plasma volume expansion and an increase in plasma angiotensin II and aldosterone concentrations might be hazardous in patients with heart disorders or a tendency to hypertension. The findings of this study suggest an important mechanism of the cardiac complications associated with oestrogen treatment and reaffirm the need carefully to evaluate cardiac and haemodynamic state in patients with prostatic cancer before deciding on the form of treatment.

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Value of routine follow up of women treated for early carcinoma of the breast

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Abstract

The value of routine follow up of women treated for early breast cancer by mastectomy with or without postoperative radiotherapy was assessed retrospectively. Over eight years 546 patients made 6863 clinic visits, during which 192 first relapses were detected. Ninety three relapses were detected at scheduled (routine) visits and 99 at unscheduled (interval) visits. First relapses within the treated area or in the contralateral breast were detected significantly more commonly at routine visits than were first metastatic relapses (66/89 (74%) compared with 27/103 (26%)). Patients whose local relapse was detected at a routine visit had a significantly better survival than those whose local relapse was detected at an interval visit. A relapse that was potentially curable (local or in the contralateral breast) was detected at 66 (1%) of 6764 routine visits, but only 26 (39%) of these patients remained free of disease.

It is concluded that the intensity of follow up of such patients could be reduced without any adverse effect on prognosis but with appreciable financial and other benefits.

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Introduction

Routine follow up of patients after definitive treatment for malignant disease forms a major part of the workload of most radiotherapy and many surgical clinics. Follow up may be for a variety of reasons, including assessing the efficacy of treatment and its morbidity, helping patients to come to terms with their illness, teaching, and, especially for less common conditions, gaining an understanding of the clinical course of the disease. The main purpose of follow up, however, is to detect relapse at a stage at which effective secondary management can be begun, and it is this that generally determines the frequency of attendance. Though some patients undoubtedly find follow up reassuring, many others find it a considerable source of stress. Regular attendance is costly not only for the patient, who may have to pay for transport or take time off work, but also in terms of the use of National Health Service resources.

The value of routine follow up has been questioned,[1-3] but few studies have examined the effectiveness of follow up in detecting relapse and what influence, if any, this has on a patient's subsequent clinical course.[4,5] Breast cancer is the most common malignancy in women, and this study examined the value of routine follow up of women after primary treatment for early breast cancer by mastectomy alone or by mastectomy and postoperative radiotherapy.

Patients and methods

During 1974-7 inclusive 717 women were referred to this department with a diagnosis of carcinoma of the breast, which was clinically staged as

international stage I (TNM classification (1978) of the International Union Against Cancer $T_{1A\,2A}$ N_0 M_0). The case records of these patients were reviewed, and 171 patients were excluded from this study because they were being followed up elsewhere and no details concerning their follow up were available (98 patients); the frequency of their follow up attendances was determined by the administration of adjuvant chemotherapy or a coexisting malignancy (31); they did not receive the standard treatment of mastectomy with or without postoperative radiotherapy (30); or they had been treated previously for carcinoma of the contralateral breast (12).

The 546 patients in the study had a mean age at presentation of 53·6 (SE 12·4). Two hundred and five patients (38%) were premenopausal, 238 (44%) were postmenopausal, and 87 (16%) were perimenopausal (within five years of their menopause); in 16 (3%) the menopausal state had not been recorded.

TABLE I—*Number of first relapses recorded according to site of tumour and type of visit at which relapse was detected during each year of follow up*

	Year of follow up							
	1	2	3	4	5	6	7	8
Metastatic:								
Routine visit	6	8	3	4	4	1	0	1
Interval visit	11	20	14	10	8	5	4	4
Contralateral breast:								
Routine visit	0	2	2	3	1	1	0	1
Interval visit	0	0	0	0	2	2	0	0
Local:								
Routine visit	18	15	10	5	6	1	1	0
Interval visit	3	7	2	1	3	3	0	0

TABLE II—*Proportion of patients relapsing according to site of tumour during each year of follow up. (Values are numbers of first relapses expressed as percentage of patient years at risk)*

	Years of follow up							
	1	2	3	4	5	6	7	8
No of patient years at risk	524	462	388	330	282	222	156	91
Metastatic	3·24	6·06	4·38	4·24	4·26	2·70	2·56	5·49
Contralateral breast		0·43	0·52	0·91	1·06	1·35		1·10
Local	4·01	4·76	3·09	1·82	3·19	1·80	0·64	

Survival rates were calculated with the actuarial method, excluding deaths from intercurrent disease. Thus patients free of breast disease at death were eliminated from the study at death.

