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Modelling the future costs of breast screening

K. Johnston*

Health Economics Research Centre, University of Oxford, Institute of Health Sciences, Headington, Oxford OX3 7LF, UK

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Abstract

The aim of this paper was to estimate the future breast cancer and non-breast cancer costs associated with breast screening. The Nottingham prognostic index (NPI) was used to stratify patients into different prognostic groups and to predict the impact of breast screening on future costs. A Markov model was used to estimate breast cancer and non-breast costs for each prognostic group. Breast cancer costs were found to increase as the severity of prognosis increases. The opposite pattern was found for non-breast cancer costs. The total future costs (breast cancer and non-breast cancer costs) for each prognostic group was between £10 000 and £11 000. As a percentage of the costs of screening, the savings in future breast cancer costs were 20.9%. Inclusion of non-breast cancer costs cancelled out any potential savings in future breast cancer cost resulting from a better prognosis and resulted in an increase of 5.7% in future costs. Whether to include the latter type of cost remains a methodological issue of debate in economic evaluation.

Keywords: Costs; Breast; Screening; Cancer

1. Introduction

1.1. The impact of breast screening on the treatment costs of breast cancer

The aim of breast screening is to reduce mortality from breast cancer through identifying and treating breast cancer at an earlier stage than would otherwise be the case without screening. One consequence of this is that it may prevent treatment for late stage breast cancer with a possible reduction in treatment costs. Although the total number of women with breast cancer will not change with screening, two factors may independently affect treatment costs: the timing of treatment and the number of women receiving treatment for advanced disease. The impact of these two factors on the magnitude of difference in treatment cost between screening and no screening is uncertain and the issue of whether breast screening results in treatment cost savings is a contentious one. For example, it has been argued that the belief that there is a wide difference between lifetime treatment costs for breast cancer detected early and late is "almost surely fallacious" as there is little empirical evidence to support it [1]. Several empirical studies have, however, addressed this question and have found the proportion of the costs of screening offset by changes in treatment costs to be between 33 and 47% [2]; between 8 and 36% [3]; 18% [4] and an increase of 0.5% [5]. Although these studies have used slightly different methods, including different definitions of staging of breast cancer and different definitions of cost saving, it is clear that there is no consensus on the issue of whether screening results in savings with regard to treatment costs.

1.2. Future health service costs

Potential savings in treatment costs of breast cancer as a result of screening are a type of future cost. Future costs may be either health service or non-health service costs (such as changes in future productivity costs). Since this paper adopts a health service perspective, only future health service costs are considered. Future health service costs may occur in life years lived anyway or life years gained [6]. Costs incurred in life years lived anyway are the costs of treatment that would be incurred without the intervention. Costs in life years gained are the costs of treatment with the intervention. An additional type of future cost is other health service

* Tel.: +44-1865-226-692; fax +44-1865-226-842.
E-mail address: kathy.johnston@ihs.ox.ac.uk (K. Johnston).

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costs incurred in the life years gained from the intervention. There is debate about whether this latter type of future cost should be included in economic evaluations [6,7]. One argument for their inclusion is that since, on the effects side, the life years gained are attributed to the intervention, so should all the costs in the life years gained be thus attributed [8]. A further argument for inclusion is that if they are not included, interventions extending life appear more cost-effective than those improving quality of life [7]. Whether to include other health service costs in life years gained has been debated in the context of breast screening. For example, it has been argued that inclusion of such costs implies that it will almost always be more cost-effective to do nothing rather than to screen for breast cancer and attempt cure [9]. One study of the costs of breast screening has included other health service costs in life years gained [10] and stated their reason for doing so as providing "as comprehensive a measure of health service costs as possible". They further argue that only if breast screening made no difference to prognosis or if the other health service costs of women with breast cancer were independent of their life expectancy would the other health service costs in life years gained be unaffected by screening [10]. Recent guidelines on economic evaluation have recommended that such costs be included in a sensitivity analysis in order to determine their quantitative importance [6]. Several recent economic evaluations have included such costs [11,12], but their inclusion is still a methodological issue of debate in economic evaluation.

