Pergamon

European Journal of Cancer, Vol. 34, No. 12, pp. 1889–1893, 1998

Printed in Great Britain
0959-8049/98/$—see front matter

PII: S0959-8049(98)00232-9

Original Paper

Stage-specific Treatment Costs for Cervical Cancer in the United Kingdom

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In order to examine the relationship between stage at initial diagnosis and management costs for cervical cancer, a detailed cost audit over 5 years was conducted on a sample of patients diagnosed in 1990 in one U.K. region. The mean costs of managing pre-invasive carcinoma (£386) were found to be significantly lower than those of stage 1 invasive carcinoma (£6623) and both were lower than the costs of invasive cancer at stages 2–4 (£10 910, £10 579 and £11 035, respectively). A comparison of management costs for cervical cancer with those of breast cancer by stage revealed both that the former are invariably higher and that the cost-by-stage profiles for the two diseases are dissimilar. © **1998 Elsevier Science Ltd. All rights reserved.**

Key words: cancer, cervical cancer, cost, economic evaluation
Eur J Cancer, Vol. 34, No. 12, pp. 1889–1893, 1998

INTRODUCTION

As with both breast and colorectal cancer, a tumour staging classification has been established for cervical cancer [1] and 5-year survival rates appear to be closely associated with cancer stage at initial diagnosis and treatment. For cervical cancer in particular, expected 5-year survival rates following primary treatment range from virtually 100% for the pre-invasive cervical intra-epithelial neoplasia (CIN) phases, to around 80% for stage 1 invasive cancers, failing to below 10% for cancers at stage 4 [2]. As a consequence, an improvement in the staging distribution on detection can be expected to yield benefits in survival, and this is the logic behind the mass population screening programmes introduced into many industrialised countries following the development of the Papanicolaou smear test in the 1940s. In the U.K., the screening programme is believed to have relieved the burden of incidence of invasive cancers which might otherwise have occurred, especially amongst younger-to-middle-aged women [3].

Whilst the association between earlier stage at detection and improved survival prospects is now virtually beyond debate, the question as to how the stage at detection influences the cost of resources employed in patient management remains less clear-cut. This arises owing to, in part, a relative lack of research in the field and, in part, to the wide variety of diagnostic and treatment techniques which might be employed in patient management. In the U.K., for example, the preponderance of new cases of cervical cancer in any 1 year will have been detected by screening in general practice. All patients will be referred to hospital for a clinical examination, usually entailing colposcopy and biopsy, and a number of further investigations, such as computed tomography (CT) scanning, ultrasound and pyleography, may be required to assess the extent of tumour spread in any particular case. Thereafter, the staging of the disease at diagnosis is an important determinant of subsequent management. In confirmed pre-invasive cases, treatment usually entails full cone biopsy, laser ablation or cryosurgery, although a simple hysterectomy might be recommended. For carcinomas at the early invasive stages, surgery and/or radiotherapy represent the principal management modalities, whilst carcinomas at the later stages are generally treated by radiotherapy alone. Short remissions appear to be obtainable as a result of the use of chemotherapy. Naturally, all therapeutic procedures carry a risk of complications, necessitating additional treatment, as appropriate. Owing to the risks of recurrence, all cervical cancer patients will be followed up by means of clinical examination and regular smears, with such recurrences being treated by any or all of the above modalities, as each case demands. The risks of recurrence diminish over time from primary treatment and, by 5 years, the mortality

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Received 22 Jan. 1998; revised 5 May 1998; accepted 19 May 1998.

rates of cervical cancer patients parallel those of the general population [4].

In this study, we attempted to shed further light on the cost of management by estimating the stage-specific costs of cervical cancer diagnosis and treatment for a large sample of U.K. patients. Thereafter, we compared our results with those of an analogous study on the costs of breast cancer treatment, in order to determine whether the stage-specific management costs of the two cancers exhibit a common distributional pattern.

PATIENTS AND METHODS

Given that the epidemiology of cancer in the U.K. has long been documented by the regional Cancer Registries, it might be thought that a population-based resource use audit and costing exercise could be easily undertaken using precollected data. However, the Registry databases do not usually include details of either resource use or cancer stage at diagnosis. Our management cost analysis was accordingly based on a detailed examination of the case records of cervical cancer patients treated in the Trent region of central England, a region containing a population of some 4.8 million people.