Results

Overall, 6863 clinic visits were made by the 546 patients over a period not exceeding eight years (median 56 months). Ninety nine (1·4%) of these visits were interval, at each of which a relapse was detected. Figure 1 shows the pattern of relapse in the 192 patients (35%) who relapsed during regular follow up. Patients were analysed according to the site of their first relapse,

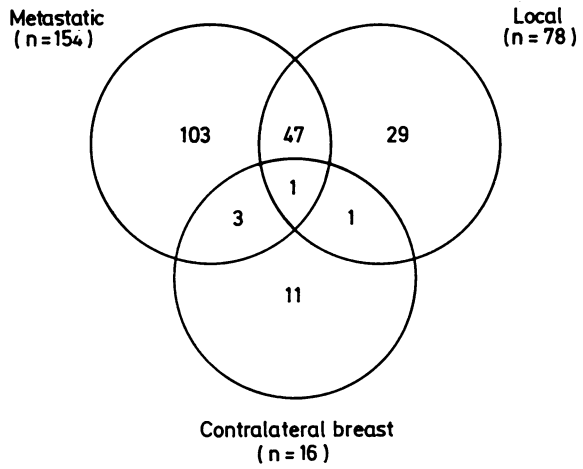

FIG 1—Pattern of relapse in 192 patients who relapsed during regular follow up.

which was local in 75 patients (14%), in the contralateral breast in 14 (3%), and metastatic in 103 (19%). The 75 patients whose first relapse was local included 15 with a synchronous metastatic relapse.

Table I shows the number of first relapses and site for each year of follow up and whether the relapse was detected at a routine or an interval visit. First local relapses and relapses in the contralateral breast were detected significantly more often at routine visits (66/89) than first metastatic relapses (27/103) ($p<0·001$). This remained significant even when synchronous local and metastatic relapses were excluded.

TABLE III—*Number (%) of routine visits at which first relapse was detected for each site of tumour for each year of follow up*

	Year of follow up							
	1	2	3	4	5	6	7	8
No of routine visits	2013	1632	1107	776	539	350	217	130
Site of relapse:								
Metastatic	6 (0·30)	8 (0·49)	3 (0·27)	4 (0·52)	4 (0·74)	1 (0·29)		1 (0·77)
Contralateral breast		2 (0·12)	2 (0·18)	3 (0·39)	1 (0·19)	1 (0·29)		1 (0·77)
Local	18 (0·89)	15 (0·92)	10 (0·90)	5 (0·64)	6 (1·11)	1 (0·29)	1 (0·46)	

Tumour size had been recorded in all but 19 cases, and the distribution by tumour classification was T_{1A} for 212 patients (39%) and T_{2A} for 315 patients (58%). One hundred and thirty four patients (25%) were managed by mastectomy alone; the remaining 412 patients also received postoperative radiotherapy. Axillary nodes were not sampled in most patients (328) but were found to be invaded by tumour in 66 (12%) and to be free of tumour in 152 (28%).

Follow up data abstracted from the case records comprised the number of clinic visits each year of follow up until first relapse, death, regular follow up was stopped, or 31 December 1982, whichever was the earliest. For those patients who relapsed the site of relapse was recorded as local (ipsilateral anterior chest wall or nodes in the ipsilateral axilla or supraclavicular fossa), in the contralateral breast, or metastatic. As routine follow up examinations were principally directed towards detecting local relapses or relapses in the contralateral breast patients relapsing with metastatic disease at the same time as local disease were classified as having local relapse. Also recorded were whether the relapse was detected at a scheduled (routine) or interval follow up visit, the time since the previous routine visit, the presence or absence of symptoms, who had referred the patient back to the clinic (for interval visits only), and the patient's subsequent clinical course.

