, and the money saved can be spent on those that are effective. The problem is that, although effectiveness is a useful word to describe what is wanted, it is difficult to define. Its meaning varies according to context.

In medicine we can at least use the gold standard of the randomised controlled trial to show that a new medical intervention is better than no intervention or than an existing intervention.[1] Long established interventions are often time honoured rather than proved by randomised controlled trials, although lack of evidence of effectiveness is not the same as evidence of lack of effectiveness. Will medical decisions not supported by randomised controlled trials continue to be purchased, and, if so, for how long? Are we wrong to continue to support these decisions? Who will investigate their effectiveness? And should one randomised controlled trial showing lack of effect outweigh the testimony of experience?[2] If this is hard going for single interventions how much harder is it for a service in which multiple interventions are provided?

For such services we assume that randomised controlled trials are again the gold standard to establish effectiveness, even if the interventions that make up the service are not proved by such trials. The provision of "hospital at home" services is a good example. There are no randomised controlled trials of hospital at home. Despite this the four counties of the former Oxford Regional Health Authority will spend £1·6m on hospital at home in 1994-5. The design and conduct of a randomised controlled trial funded jointly by Northamptonshire Health Authority and Anglia and Oxford Regional Health Authority initially presented formidable problems (S Shepherd, personal communication).

This week's journal reports the failure of an attempt to evaluate a palliative care service with a randomised controlled trial (p 1340).[5] The trial was done to "strengthen the case for continued funding." It failed because of difficulties in recruitment and problems inherent in the design. The wider issues raised by the authors are important. First is the idea that doing a randomised controlled trial in palliative care is so difficult that palliative care, and by analogy any other specialty in which it is difficult, should be "excused" from doing randomised controlled trials. The second is that the rarity of successful ran-