According to the Trent Cancer Registry, 378 women in the region were diagnosed with invasive cervical cancer in 1990. We selected this particular year as the study baseline, on the grounds that it would permit us to construct a resource audit for each patient for up to 5 years, a period following diagnosis during which the majority of cancer recurrences and treatment complications would be likely to occur. An attempt to retrieve the full treatment record of all these cases revealed that 15 were untraceable, whilst 25 cases had been misclassified, either by diagnosis or by year. An examination of the remaining 338 patient records revealed that insufficient data were available to determine cancer stage in 77 cases, leaving 261 records amenable to analysis.

A full audit of resource-using healthcare events was compiled for each of these patients, for 5 years following initial diagnosis or until death, if occurring earlier. The unit costs of these events were obtained from a survey of 11 of the region's principal service providers, each of whom was sent a form requesting the cost of the various activities, as performed at their site. Since 1993, all National Health Service (NHS) providers have been required to follow a uniform accounting protocol, requiring that their services be costed at full cost, i.e. all service-specific variable costs, with the inclusion of the relevant components of fixed and overhead costs [5]. We employed the mean of the reported costs of each event in our estimates, converted back to 1990 prices using the NHS pay and price index. Given that management events were occurring across time, the costs of events occurring in years 2–5 following diagnosis were discounted at 6%. In other words, mean 5-year costs were expressed as a 1990 present value, to represent the prospective cost implications from the perspective of the baseline year.

Considerable diversity with respect to cost-events was evident on a patient-by-patient basis. For example, a total of 22 distinct diagnostic events were found to have occurred amongst the 261 cases, including cytology, colposcopy and various X-rays and scans. In some cases, many or all of the diagnostic events were undertaken on an in-patient basis, whilst in others, some or many of the tests were administered on an out-patient or day-case basis, with differential consequences for costs. Surgery was of two types, namely Wertheim's and conservative hysterectomy, whilst radiotherapy was palliative or radical, external beam, intracavity or a combination. Patient-specific radiotherapy costs varied with type (e.g. low energy, simple, complex), number of fractions and setting (e.g. in-patient or out-patient). After primary treatment, each patient received one or more of up to 18 forms of immediate procedure or further investigation, for example, investigation for fistulas, blood transfusion or emergency in-patient admission. Within the sample, seven different chemotherapy drugs were employed, in combinations, dosages and settings specific to each of the patients so treated.

As a consequence of the clear diversity of management routes, the cost audits of patient-specific events rapidly assumed great complexity. Space precludes a full description of the cost algorithms developed, although these are available from the authors on request.

For pre-invasive cancers, the regional Registry holds records only for CIN3 cases, although details of management are not included. In order to estimate management costs for pre-invasive cancers, we were, therefore, constrained to the analysis of activity at one particular site. We audited the case records of 141 patients diagnosed with CIN1–CIN3 at the Queen's Medical Centre, Nottingham, over the period June 1990 to June 1991. This time period was chosen to approximate to the baseline year of the invasive cancer sample. Understandably, the range of diagnostic, management and follow-up events for the pre-invasive cancers was comparatively narrow, being confined to smears, colposcopy and biopsies (11 distinct events in total), and no patient required an in-patient episode. In principle, these events were costed as for the invasive carcinomas.

RESULTS

Table 1 presents summary data of the characteristics of the invasive cancer sample, whilst Table 2 presents the mean discounted 5-year costs of invasive cervical cancer, by stage. Total historic (undiscounted) costs are also presented. The proportions of the total 5-year costs incurred in the first year following diagnosis were 83, 81, 88 and 98% for stages 1–4, respectively. With such high proportions, the impact of discounting on mean historic costs was small, as is evident from the results.

All differences between mean discounted costs were tested by one-way analysis of variance (Duncan's multiple range test at 5%). Within the sample, stage 1 costs for diagnosis ($P = 0.01$), radiotherapy ($P = 0.00$), chemotherapy ($P = 0.03$) and in-patient palliative care ($P = 0.00$) were significantly lower than those for stages 2–4. Grouping the two principal palliative cost categories (palliative radiotherapy and in-patient palliative care) together, stage 4 palliative costs were significantly higher ($P = 0.00$) than those for stages 2 and 3, and all three were higher than those for stage 1. Grouping the primary treatment cost categories (surgery, radical radiotherapy, investigations, hormone replacement and chemotherapy), stage 4 primary treatment costs were significantly lower than those of stages 2 and 3, whilst stage 1 costs were lower ($P = 0.00$) than those of stage 2. Overall, analysis of variance revealed that the mean 5-year total cost for stage 1 invasive cancer was significantly lower ($P = 0.00$) than that for stages 2–4.