The number of relapses detected routinely in any given year of follow up depends on the proportion of patients relapsing and the frequency of visits. Table II summarises the proportions of patients relapsing: the number of first relapses by site is shown as a percentage of the patient years at risk for each year of follow up. Table III shows the proportion of routine visits at which a relapse was detected for each year of follow up. Table IV shows the presence or absence of symptoms in relation to the site of first relapse and the kind of visit at which it was detected. This information was not available for 37 (19%) of the patients, but among the remainder relapses detected at interval visits were always symptomatic, and 23/44 (52%) of the local relapses and relapses in the contralateral breast detected at routine visits were in asymptomatic patients. Only one metastatic relapse was asymptomatic.

Referral back to the clinic for an interval visit was most often made by the patient's general practitioner (64/99), sometimes by a consultant in another specialty (28), and occasionally by the patient herself (seven).

Actuarial survival for all patients was 94·4% at two years and 80·9% at five years.

TABLE IV—*Presence of symptoms in patients at first relapse according to site of tumour and type of visit at which it was detected*

Type of visit at relapse	Symptoms		
	Present	Absent	Not known
	Local relapse		
Routine	17	20	19
Interval	16		3
Total	33	20	22
	Relapse in contralateral breast		
Routine	4	3	3
Interval	3		1
Total	7	3	4
	Metastatic relapse		
Routine	24	1	2
Interval	67		9
Total	91	1	11

For local relapses the median time since the previous visit was three months, being less when relapse was detected at an interval visit (two months) than at a routine visit (three months). The median time since the previous visit for relapses in the contralateral breast was five months for both interval and routine visits. The median time since the previous visit for patients with first metastatic relapse was two months (three months for routine visits and two months for interval visits).

Fifty four patients with local relapses (72%) received treatment for their recurrence, 10 by radiotherapy, 20 by hormonal manipulation (most commonly tamoxifen or oophorectomy), eight by surgery alone, and 16 by combination treatment (including cytotoxic chemotherapy in four cases).

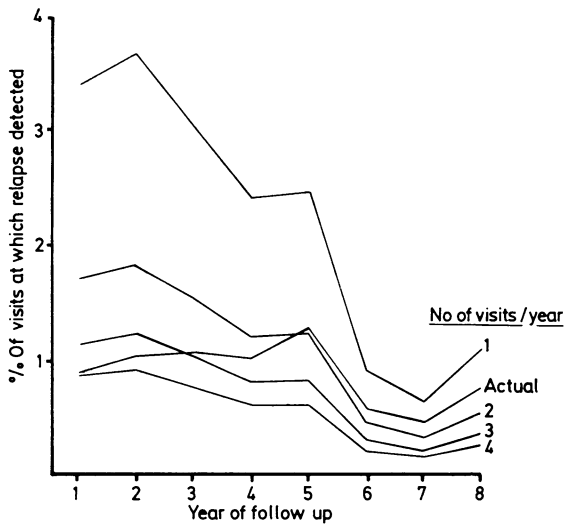

FIG 2—Observed percentage of routine visits at which first relapse was detected compared with estimated percentage for different numbers of visits a year.

Local disease remained controlled in 21 patients at their last follow up visit, and one patient died of intercurrent illness while free of local disease. Six patients remained alive with uncontrolled local disease or died of an intercurrent illness with local disease still present. The remaining 47 patients developed metastases, of whom 38 died. Actuarial survival after local relapse was 64·4% at two years and 43·2% at five years.

Ten of the 14 patients with a first relapse in the contralateral breast responded successfully to treatment. The four other patients died of metastatic disease. The two year actuarial survival rate after relapse in the contralateral breast was 84·6%.

