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## Contra:

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ALTHOUGH THERE may be an adjuvant benefit for patients with colorectal cancer who are given 5-fluorouracil, breast cancer is the only solid tumour in which adjuvant therapy has been confirmed as effective. The second meta-analysis of the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) has led to a change of attitude towards adjuvant therapy in older women [1]. The overview shows clearly that the magnitude of the effect of tamoxifen is equally large in postmenopausal women of all age groups and indeed that there may be a slightly larger mortality reduction in women aged over 70 years, as summarised in Table 1.

Additionally, the meta-analysis shows that there is a significant but smaller effect of chemotherapy in women aged 50-69 years. It is not possible to give an accurate estimate of the effect in those over 70 years of age because of the small

numbers in this age group randomised within controlled trials. The likelihood of benefit for all subgroups with breast cancer has meant that the more hawkish medical oncologists have argued that older women should be given adjuvant chemotherapy, particularly those with oestrogen receptor-negative cancers.

To address this problem, Desch and associates created a Markov model to assess the survival benefit and cost-effectiveness of adjuvant chemotherapy in older women with node-negative breast cancer [2]. Recurrence rates were based upon the EBCTCG meta-analysis, together with likelihood of recurrence in node-negative cases using data from the NSABP B13 study [3]. Chemotherapy was assumed to comprise cyclophosphamide, methotrexate and 5-fluorouracil (CMF). Other assumptions were that chemotherapy would

Table 1. Meta-analysis of the reduction in odds of relapse and death in postmenopausal women treated with adjuvant tamoxifen and polychemotherapy, EBCTCG 1992 [1]

Age (years)	Tamoxifen		Polychemotherapy	
	Relapse	Death	Relapse	Death
50–59	28%	19%	29%	13%
60–69	29%	17%	20%	10%
70+	28%	21%	?	?

affect only the risk of first relapse and that the patients did not have severe comorbidity. After carrying out a baseline analysis this was then adjusted for active life expectancy, as shown in Table 2.

In the baseline analysis, there is some small gain (2 months) of life expectancy in those over 70 years of age. However, this was achieved at great cost per quality of life year (QALY). This gain was almost obliterated after adjustment for life expectancy and this led to a significant amplification of cost/QALY. When compared with other procedures with known cost/QALY, this was equal to that of liver transplantation and 12 times the cost/QALY of adjuvant tamoxifen or coronary artery bypass.

This would argue strongly against use of adjuvant chemotherapy for breast cancer in this age group. Furthermore, since chemotherapy has even less adjuvant activity in other solid tumours, it is difficult to assign any role in the elderly.

To demonstrate a cost-effective role for adjuvant chemotherapy in the elderly would be a Herculean task. Suitable can-

Table 2. Benefit and cost-effectiveness of adjuvant chemotherapy in elderly women. Desch and associates [2]

Age (years)	Baseline analysis		Adjusted for life expectancy	
	Months gained	Cost/QALY	Months gained	Cost/QALY
60	2.8	\$28 200	?	?
65	2.8	\$31 300	1.3	\$59 300
70	2.2	\$36 300	1.0	\$75 000
75	1.8	\$44 400	0.7	\$96 000
80	1.4	\$57 100	0.4	\$212 500

didates would have oestrogen receptor-negative cancers, with nodal involvement and be prepared to be randomised to either chemotherapy or tamoxifen. Quality of life instruments would be required to assess endpoints other than relapse and death. Perhaps a determined clinical researcher with equally determined patients will be able to complete such a study. Until this has happened it is going to be very difficult to justify the routine use of any adjuvant chemotherapy other than tamoxifen.

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## Arbiter:

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AS THE article by Professor Fentiman indicates, chemotherapy cannot be considered a standard treatment for elderly women ( $\geq 70$  years of age) with breast cancer because the number of patients who have entered clinical trials of chemotherapy is too small (less than 300) to draw any definitive conclusions, and, as pointed out by Dr Balducci and Dr Extermann, there is a trend in a reduction of efficacy of chemotherapy with increasing age [1]. However, in considering this controversial topic, it is clear that the available data on which opinions are based come from studies of postmenopausal women under the age of 70 years because no trial has yet been performed specifically in older women. Why is there no trial of this kind in the literature?

There are many reasons for this. Firstly, a number of variables could affect the design and analysis of such trials, e.g. schedule of combined chemotherapy and tamoxifen (concomitant or sequential), drug interactions in the case of concomitant administration, and oestrogen receptor (ER) expression [2]. Overall, the net benefit that one can expect from the addition of chemotherapy to tamoxifen may be very little. This is because of the trend both towards reduction in efficacy of chemotherapy with increasing age of patients and to increasing efficacy of tamoxifen with increasing numbers of ER-positive tumours, which should account for approximately 81% of cases among patients older than 65 years [3]. Toxicity—the biological and human cost of adjuvant chemotherapy—that always plays an important role in the cost/benefit balance, may be more frequent and more severe among elderly patients than among younger patients. Furthermore,