Table 1—*Data available from trial comparing short term (five years') treatment with adjuvant tamoxifen with longer term treatment (eight years and seven months) for breast cancer. Figures are numbers of women except where otherwise stated*

	Short term treatment	Long term treatment
Survival (%)	96	94 (P = 0.11)
Event free survival (%)	92	86 (P = 0.016)
Recurrence	10	23
Death	13	23
Cancer in contralateral breast	5	6
Second primaries	16	24

unpublished data. Table 1 gives the data, which are available under the American Freedom of Information Act.

Baum and Cuzick believe that the statistical analysis is highly unreliable and that the National Surgical Adjuvant Breast and Bowel Project, the National Cancer Institute and its independent data safety monitoring committee, and the Food and Drug Administration met "to influence policy on the European side of the Atlantic." A more charitable view might be that they issued their clinical announcement for the benefit of patients.

There will be consternation among the Californian panel on carcinogenesis and a second group of experts who met recently at the International Agency against Cancer in Lyons. Their conclusion, that tamoxifen is a carcinogen,[3 4] is dismissed as "absurd" by Baum and Cuzick. Newbold *et al* have recently shown that tamoxifen induces proliferative changes in the oviduct and uterus of mice treated with tamoxifen (100%) and at 12 months of age there is an increased incidence of endometrial cancer.[5] They might be well advised to withdraw their abstract before Baum and Cuzick take them to task.

Sasco and Gendre point out that drugs other than tamoxifen are also carcinogenic.[6] This does not stop such compounds being used, but they must be used with care rather than handed out like sweets, and the recipients should be informed of the risks involved.

Helena Earl and colleagues' letter about the aTTom trial states that there is "an ethical and scientific imperative to determine the optimum duration of treatment."[1] The design of their trial, however, does not seem to address the problem that some volunteers will not benefit from treatment and that the prognosis in others is so favourable that they also are not appropriate candidates for adjuvant treatment. Nor will the trial determine the costs of the treatment in terms of side effects, which Baum and Cuzick believe to be "anecdotal," since the end point is the number of dead in each arm.

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1 Adjuvant treatment with tamoxifen [letters]. *BMJ* 1996;**312**:1036-7. (20 April.)
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Informed consent and follow up in aTTom trial are inadequate

EDITOR,—The fact that women will be given adjuvant tamoxifen for more than five years despite the National Cancer Institute's warning that longer term treatment may do more harm than good is not the only reason why doctors and the public should reject the controversial aTTom (adjuvant tamoxifen treatment—offer more?) trial in breast cancer and its international counterpart, ATLAS (adjuvant tamoxifen—longer against shorter).[1 2]

The megatrial was designed to "impose no extra workload on collaborators, other than randomizing and treating their patients, so that even the busiest clinicians can participate. There are no forms at all to complete, and no regular follow-up information is required—survival information will be obtained from national registries." There will be "no extra investigations, no extra clinic visits, infrequent follow-up, and no requirements for detailed documentation of initial status, toxicity, treatment compliance, health economic aspects, quality of life, and so on."[3] Although patients are randomised "to at least 5 years of tamoxifen while some may be rerandomized after 5 years to lifetime tamoxifen,"[4] the designers believe that it is not necessary to ensure that the 20 000 women are closely and uniformly monitored for gynaecological conditions associated with tamoxifen, including endometrial cancer. Nor will clinicians be required to monitor the women routinely and report other second tumours, liver toxicity, thromboembolism, ocular toxicity, depression, or bone loss in premenopausal women—conditions associated with longer term tamoxifen in clinical trials.

The process of gaining informed consent for the aTTom and ATLAS trials also leaves much to be desired, as is evident from a flyer issued by Wandsworth Health Authority's local research ethics committee in 1995:

Tamoxifen does cause some minor side effects in a few women, which either lessen if the treatment is continued or cease when the treatment is stopped. There is some evidence that there may be a small risk of an increase in diseases of the liver and womb if tamoxifen is taken for many years. Nobody knows for sure....

It is unclear if the invitation's wording is the product of a single research ethics committee's interpretation of the world literature or stems from a model developed by the national trialists, who have argued that "the recent trends towards extensive informed consent, careful quality of life assessment and measurements of economic costs of treatments in trials are often seriously inappropriate."[5] The *BMJ* is to be commended for publishing an editorial questioning the ethics of such extended trials of tamoxifen.[1]

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Specialist surgeons and survival in breast cancer

Observational studies are essential

EDITOR,—Several letters[1] have criticised the methods used and the conclusions drawn in Charles R Gillis and David J Hole's study, which showed substantial improvements in survival from breast cancer among women referred to specialist surgeons.[2] The study used observational data from the West of Scotland Cancer Registry. It is argued that such data can never be appropriately controlled for differences in case mix and that only data from randomised controlled trials can be used to provide reliable evidence. We believe that this objection is invalid and negates the underlying importance of observational studies in health services research, which Nick Black has highlighted.[3]

We do not deny the obligatory role of randomised controlled trials in evaluations of alternative treatments. Specialist care, for which specialist surgeons were a marker in the Scottish study, is not simply about improved surgical technique or the optimum deployment of adjuvant treatment but includes treatment by a multidisciplinary team with access to all oncological and nursing facilities. This overall context can rarely, if ever, be evaluated by randomised controlled trials.

The evidence review prepared for the National Clinical Outcomes Subgroup on Breast Cancer Guidance (chaired by one of us (RAH)) identified 27 observational studies relating case volume and process to outcome, of which nine dealt with breast cancer. Five further studies dealt with the effect of specialisation on survival or mortality of patients with breast cancer. While a few studies were relatively small (under 1000 patients), four had over 5000 patients, of which two had over 10 000 patients. Controlling for case mix and patients' characteristics is a major problem, although in our analysis of survival in breast cancer among 13 000 women in Yorkshire, adjustment using crude but consistent indicators of prognosis had no impact on the results.[4] This may be because potential biases that may operate with smaller numbers are minimised when large numbers are studied in a population context.

Population based research that uses data from sources such as cancer registries can quantitatively assess the experience of an entire community and compare it with that of another community. Such communities may live in different areas and be served by different hospitals or may live in the same area but follow different referral pathways from their general practitioners. Observed differences require explanation and in some cases may be artefactual. The observations need to be made, however, as a necessary component of rigorous evaluative research. This is not just a plea from academic research workers but also an increasing demand from patient and community groups.

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Treating a specified number of patients is no guarantee of quality

EDITOR,—The NHS Executive has recently written to trust executives about the development of