For 103 patients the first relapse was metastatic only, and 81 of these patients died. A total of 154 patients relapsed with metastatic disease, and of these, 44% survived one year after the development of metastases and 25% survived two years.

Patients whose local relapse was detected at a routine visit had a significantly better survival than those whose local relapse was detected at an interval visit ($p<0·05$, log rank test), with two year survival rates of 72·7% and 39·0%, respectively. A significantly higher proportion of patients whose local relapse was detected at an interval visit had synchronous metastases (9/19, compared with 6/56 with local relapses detected at a routine visit) ($\chi^2=9·7$, $p<0·01$). There was no significant difference, however, in the overall proportion of patients developing metastases (15/19 whose relapses were detected at interval visits and 32/56 whose relapses were detected at routine visits). A significantly higher proportion of patients whose local relapse was detected at a routine visit had treatment for their local disease (46/56, compared with 10/19 whose relapse was detected at an interval visit; $\chi^2=5·1$, $p<0·05$), but among those who responded successfully to secondary management no significant advantage was associated with detection at a routine visit.

Among patients whose relapse was detected at a routine visit a higher proportion of those with relapse in the contralateral breast than with local relapse were treated successfully (7/10 compared with 19/50), although this difference just failed to reach significance. Patients with relapses in the contralateral breast had little advantage in terms of survival after relapse so that the numerical advantage may have been related to time to first relapse, which was longer for relapses in the contralateral breast than for local relapses.

In summary, a relapse (local or in the contralateral breast) that was potentially curable was detected at 66 (1%) of the 6764 routine visits. Of these 66 patients, however, only 26 (39%) were free of disease at their most recent review (19 after local relapse and seven after relapse in the contralateral breast). Thus, at best, a relapse that was successfully treated was detected at only 0·4% of routine visits—that is, 260 routine patient visits were made for every patient successfully retreated.

Discussion

Routine follow up of all patients is recommended after definitive treatment for breast cancer,[6] and specific programmes of follow up have been devised.[7-8] As the main purpose of follow up is to detect relapse at a stage at which it can be successfully treated it is, in effect, a screening programme of a population at high risk of relapse. There is no effective curative treatment for patients with metastatic disease so failure of routine follow up to detect metastases (only 26% of first metastatic relapses were detected routinely) is not relevant to an assessment of the effectiveness of routine follow up as a screening programme.

A relapse (local or in the contralateral breast) that was potentially curable was detected at 1% of routine visits, but only 39% of these patients were still free of breast disease at their most recent review. Even this is probably an overestimate as, in this series, the proportion of patients developing metastases after local relapse (64%) was lower than the 83-88% found in other series with a longer follow up.[9-11]

Overall, relapse in the contralateral breast occurred in 0·6% of patients a year, although if the first year is disregarded (as the patients all had stage I disease and bilateral cancers had been excluded) this rate would be 0·8% a year, which is comparable with results of other series.[12,13] Relapses in the contralateral breast are, however, important as, although they are less common than local relapses, a higher proportion may be successfully treated.

If the patients had been seen less often for follow up how might this have affected the outcome? Figure 2 shows the actual percentage of routine visits at which local relapses and relapses in the contralateral breast were detected compared with the estimated percentage of visits at which the same number of relapses would have been detected at different annual frequencies of attendance. If the frequency of visits is reduced then the percentage of visits at which relapse is detected rises, although by less than the proportion shown as some relapses would probably be detected earlier at interval visits. The benefit would be a considerable reduction in the clinic's workload, but the cost would be the risk of some relapses remaining unobserved for longer. In this series almost half of the local relapses and relapses in the contralateral breast detected routinely were symptomatic, and better counselling of patients and training in self examination, especially for tumours of the contralateral breast, might increase the number of patients who refer themselves back to the clinic.