A further analysis of cost by therapeutic regimen (surgery versus non-surgery) was conducted on the 126 stage 1 and 69 stage 2 patients where interventions were intended to be

Table 1. *Sample characteristics*

	Stage 1 ($n=128$) *n* (%)	Stage 2 ($n=76$) *n* (%)	Stage 3 ($n=42$) *n* (%)	Stage 4 ($n=15$) *n* (%)
Five-year survivors	61 (48)	25 (33)	5 (12)	3 (20)
Local recurrences	10 (8)	28 (37)	14 (33)	1 (7)
Mean ± S.D. time to recurrence (months)	21 ± 14	18 ± 14	9 ± 11	3
Metastases	4 (3)	12 (16)	5 (12)	5 (33)
Mean ± time to metastases (months)	31 ± 16	17 ± 18	12 ± 18	3 ± 4
Mean length of in-patient stay (days)	26	47	48	64

S.D., standard deviation.

Table 2. *Five-year costs of diagnosis, treatment and follow-up, by stage* (1990£)

	Stage 1		Stage 2		Stage 3		Stage 4	
	Mean ± S.D.	% of total	Mean ± S.D.	% of total	Mean ± S.D.	% of total	Mean ± S.D.	% of total
Diagnosis	1481 ± 1546	22.4	2401 ± 3479	22.0	2824 ± 1921	26.7	2621 ± 3991	22.7
Surgery	1159 ± 1177	17.5	795 ± 1594	7.3	98 ± 442	0.9	–	0.0
Radical radiotherapy	2295 ± 2704	34.7	3817 ± 2597	35.0	3595 ± 2849	34.0	946 ± 2509	8.2
Palliative radiotherapy	79 ± 540	1.2	203 ± 904	1.9	683 ± 1612	6.5	2727 ± 2951	23.6
Chemotherapy	75 ± 506	1.1	367 ± 1031	3.4	251 ± 726	2.4	–	0.0
Hormone replacement therapy	39 ± 71	0.6	37 ± 65	0.3	3 ± 16	0.0	–	0.0
Investigations	719 ± 2790	10.9	1457 ± 5129	13.4	1336 ± 3314	12.6	1208 ± 3811	10.5
In-patient palliative care	150 ± 733	2.3	1267 ± 3509	11.6	1443 ± 4457	13.6	3841 ± 9326	33.3
Follow-up	626 ± 342	9.5	566 ± 420	5.2	346 ± 381	3.3	192 ± 363	1.7
Total	6623 ± 4753	100.0	10 910 ± 9076	100.0	10 579 ± 17121	100.00	11 535 ± 11 724	100.0
(95% confidence interval)	(5789–7452)		(9937–12985)		(8590–13 085)		(5042–18027)	
Undiscounted total costs	6807 ± 5033		11217 ± 9502		10736 ± 7367		11577 ± 11729	

S.D., standard deviation.

curative rather than palliative. For these stage 1 cancers, 57% received surgery, with a mean 5-year cost of £5795 (all palliative treatments excluded) and a 5-year survival rate of 47%. The corresponding mean cost for those treated non-surgically was significantly higher at £7929 (*t*-test, $P=0.01$), with 5-year survival at 50%. For stage 2 cancers, 32% received surgery, at a mean cost of £10 404 and a 5-year survival of 55%. The mean cost for those treated non-surgically, £12 202, was not significantly higher (*t*-test, $P=0.45$), whilst mean 5-year survival was 30%. Sample sizes for the remaining stages were too small to enable comparisons to be made.

The pre-invasive cancer sample comprised 15, 31 and 95 cases at CIN1–CIN3, respectively. The differences between mean costs for the management of pre-invasive carcinomas at each of these grades were insubstantial (< 1%). Averaged across all the CIN grades, therefore, the mean cost of management was estimated at £386 (standard deviation (S.D.) 66). This comprised costs of diagnosis (19% of the total mean cost), including initial smear, colposcopy (13%) and punch biopsy; costs of treatment (62%), including loop cone (44%), knife cone (10%) and laser biopsies; and costs of follow-up (19%), entailing further smears, colposcopy and biopsies. Analysis of variance revealed that the mean total cost of pre-invasive carcinoma of the cervix was significantly lower ($P=0.00$) than that for all stages of invasive cancer.