1.3. Aims

The first aim of this paper was to estimate future breast cancer costs (costs of treating breast cancer following a breast cancer diagnosis) and non-breast cancer costs (costs of treating other illnesses in the life years following a breast cancer diagnosis) by a staging indicator of breast cancer. The second aim was to judge the quantitative importance of non-breast cancer costs relative to breast cancer costs. The final aim was to estimate the impact of breast screening on future costs by estimating the difference in the future costs of screen-detected, as opposed to symptomatically-detected, cancers.

2. Patients and methods

2.1. Nottingham prognostic index

The staging indicator used to predict future costs was the Nottingham prognostic index (NPI) [13,14]. The NPI is assigned at diagnosis and incorporates three prognostic factors: tumour size, nodal status and histological grade. The NPI is derived from a Cox regression model and is estimated as follows: (0.2×size + lymph node status + grade) [14].

The NPI is a continuous index, but can be categorised into four main prognostic groups: excellent, good, moderate and poor. In addition to these groups, a further group for Ductal Carcinoma *In Situ* (DCIS), is also identifiable. Consequently, there are five potential prognostic groups (PGs) a woman can be classified into at diagnosis (Table 1). The key advantage of the NPI over other staging indicators such as TNM staging, is that it includes grade of cancer, a factor that has been shown to correlate highly with prognosis [15]. The NPI has been shown to be stable [13] and the factors that comprise the NPI have been shown to pick up the effects of screening [16]. A further advantage of using the NPI is that it allows separate identification of DCIS non-invasive cancers, a type of cancer commonly detected with screening. The NPI is increasingly being used as the surrogate endpoint for breast screening trials (for example the breast screening frequency trial in the UK) [17]. Although the NPI was developed in the UK, it can be applied internationally assuming the relevant prognostic information has been recorded.

2.2. Markov model

Markov modelling [18,19] was used to estimate future costs for each of the five PGs. Fig. 1 shows the Markov state diagram used for each PG, with the arrows representing allowable transitions. The model begins at the point where breast cancer has been diagnosed and NPI assigned. There are five states in the model: breast cancer diagnosed; local recurrence; regional recurrence; distant recurrence; and dead. The three types of recurrence refer to the following: local recurrence is recurrence in the ipsilateral breast or mastectomy flaps; regional recurrence is recurrence in the regional lymph nodes (that is internal mammary, axillary and/or intra clavular nodes); and distant recurrence is the spread of disease beyond the above sites.

The first state in the model refers to breast cancer diagnosis and the primary treatment received following the breast cancer diagnosis. It is not possible to return

Table 1
Prognostic groups identifiable using Nottingham prognostic index (NPI)

Prognostic group	Score
DCIS	n/a
Excellent	NPI $\leqslant$ 2.4
Good	2.41 $\leqslant$ NPI $\leqslant$ 3.4
Moderate	3.41 $\leqslant$ NPI $\leqslant$ 5.4
Poor	NPI $\geqslant$ 5.4

DCIS, ductal carcinoma *in situ*; n/a, not applicable.

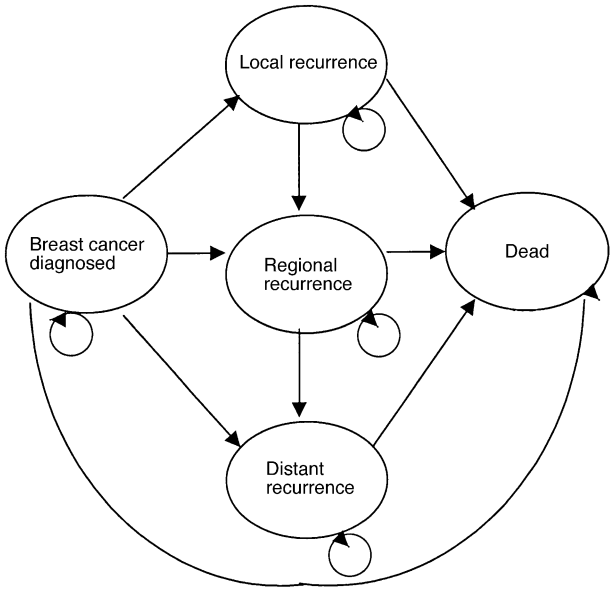

Fig. 1. Markov state diagram.

