cancer and for those who took it for more than 10 years the relative risk was virtually neutral (relative risk 1.03).² Furthermore, it seems that, even if the incidence of breast cancer is increased in current long term users, the risk of death is decreased.³

Those of us who advocate hormone replacement therapy would agree with McPherson's sentiments that on balance the current evidence continues to suggest that such therapy will probably give rise to a net gain in years of life. The American nurses' study recruited 121 700 female registered nurses aged 30 to 55 in 1976; it will be several years yet before such studies can provide us with conclusive answers.

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- 1 McPherson K. Breast cancer and hormonal supplements in postmenopausal women. *BMJ* 1995;311:699-700. (16 September.)
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Likely mode of death may be a consideration

EDITOR,—Klim McPherson uses net loss of or gain in years of life as a criterion in discussing the balance between the risks and benefits of hormonal supplements in postmenopausal women.¹ Another criterion, however, is the mode of death. A patient might choose to risk an earlier, but "easy," death from coronary heart disease rather than a later, but possibly lingering and traumatic, death from breast cancer.

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Increase in risk of breast cancer is small

EDITOR,—I am confused over how Klim McPherson reaches some of his conclusions, particularly the conclusion that long term use of hormonal supplements in postmenopausal women may be responsible for an average net loss of years of life.¹ Far more studies have been done that show benefits of hormone replacement therapy on coronary heart disease and osteoporosis than that show benefits on breast cancer. The figures for coronary heart disease, of a 50% reduction in overall mortality,² and the preventability of osteoporosis and fractures are reasonably believable.³ The studies of breast cancer show variable results, some with a small increase in incidence from long term use. If we accept the figures quoted—that for a 50 year old postmenopausal woman the lifetime risk of coronary heart disease is 45%, of fracture of the hip is 15%, and of cancer of the breast is 8%—then with the reduction in the incidence of coronary heart disease and fractures there would need to be a huge increase in breast cancer of the order of 400-500% to produce a negative net loss of years of life.

Henderson *et al* carried out a prospective study in 8881 postmenopausal residents of a retirement community who had used oestrogen for a mean of 10 years.⁴ They found that subjects with a history of use of oestrogen had a 20% reduction in all cause mortality adjusted for age compared with non-users, and current users had a 40% reduction. This included a 20% reduction in the incidence of

carcinoma, including carcinoma of the breast, although a rise in endometrial carcinoma was noted with oestrogen only treatment.

The prevention of endometrial carcinoma by the addition of a progestogen is well recognised, but the overall effects of progestogen are less well defined. Long term use (for 22 years) of combined oestrogen and progestogen was not associated with an increase in the risk of breast cancer in a study by Nachtigall *et al*.⁵

Long term use of combined oral contraceptives has been intensively studied by the Royal College of General Practitioners, among others, and only a small increase in the risk of breast cancer has been suggested. While this is in a younger age group, many of the women who started taking combined oestrogen and progestogen long term in the early 1960s must be well over 50 by now; as far as I am aware, no appreciable increase in breast cancer in this age group has been reported.

The lack of evidence for anything other than a potentially small increase in the risk of breast cancer associated with long term (15 years) use of hormone replacement therapy is far outweighed by the large benefits and reduction in overall mortality associated with hormone replacement therapy.

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- 1 McPherson K. Breast cancer and hormonal supplements in postmenopausal women. *BMJ* 1995;311:699-700. (16 September.)
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Article increased uncertainty

EDITOR,—Klim McPherson's editorial on breast cancer and hormonal supplements in postmenopausal women is important both for patients taking hormone replacement therapy and for general practitioners prescribing it.¹ But what are we supposed to do now? McPherson presents the statistics as irrefutable facts. Are they? Should we ask our patients whether they want to die of breast cancer or ischaemic heart disease? What is the actual decrease in the risk of ischaemic heart disease in women taking hormone replacement therapy? Should a family history of breast cancer become a contraindication to hormone replacement therapy? Do we now have to get consent forms signed before patients start taking hormone replacement therapy?

Perhaps McPherson should have written a review article rather than an editorial, so that he could proffer the full implications and necessary advice to practising doctors. As a profession we should be grateful that the media had other things to concentrate on at the time.

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- 1 McPherson K. Breast cancer and hormonal supplements in postmenopausal women. *BMJ* 1995;311:699-700. (16 September.)

Author's reply

EDITOR,—In general I agree with David A Viniker. The finding of an apparent deficit in the case fatality from breast cancer among women who take supplements when there is evidence of an increased incidence is to be expected early in a study because of likely selection and surveillance biases.¹ Proving a real effect is therefore difficult.

Jules Alterman points out that patients might prefer an easy death from coronary heart disease rather than a traumatic death from breast cancer. Probably for this reason, breast cancer is more feared than coronary heart disease despite its being a less common cause of death after age 55, and this is important.

With regard to C J Mugglestone's comments, if supplements affect the risk of breast cancer for a prolonged period after they are stopped and the attributable effects on coronary heart disease are less than observational studies (which might suffer from important selection bias) seem to show, then a net loss of years of life could result. Mortality from breast cancer is currently higher than that from coronary heart disease until around age 55. A 50% reduction in coronary heart disease is almost certainly largely a consequence of some selection bias.² The problem with breast cancer, as I tried to point out, is that the effects of a recent common exposure (combined hormonal supplements, for example) might be systematically underestimated until sufficient patients have been followed up long term.³ Exposure to stilboestrol during pregnancy affects the risks of breast cancer, but not at all until 20 years after exposure.⁴ Mugglestone's calculations do not take into account the differing age specific mortality patterns. What was observed during long term follow up in the United States among selected users of unopposed supplements may not be true for combined supplements, possibly taken more generally. There is, of course, a considerable increase in the incidence of breast cancer among women aged over 50,⁵ but this is due neither to oral contraceptives nor to hormone replacement therapy. And Mugglestone's confidence in only a small increase in risk with 15 years of use of hormone replacement therapy is not supported by recent data.

Finally, in answer to D J Plews's comments, I hope that I did not present the statistics as irrefutable facts; I said that "reliable information . . . is still lacking."

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Thrombolytic treatment

Pulse spray infusion works faster but is more expensive

EDITOR,—We were surprised by Marc Verstraete's comment that "thrombolytic drugs are now usually given locally with a pulse spray technique" in less than two hours.¹ The British Thrombolysis Study Group has collected information prospectively from several hospitals in Britain on the use,