As a comparator for the management costs of cervical cancer, we employed estimates obtained from an analogous resource use audit and costing, exercise, which calculated stage-specific costs for a sample of 137 women diagnosed with breast cancer in Trent in 1991 [6]. The combined data are presented in Table 3. Differences in mean costs between breast and cervical management were assessed using the Mann–Whitney test, at a more stringent significance level than normal to compensate for multiple comparisons.

As is evident, the costs for breast cancer were consistently lower on a stage-for-stage basis. The principal cause of the difference lies in the diagnosis and radical radiotherapy categories, but length of hospital in-patient stay was also a major contributory factor. For the cervical sample, 75, 79, 79 and 50% of cancers at stages 1–4, respectively, were diagnosed on an in-patient basis, with average lengths of stay of 5, 9, 11 and 16 days, respectively. All breast cancer diagnoses and staging investigations were carried out on an out-patient basis, irrespective of stage. With respect to radical radiotherapy, higher proportions of cervical cancer patients received such therapy: 53, 80 and 72% for stages 1–3, respectively, in comparison with 40, 62 and 38% for breast cancer patients, respectively. Virtually all such radiotherapy was administered to breast cancer patients on an out-patient basis: for cancers at stage 1, for example, 3% of breast cancer patients, but 45% of cervical cancer patients, received radiotherapy as in-patients. Overall, in-patient costs as a percentage of total management costs were 81, 82, 91 and 94% for stage 1–4 cervical cancer respectively, but 58, 61, 58 and 69% for stage 1–4 breast cancer, respectively.

DISCUSSION

In clinical management terms, the significant cost differential between stage 1 cervical cancer and that at more advanced stages may be explained as follows. Stage 1 cervical cancer requires fewer staging investigations to assess the

Table 3. Mean costs of management: breast cancer versus cervical cancer (1990£)

	Stage 1		Stage 2		Stage 3		Stage 4	
	Breast ($n=102$)	Cervix ($n=128$)	Breast ($n=13$)	Cervix ($n=76$)	Breast ($n=16$)	Cervix ($n=42$)	Breast ($n=6$)	Cervix ($n=15$)
Diagnosis	61	1481*	42	2401*	33	2825	21	2620*
Radical surgery	1141	1001	1457	589*	770	97*	0	0
Conservative surgery	496	158*	433	206	110	0*	0	0
Radical radiotherapy	571	2295	471	3817*	287	3595*	255	946
Palliative radiotherapy	68	79	18	203	56	683	3549	2727
Chemotherapy	67	74	133	367	248	251	280	0
Investigations	107	720	217	1457	710	1336	72	1208
Palliative care	161	150	327	1267	1013	1443	1995	3841
Follow-up	850	626	848	566	651	346	386	192
Total	3522	6584*	3946	10 873*	3878	10 57	6558	11 534*

*Significant difference at 0.5% (Mann–Whitney test).

extent of tumour spread at the time of diagnosis. The treatment of choice tends to be hysterectomy with adjuvant radical radiotherapy. In turn, such radiotherapy is less complex and is more regularly carried out on an out-patient basis. Due to superior prognosis, fewer postprimary treatment investigations are undertaken and less palliative radiotherapy and palliative in-patient care is necessary.

As is evident from the standard deviations presented in Table 2, cost variations about the mean for particular classes of events are high, with standard deviations often exceeding the means. Such a pattern is commonly observed when cohorts are costed and arises because of wide variations in treatment patterns between patients, even amongst those ostensibly exhibiting the same pattern of disease. Spread is inevitably enhanced when, as is often the case, a proportion of the cohort receives no treatment under a particular cost heading, i.e. zero costs are included in the range. It can be seen in Table 2 that, whilst certain individual items of therapy display large variances, the variance in the total is substantially smaller. This is accounted for by negative correlations between costs in the different categories, principally, the palliative/primary subdivisions as noted above.