to the breast cancer diagnosed state after movements to any of the recurrence states. Once in any of the recurrence states, it is possible to move to more severe recurrence states, but it is not possible to move backwards to less severe recurrence states. The transitions allow patients to be in remission from breast cancer, equivalent to remaining in any of the recurrence states. Although patients may progress through the different states of recurrence, the Markovian assumption [18] means that transitions are independent of what happened in any previous cycle. For example, the probability of transition to the dead state is independent of the number of regional recurrences that have occurred.

The probabilities of moving from the breast cancer diagnosed state to the different types of recurrences differed by PG and were derived from a database from the Professorial Unit of Surgery at the City Hospital, Nottingham, UK. The database has collected the information required to estimate the NPI since 1988 and follow-up data on recurrence and survival by PG for 7 years. For transitions from breast cancer diagnosed to the dead state, probabilities of dying beyond 7 years are therefore required. In order to estimate these, a trend was fitted to the survival data (several functional forms were tested and a linear trend was applied). In the absence of other information, transitions linking recurrence and survival were assumed to be the same for each PG and were obtained from the literature [20]. Data on probabilities of death by other causes were derived from life tables of deaths of females in England and Wales in 1995 from the Office of National Statistics.

Table 2 reports the transition probabilities that differ by PG for each PG. A transition probability of zero indicates that it was not an allowable transition. Table 3 reports the transition probabilities assumed to be the same by PG. The Markov model begins with all patients in the breast cancer diagnosed state at age 50 years. A cycle length of 1 year was chosen since follow-up after breast cancer diagnosis and treatment is annual. The model was run for 50 cycles to represent a lifetime. A cohort analysis was used to evaluate the model, that is, a hypothetical cohort of 10 000 individuals was run through the model [18].

2.3. Breast cancer costs

Breast cancer costs, that is, the costs of treating breast cancer following a breast cancer diagnosis, were estimated from the City Hospital, Nottingham. The Nottingham database does not record patient-specific resource use and only has information on the type of primary treatment for breast cancer, but no details of the treatment. Consequently, standard treatment protocols for the City Hospital were used to estimate treatment costs. Costs were estimated for primary treatment,

Table 2
Annual transition probabilities differing by prognostic group

Transition/PG	DCIS	Excellent	Good	Moderate	Poor
BCD to LR	0.0044	0.0015	0.0069	0.0110	0.0279
BCD to RR	0.0054	0.0045	0.0080	0.0155	0.0257
BCD to DR	0	0	0.0074	0.0155	0.0764
BCD to dead (breast cancer) Age 50–59 years	0	0.0039	0.0097	0.0602	0.2770
BCD to dead (breast cancer) Age 60–69 (years)	0	0.0051	0.0100	0.0837	–
BCD to dead (breast cancer) Age 70–79	0	0.0061	0.0112	–	–
BCD to dead (breast cancer) Age 80–89 (years)	0	0.0069	0.0121	–	–
BCD to dead (breast cancer) Age 90–99 years	0	0.0073	0.0132	–	–

BCD, breast cancer diagnosed; LR, local recurrence; RR, regional recurrence; DR, distant recurrence; DCIS, ductal carcinoma *in situ*. – indicates no one survives over the period.

Table 3
Annual transition probabilities for recurrences and death

Transition	Transition probabilities
Local recurrence to regional recurrence	0.0400
Local recurrence to distant recurrence	0.2258
Local recurrence to death	0.2152
Regional recurrence to distant recurrence	0.2258
Regional recurrence to death	0.2438
Distant recurrence to death	0.7450
Other causes death aged 50–59 years	0.0091
Other causes death aged 60–69 years	0.0266
Other causes death aged 70–79 years	0.0423
Other causes death aged 80–84 years	0.0719
Other causes death aged 85+ years	0.1166

recurrences and follow-up. Annual costs were estimated and attached to the appropriate Markov states and transitions. Table 4 reports these costs. Initial state rewards accrue at the beginning of the model; incremental state rewards accrue each time a state is entered; transition rewards accrue each time the movement between states occurs. The source of the unit costs of surgery and outpatient visits was the Nottingham City Hospital finance department. The source of the unit costs of adjuvant hormone treatment and chemotherapy treatment was the British National Formulary. Costs were discounted at 6% in the model [21], the recommended rate in the UK. Costs were also discounted at 3% in a sensitivity analysis.