The actual frequency of follow up in this study was roughly four times a year for the first two years, three times a year for the next two years, twice in the fifth year, and once a year thereafter. If, for example, all these patients had been seen three times a year for two

years, twice a year for the next three years, and once a year thereafter then there would have been 1335 fewer routine visits, a reduction of 20%. The cost would have been a mean delay in detecting relapse of less than one month in those 26 patients whose relapse was detected at a routine visit and who were subsequently successfully retreated but over one month for all patients whose relapse was detected at a routine visit. If the patients had been seen twice a year for two years and once a year thereafter there would have been a 49% reduction in the number of visits, but the cost would have been a mean delay in detecting relapse of over four months for the subgroup of 26 patients and almost five months for all patients whose relapse was detected at a routine visit.

If the patients had been seen more often would the outcome have been any different? We doubt it. The median time since the previous visit for local relapses detected at interval visits was shorter than that for local relapses detected at routine visits, so that a considerable increase in the frequency of visits would be needed to detect these earlier. Patients whose local relapse was detected at an interval visit had a particularly poor prognosis, which is consistent with their tumours being fast growing and suggests that the relapses developed after the previous routine visit rather than that they had been missed at their previous visit. A similar finding was observed in screening normal populations for breast cancer.[14]

This study confirms results from other series that despite intensive follow up few patients are successfully retreated.[4,5] We conclude, therefore, that for patients with early breast cancer treated by mastectomy, with or without postoperative radiotherapy, routine follow up might be less frequent. Patients should, however, be encouraged to return to the clinic early if they detect any change within either the treated area or the contralateral breast. Careful examination of the contralateral breast is particularly important as a tumour there may respond more successfully to treatment than would a local relapse.

We are grateful to colleagues past and present for allowing us access to the case records of their patients.

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Sugar, fat, and the risk of colorectal cancer

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Abstract

The habitual diet of 50 patients with large bowel cancer, as assessed by a dietary history method, was compared with that of 50 closely matched controls. Patients were included only if their symptoms were unlikely to have changed previous eating habits. The mean daily intakes of all major nutrient classes and of dietary fibre were estimated. Patients with large bowel cancer consumed 16% more energy than controls (mean (SEM) daily intake 9·92 (0·41) *v* 8·56 (0·32) MJ (2370 (98) *v* 2046 (76) kcal), respectively; $p<0·0001$), mainly in the form of carbohydrate (21% more; 282·6 (13·7) *v* 233·4 (10·5) g; $p<0·0001$) and fat (14% more; 100·8 (4·3) *v* 88·4 (3·2) g; $p<0·001$). The extra carbohydrate was largely in the form of sugars depleted in fibre and the extra fat as combinations of fat and such sugars.

As the selection criteria used make it unlikely that this eating pattern was caused by the disease the data suggest that a high intake of sugars depleted in fibre and fat predisposes to the development of large bowel cancer.

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Introduction

The incidence of large bowel cancer varies greatly among countries and correlates with the average consumption of several dietary variables such as meat, fat, sugar, and energy.[1-3] Correlations with dietary fibre have not been calculated, largely because there is scanty data on the intake of fibre among different communities.

Another method of identifying possible aetiological factors is a case-control study in which patients with a disease are compared with a healthy control population for exposure to postulated environmental agents. There have been about 12 such studies of patients with colorectal cancer,[4-15] and the results are inconsistent. For example, some have implicated meat and dairy products as risk factors[7 9 15] whereas others have not[11 12 14] and, similarly, evidence of a protective effect of vegetables has been noticed in some studies[8 12 14 15] but not in others.[5 11] Some of these inconsistencies may have arisen because the disease itself had modified eating habits and dietary recall.[16] Common symptoms of this cancer include loss of appetite, vomiting, and pain after meals, all of which can reduce the intake of food in patients with cancer. In published case-control studies no attempt has been made to eliminate these variables. A further problem with many studies is that the control subjects have been loosely matched.

We therefore undertook a case-control study that differed from these earlier ones in four respects: (*a*) in recruiting patients we excluded any with symptoms or pre-existing disorders that were likely to modify their eating habits; (*b*) the control population was closely matched; (*c*) the dietary data obtained were analysed in terms of nutrient composition rather than as individual foodstuffs;