In addition to the invasive cancers identified in the Cancer Registry data, 1867 cases of pre-invasive cancer were detected in 1990, as a result of the screening programme. Assuming that the full population of invasive cancers was staged according to our sample, the gross 1990 discounted 5-year costs of the management of cervical cancer in Trent amounted to approximately $4.2 million, equivalent to slightly less than £1 per head of population. For cervical cancers as a whole, the invasive cases comprised just 16% of the total. yet were responsible for 83% of the costs of diagnosis, treatment and follow-up. Sizeable cost economies in the management of cervical cancer may evidently be realised by detection at earlier stages; for example, had all the invasive cancers been detected at stage 1 then the total diagnosis and treatment costs for Trent would have been around 21% lower. Perhaps more improbably, had all the cancers been detected by screening at the pre-invasive stage, then the total diagnosis and treatment costs for Trent would have amounted to only around £0.9 m, representing a saving of £3.3 million or 79% of cervical cancer management costs. Naturally, these potential treatment cost savings would have to be offset against the costs of the screening programme.

The results of our analysis of cervical cancer management costs bear comparison with those of other, earlier studies. One study undertaken in the U.S.A. [7] produced figures for stage 1 cancer of around £6000 (converted into 1990£ via the exchange rate) and, for stage 4, of around £10 000. However, and unlike the results of our study, stage 2 and 3 costs were closer to those of stage 1 than they were to those of stage 4. A later US study [8] cited results with a far closer similarity to ours, stage 1 at around £7000 with stages 2–4 at £10 000–11 000, whilst another [9] produced translated estimates of around £6700 for early stage, and of around £9700 for late stage cancer. In a New Zealand study [10], the average treatment costs for all invasive cancers across all stages was estimated at around £8000.

Suggestive as these findings are, it must be borne in mind that the comparison of cost results across healthcare systems is intrinsically problematic. Currency conversions are essentially arbitrary and, especially in the U.S.A. charges and prices are frequently used in place of resource costs. Perhaps most important of all in the present context, none of the above studies provides either sufficient detail of the methods of cost-accounting employed, or information at a disaggregated level, to enable us to identify the sources of similarities and differences between their estimates and our own. The following studies are far more transparent, however.

One early U.K. study [11] employed a case record approach to costing similar to ours and examined 80 pre-invasive and invasive cases. Converted into 1990 prices, the estimates were £376 and £1969 per case, respectively, and the pre-invasive estimate corresponds closely with our own. The invasive estimate, however, is considerably lower, and this is accounted for by the use of a 1-year, rather than a 5-year, time frame, the omission of many chemotherapy and radiotherapy costs and the use of, in our view, an unrealistically low estimate of in-patient hospital stay (less than 10% of the values we observed, even after allowance for inflation). A more recent study [12], which used only length of stay as an indicator of resource usage for invasive cancer, produced an order-of-magnitude estimate of £3000 per case per annum (1990 prices), i.e. £15 000 over 5 years.

Of the existing studies, the two which come closest to ours in terms of methodology were based in Holland. One which assessed the cost of management of invasive cancer at stages 3 and 4 [13] produced an estimate in local currency which

translated to £9034, proximate to our estimate of around £10 500. However, another which assessed the cost of CIN3 pre-invasive carcinomas [14] produced an estimate of £1153 in 1990 prices. This figure is considerably higher than our estimate, yet the transparency of the Dutch study permits us to explain the difference, which derives essentially from variations in patient management between the samples. In the Dutch study, 33% of women had conservative treatment (laser ablation, cryotherapy and loop diathermy), 56% had conisation with an average length of in-patient stay of 2.7 days and 11% underwent hysterectomy, with an average length of stay of 1.3 days. In the Trent sample, however, no CIN3 case underwent hysterectomy, 95% had conisation and only 5% had conservative treatment. Neither of these last two procedures required in-patient stays as all were carried out on either an out-patient or day-case basis. This comparison clearly indicates that, whilst costs inevitably differ within a healthcare system on a patient-by-patient basis, systematic cost differences can be observed across healthcare systems, owing to the acceptance of different management protocols.

Our comparison of the cervical cancer management costs with those of breast cancer clearly indicates not only that the former are significantly higher but that the implications of stage progression for management costs differ between cancer sites. Broadly speaking, for cervical cancer, a cost plateau is reached after stage 1 and interstage cost variations thereafter are insubstantial. For breast cancer, the cost plateau occurs across the first three stages and costs subsequently rise at stage 4. As a consequence, shifting detection of disease to the earliest invasive stage exerts a greater relative impact on overall management costs for cervical cancer than it does on those for breast cancer.

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Acknowledgements—The authors gratefully acknowledge R. Hammond, Consultant, Queen's Medical Centre, for permission to access the records of pre-invasive cancer cases and K. Thornhill and S. Smith, for assistance with the invasive cancer data collection. This research was supported by a grant from NHS Executive Trent.