2.4. Non-breast cancer costs

Non-breast cancer costs, that is, the costs of treating other illnesses in the life years following a breast cancer diagnosis, were estimated using information on life years, average health service costs by age and ages of women. Estimates of life years by PG were obtained from the Markov model by ensuring that each stage spent in a live state was awarded an incremental reward of 1 life year. Estimates of average annual NHS hospital and community health services expenditure per person by age were used [22]. The average annual

Table 4
Breast cancer costs

State	Type of reward	Annual cost £ (1998/1999)
Primary treatment[a]		
Primary treatment of DCIS	Initial state reward	2699
Primary treatment of excellent prognosis	Initial state reward	2700
Primary treatment of good prognosis	Initial state reward	2935
Primary treatment of moderate prognosis	Initial state reward	3156
Primary treatment of poor prognosis	Initial state reward	3262
Follow-up[b]		
Follow-up after primary	Incremental state reward	71
Treatment for recurrence[c]		
Treatment for local recurrence	Transition reward	2502
Treatment for regional recurrence	Transition reward	3327
Treatment for distant recurrence	Transition reward	5249
Follow-up after recurrence[d]		
Follow-up after local and regional recurrence	Incremental state reward	163
Follow-up after distant recurrence	Incremental state reward	4336
Palliative care		
Palliative care	Transition reward	2750

CT, computed tomography; MRI, magnetic resonance imaging; DCIS, ductal carcinoma *in situ*.

[a] Primary treatment costs are based on proportions having different treatment combinations of surgery and adjuvant treatments. Surgery costs include the costs of operation (anaesthesis time, theatre time, overheads and consumables) and ward costs and are as follows: £2539 for mastectomy; £2461 for lumpectomy; £2515 for subcutaneous mastectomy. Adjuvant hormone treatment is tamoxifen 20 mg a day for 5 years and four outpatient visits per year (£222, discounted). Adjuvant chemotherapy treatment is based on CMF (cyclophosphamide, methotrexate and 5-fluorouracil) repeated at 28 day intervals for six cycles (£938) with six outpatient visits per year. Adjuvant radiotherapy consisted of radiotherapy to the breast (50 Gy, 25#, for breast conservation and simple mastectomy, cost of £1331) and 45 Gy, 15# for subcutaneous mastectomy (cost of £868) with four outpatient visits per year.

[b] Annual outpatient visit £71.

[c] The costs of treating recurrence are based on the proportions having different investigative procedures and treatments [30–32]. Investigative procedures for local and regional recurrence are core biopsy (£94) or open biopsy (£873). Investigative procedures for distant recurrence are bone scan (£83); liver ultrasound (£21); CT scan (£73); chest X-ray (£16); biochemistry tests (£7); skeletal survey (£27); blood count (£5); MRI (£44). Costs of treatment for local and regional recurrence are based on surgery and adjuvant treatment costs above. Costs of distant recurrence are based on proportions having first-line chemotherapy (£2015) and second-line chemotherapy (£4336) [32].

[d] Follow-up after local and regional recurrence is based on two outpatient visits per year and one mammogram (total cost of £163); follow-up of distant recurrence involves second-line chemotherapy (£4336) [32].

NHS expenditure is £383 for the age group 45–64 years; £805 for the age group 65–74 years; £1435 for the age group 75–84 years; £2274 for aged 85 years and over. Information on the proportion of women in the different age groups was obtained from the results of the cohort analysis of the Markov model. Since the Markov model begins for women aged 50 years and each cycle is 1 year, the cycle number can be used to index age and the proportion of life years in each age band easily identified. Costs were discounted at 6% in the model [21], the recommended rate in the UK. Costs were also discounted at 3% in a sensitivity analysis.

