

and vascular invasion is adequately assessed only in resected specimens. For that reason any woman having conservation surgery should be warned that if histological examination of the resected specimen shows adverse factors she will need a mastectomy later.

While I accept that there may be no definite evidence at present associating better local control with improved survival, I think that most of us feel uneasy when we see local recurrence in a conserved breast and wonder whether we have jeopardised that patient's chances of long term survival.

Finally, and until we have a cast iron method of detecting occult axillary lymph node metastasis before surgery, a level II or III axillary dissection must be performed in all patients having conservation surgery for invasive carcinoma.

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Use of aspirin in secondary prevention of coronary heart disease is rising

EDITOR,—We can confirm Ray King and Jonathan Denne's findings of an increased use of low dose aspirin in secondary prevention of cardiovascular disease¹ and have a suggestion for why there may be a difference in the prevalence of such treatment between the sexes and how this might be overcome.

Throughout 1994 and 1995 the Burn Brae Medical Group, a practice of six partners with 8200 patients in a market town, carried out three audits of the subject. A computer search followed by analysis of both computer and written notes identified 531 patients with cardiovascular disease (myocardial infarction 111, angina 304, transient ischaemic attack or cerebrovascular accident 92, and peripheral vascular disease 91; many patients had more than one vascular disease). Initially 255 patients were taking aspirin (men 148/280 (53%), women 107/251 (43%)). At the end of the second audit, after telephone contact or postal questionnaire and invitation to a specific consultation with their general practitioner, the number receiving low dose aspirin had increased to 342, with a significant difference between the sexes (197 (70%) men, 145 (58%) women; $P < 0.01$). In July 1995 we therefore carried out a third audit of 100 patients from the original cohort. All were aged under 75 (50 men; 50 patients taking aspirin). The response to a telephone or postal questionnaire (85% response rate) showed no difference between the sexes in the advice offered by general practitioners, and heeded by patients, about stopping smoking, taking exercise, reducing dietary fat, and taking low dose aspirin. As would be expected, those not taking aspirin were less likely to have been given this advice (26/41 (66%) v 42/44 (95%) for both sexes). Women were more likely to complain that aspirin upset their stomach (7/43 (16%) v 3/42 (7%)).

One of the most interesting findings was that, while the vast majority of patients (75) confirmed that television, radio, newspapers, and magazines were other sources of information about the benefits of stopping smoking, taking exercise, and reducing cholesterol, a considerable number (24) specifically commented that they had not seen similar information about low dose aspirin.

We suggest that, although low dose aspirin is being increasingly prescribed, general practitioners should give specific advice to take aspirin to all high risk patients. Possibly women are less tolerant of low dose aspirin than men. Finally, national health educational bodies should target the media to increase society's knowledge of the benefits of low dose aspirin in the secondary prevention of cardiovascular disease.

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Misoprostol in patients taking non-steroidal anti-inflammatory drugs

Analysis excluded important events

EDITOR,—N Maiden and R Madhok's editorial¹ highlights the rough halving of the incidence of serious gastrointestinal complications associated with non-steroidal anti-inflammatory drugs that was achieved with coadministration of misoprostol in a recent trial in almost 9000 patients.² The authors point out the relevance of these results to clinical practice by adopting the valuable "numbers needed to treat" approach advocated by Cook and Sackett.³ They do not, however, take into account that the study's statistical power was based on the overall rate of serious upper gastrointestinal events, incorrectly asserting that bleeding was no less common in patients taking misoprostol. They therefore focus inappropriately on, and apply the number needed to treat values solely to, one subgroup of events (perforation and gastric outlet obstruction). Consequently, the risk-benefit implications of the overall results are not explored fully. This exclusion of events regarded as serious by predefined criteria gives a misleading perspective.

The serious events comprising the primary end point (perforation, gastric outlet obstruction, and bleeding) showed a 68% higher incidence in the group unprotected by misoprostol; this was attributable to 17 additional cases, of which eight were associated with bleeding. Number needed to treat analysis, if it is to help determine the overall benefit to the community in both medical and cost terms, must at least take account of all the events on which the primary end point was based.

On an annualised basis the number who would have to be treated with misoprostol to prevent one such serious event was 132. Within this figure there was substantial variation among high risk groups (table 1). These data suggest that age groups other than just those over 75 receive significant benefit from coadministration of misoprostol, and the data are comparable to those

Table 1—Number of patients who would need to be treated for one serious event to be prevented

Patients	No to be treated to prevent one serious event		
	All ages	Age ≥ 65	Age ≥ 75
All	132	110	150
With previous cardiovascular disease	102	71	72
With previous peptic ulcer disease	26	20	11
With previous gastrointestinal bleeding	20	16	7

for other prophylactic treatments, such as anti-hypertensive drugs, that are routinely used to prevent complications of comparable severity.⁴ Furthermore, an annualised rate of 1.5% for serious iatrogenic gastrointestinal complications² suggests that these complications are arguably relatively common, rather than "relatively rare" as the editorial suggests. Complications induced by non-steroidal anti-inflammatory drugs are, for example, 50-100 times more common than thromboembolism in women taking oral contraceptives and carry a fivefold greater risk of death, with an annual mortality of the same order as that from carcinoma of the cervix or asthma. The 40-50% reduction in serious complications provided by misoprostol needs to be considered in this context.

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This reduction in risk is deemed worth while in other circumstances

EDITOR,—In their editorial N Maiden and R Madhok discuss the prophylactic use of misoprostol in patients over 65 who are taking non-steroidal anti-inflammatory drugs.¹ They conclude that 493 patients would need to be treated to prevent one gastrointestinal complication (defined as perforation or gastric outlet obstruction). Despite acknowledging the potential deaths arising from such events they do not recommend universal prescription of misoprostol, stating as a major reason the relatively large number who would have to be treated, along with the side effects and cost.

This reduction in risk could, however, be compared favourably with other, better established, aspects of prevention in medicine. For example, the Medical Research Council's trial of treatment of mild hypertension in 1985 concluded that one stroke could be prevented for every 850 patient years of treatment with antihypertensive drugs.² Yet few people would deny the potential side effects or cost involved in this commonplace primary care intervention. Another, more topical example concerns dilemma faced by those women deciding whether to continue to take a third generation oral contraceptive. In fact, over 330 000 women would have to change their pill from one containing gestodene or desogestrel to an older combined pill to prevent one death from venous thromboembolism a year.³ Nevertheless, this small scale of risk does not seem to have prevented the prompt issue of specific warnings from the Committee on the Safety of Medicines to the public⁴ or from the Family Planning Association to the profession.³

The decision to intervene therapeutically in any given situation obviously depends on a variety of medical and social factors. Being consistent with regard to the true risks and benefits is evidently still a long way down on our list of priorities.

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