2.5. Impact of breast screening on future costs

The impact of breast screening on future costs was estimated by applying the breast cancer and non-breast cancer cost estimates to the distribution of cancers in different PGs for both screen-detected and symptomatically-detected cancers. In a sample of 195 screen-detected cancers, 23.1% were in the DCIS PG; 35.4% were in good PG; 37.4% were in the moderate PG; and 4.1% were in the poor PG [23]. In a sample of 315 symptomatically-detected cancers, 2.9% were in the DCIS PG; 23.8% were in good PG; 51.7% were in the moderate PG; and 21.6% were in the poor PG [23]. No information was provided on the proportions in the excellent PG. The proportions were weighted by the average total future cost per PG and then applied to the number of cancers detected. In 1997/1998, the number of cancers detected in the breast screening programme was 7932 [23]. The number of women screened for the same period was 1 350 204 and the number of women recalled for assessment was 71 255 [23]. The net difference in future costs between screen-detected and symptomatically-detected cancers was calculated and also expressed as a percentage of the costs of screening. The total costs of screening were estimated by multiplying the number of invitations, screens and assessments by their unit costs (£8.73, £11.97 and £55.12 respectively, 1998/1999 prices) [24].

3. Results

Table 5 presents the average total future costs for each PG, discounted at both 6 and 3%. For both discount rates, the results show that the magnitude of the breast cancer cost increases with severity of the PG, whilst the magnitude of non-breast cancer cost decreases as the severity of prognosis increases. Non-breast cancer costs are lowest for the poor PG, where life expectancy is lower. Similarly, the non-breast cancer costs are highest for the DCIS group and excellent PGs, where life expectancy is higher. Average breast cancer and non-breast cancer costs increase for all PGs when costs are discounted at 3% compared with 6% but the increases are larger for non-breast cancer costs. When costs were discounted at 6%, the average total future cost (breast cancer and non-breast cancer costs) by PG is very similar across the PGs, at approximately £10 000 to £11 000. Table 5 shows that the average total future costs are substantially higher for the DCIS, excellent and good PGs than for the moderate and poor PGs when costs are discounted at 3% compared with 6%.

Table 6 presents the future costs for screen-detected and symptomatically-detected cancers, discounted at 6%. Total breast cancer costs are highest for the DCIS group and good PG for screen-detected than symptomatically-detected cancers. This pattern is reversed for the moderate and poor PGs. The total difference in breast cancer costs is a saving of approximately £7.7 million with screening. Total non-breast cancer costs are higher for the DCIS group and good PG for screen-detected than symptomatically-detected cancers. The total difference in non-breast cancer costs is an increase of approximately £9.8 million with screening. The total difference in future costs is an increase of approximately £2.1 million for screen-detected cancers compared with symptomatically-detected cancers. The total costs of screening are approximately £36.9 million. As a percentage of the costs of screening, the savings in breast cancer costs were 20.9% (−£7.7 million divided by £36.9 million). Once non-breast cancer costs were included an increase of 5.7% in total future costs as a percentage of the costs of screening results (£2.1 million divided by £36.9 million). The corresponding figures for a 3% discount rate (not shown in table) were savings in breast cancer costs of 17.3% (−£7.1 million divided by £36.9 million) and an increase of 7.0% in future costs as a percentage of the total future costs of screening (£2.6 million divided by £36.9 million).

Table 5
Average total future costs by prognostic group (£1998/1999)

Prognostic group	Average total breast cancer cost	Average total non-breast cancer cost	Average total future cost
6% discount rate			
DCIS	4816	6198	11 014
Excellent	5463	5259	10 722
Good	6298	4656	10 954
Moderate	7368	2711	10 079
Poor	9278	946	10 224
3% discount rate			
DCIS	5554	9899	15 453
Excellent	6472	7957	14 429
Good	7341	6850	14 191
Moderate	8192	3400	11 592
Poor	9724	1031	10 755

DCIS, ductal carcinoma *in situ*.

Table 6
Impact of screening on future costs (discounted at 6%) (£ 1998/1999)

	Costs for screen-detected cancers (£)	Costs for symptomatically-detected cancers (£)	Difference in costs between screen-detected and symptomatically-detected cancers(£)
Costs of screening			
Invitation	16 835 589	n/a	
Screening	16 163 972	n/a	
Assessment	3 927 401	n/a	
Total	36 926 962	n/a	+36 926 962
Breast cancer costs of cancers detected			
DCIS PG	8 815 915	1 091 494	
Good PG	17 676 138	11 893 882	
Moderate PG	21 879 613	30 243 249	
Poor PG	3 019 107	15 886 254	
Total	51 390 773	59 114 879	−7 724 106
Non-breast cancer costs of cancers detected			
DCIS PG	11 345 201	1 404 644	
Good PG	13 068 031	8 793 189	
Moderate PG	8 050 085	11 127 287	
Poor PG	307 843	1 619 840	
Total	32 771 160	2 294 460	+9 826 200
Total future costs of cancers detected			
DCIS PG	20 161 115	2 496 138	
Good PG	30 744 169	20 687 070	
Moderate PG	29 929 698	41 370 536	
Poor PG	3 326 950	17 506 094	
Total	84 161 933	82 059 838	+2 102 095

DCIS, ductal carcinoma *in situ*; PG, prognostic group; n/a, not applicable.

4. Discussion

The results show that breast cancer costs increase as the severity of prognosis increases, irrespective of the discount rate. This finding is similar to those found in four studies reporting breast cancer costs by TNM staging. Two studies found costs to increase across all stages [3,25] one study found costs to rise to TNM stage 3 and fall to TNM stage 4 [26] and one study found costs to rise to TNM stage 2, fall to TNM stage 3 and rise to TNM stage 4 [5]. A limitation of this study is that patient-specific resource use (and hence costs) could not be estimated and consequently treatment cost estimates had to be based on average treatment protocols. This meant that variations in cost within PGs could not be addressed.

A limitation of the model is that transition probabilities between types of recurrence and between recurrence and death were not available by PG and were assumed to be constant across PGs. There is some uncertainty surrounding the estimates used for transitions between recurrences. For example, the annual probability of regional recurrence following local recurrence is 4% per year [20] and it has been suggested that this estimate is relatively high because it is based on data from women at high risk [27]. One advantage of the modelling approach adopted is that it uses a combination of prognostic factors to model future costs rather than single prognostic or predictive factors.

The study shows that non-breast cancer costs are quantitatively important relative to breast cancer costs. Irrespective of the discount rate, the pattern of breast cancer and non-breast cancer costs differed amongst PGs with non-breast cancer costs being lowest for the poorer prognostic groups because fewer life years could be gained. The estimates of non-breast cancer costs were based on the Department of Health estimates for annual health expenditure which, although fairly crude estimates, have been used in other studies [12,28] and were used in this paper because no other estimates exist for the UK. A limitation of these costs is that they may already include some breast cancer costs, but since the percentage of NHS expenditure spent on all cancers is 3% [29], the impact of this on non-breast cancer costs is likely to be limited.

Although there is some uncertainty surrounding the cost estimates used, the implications of the differences in future costs by PG were identified. When the distribution of cancers detected by PG with screening and symptomatic presentation were applied, savings in breast cancer costs resulted. As a percentage of the costs of screening, the savings in breast cancer costs were

20.9%. Once non-breast cancer costs were included an increase of 5.7% in total future costs as a percentage of the costs of screening resulted.

This paper has estimated costs for each PG within the NPI, a surrogate endpoint increasingly being used in clinical trials. The costs estimated here could be used in other trials using the NPI as an endpoint. Although the estimation of costs beyond the surrogate endpoint is not a substitute for longer term follow-up, the modelling of future costs performed is preferable to failing to address such costs. The implication of including future costs for screening is that some of the costs of breast screening could be offset by savings in future breast cancer costs. Including non-breast cancer costs increases the total future costs and would ultimately make breast screening appear less cost-effective. Inclusion of such future costs, however, remains a methodological issue of debate in the economic evaluation.

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