



# Estimates of the lifetime costs of breast cancer treatment in Canada

B.P. Will<sup>a</sup>, J.-M. Berthelot<sup>a</sup>, C. Le Petit<sup>a</sup>, E.M. Tomiak<sup>b</sup>, S. Verma<sup>b</sup>, W.K. Evans<sup>b,\*</sup>

<sup>a</sup>The Health Analysis and Modelling Group, Statistics Canada, 24-Q, R.H. Coats Building, Ottawa, ON, K1A 0T6, Canada

<sup>b</sup>The Ottawa Regional Cancer Centre, Cancer Care Ontario and the University of Ottawa, 501 Smyth Road, Ottawa, ON, K1H 8L6, Canada

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## Abstract

A comprehensive understanding of the cost components of common illnesses is a necessary first step towards ensuring optimal use of scarce healthcare resources. Since breast cancer is the commonest malignancy affecting Canadian women, we estimated the direct healthcare costs associated with the lifetime management of a cohort of 17 700 women diagnosed in 1995. Using a multiplicity of data sources, treatment algorithms, follow-up and disease progression patterns were determined by age ( $< 50$ ;  $\geq 50$  years) for all four stages of breast cancer at diagnosis, as well as for the management of local and distant recurrence. Statistics Canada's Population Health Model (POHEM) was used to integrate the data from the different sources and to estimate the lifetime costs, discounted at 0, 3 and 5% rates. The average undiscounted lifetime cost per case of treating women diagnosed with breast cancer varied by stage, from \$36 340 for stage IV or metastatic disease, to \$23 275 for stage I patients. The total cost of treatment for the cohort diagnosed in 1995 was estimated to be over 454 million Canadian dollars. Hospitalisation (mainly for initial treatment and terminal care) represented 63% of the lifetime costs of care delivery. Disease costing models are valuable tools for optimising the use of scarce resources without compromising the health status of individual patients. The breast cancer costing model has recently been used to assess the cost impact and cost-effectiveness of providing radiotherapy to all patients undergoing breast surgery, and of performing outpatient breast surgery. © 2000 Published by Elsevier Science Ltd. All rights reserved.

**Keywords:** Breast cancer; Microsimulation model; Direct care costs; Disease costing

## 1. Introduction

Canada is currently facing many challenges within its healthcare delivery system. Government debt, the globalisation of the economy and the ageing of the population are creating pressures to provide more efficient healthcare delivery to the Canadian population. Decisionmakers and health policy analysts require information on the current and future costs and outcomes resulting from the management of specific diseases, in order to evaluate the impact of proposed health policy changes.

Breast cancer is the most common female cancer in Canada in terms of incidence and the second most important in terms of mortality. It is estimated that in 1995, approximately 17 700 women were diagnosed with

breast cancer and that 5400 women died from this disease [1]. Breast cancer is generally a slowly progressive disease. As a result, the phases of disease progression are measured in years and sometimes in decades. In order to have a full understanding of resource consumption, it is necessary to understand not only the therapeutic options at first diagnosis, but also, the frequency and types of follow-up procedures, and the management of recurrent or metastatic disease, including terminal care. In this paper, we present original research by Statistics Canada and oncologists at the Ottawa Regional Cancer Centre, culminating in a comprehensive model of breast cancer management. Once this information was incorporated into the Population Health Model or POHEM [2,3], we estimated the costs of treating all phases of this disease in Canada. Studies of the economic burden of illness can demonstrate the impact of diseases like breast cancer on society, can serve as a benchmark against which new therapeutic interventions can be assessed, and can aid in determining priorities for medical research [4].

\* Corresponding author. Tel.: +1-613-737-7700; fax: +1-613-247-3503.

E-mail address: bevans@cancercare.on.ca (W.K. Evans).

## 2. Patients and methods

A model for all phases of breast cancer therapy requires data on initial treatment, follow-up patterns, treatment at recurrence and care during the terminal phase of the disease. Information on the types of medical services (surgery, chemotherapy, radiotherapy, supportive care) and their costs, and on the duration of each phase of the disease is also needed. Given the current state of health information systems in Canada, these data are only available from a multiplicity of sources.

### 2.1. Initial treatment, follow-up patterns and their costs

We have previously reported on the methodology used to estimate the cost of initial diagnosis and treatment of non-metastatic (stages I, II and III) breast cancer, including adjuvant therapies [5]. Breast cancer treatment is dependent on the stage of the disease at initial diagnosis. Stage groupings are based on tumour size (T), extent of lymph node involvement (N), and evidence of distant metastasis (M) [6]. In brief, treatment algorithms for these three stages of the disease by age group ( $< 50$  or  $\geq 50$  years of age) were derived from national databases such as the Canadian Cancer Registry, Statistics Canada's national person-oriented database of hospital discharges [7] and national surveys of medical, surgical and radiation oncologists [8]. Provincial cancer registry data, provincial fee schedules and special costing studies and chart reviews were used to augment the national databases and to determine costs (see Table 1 for a complete list of data sources).

Our earlier work has now been refined by adding costs associated with initial diagnosis and treatment of all stages of the disease (including stage IV or metastatic breast cancer), follow-up, recurrent breast cancer, as well as the costs and duration of palliative and terminal care. In the remainder of this section, details are provided on how the new components of the model were developed.

### 2.2. Costs associated with the diagnosis, treatment and follow-up of local recurrence

Current diagnostic and therapeutic practice in the management of recurrent breast cancer was determined from a retrospective review of all cases of local or distant recurrence diagnosed between 1985 and 1992 at the Saskatchewan Cancer Foundation. This cancer registry was used because it is a comprehensive registry of all cancer cases diagnosed provincially and because charts were more readily available for extraction. Based on the therapeutic modalities used, costs were determined from sources such as the Canadian Institute for Health Information (CIHI), the Ontario Health Insurance Plan

(OHIP), and the Ontario Case Cost Project (OCCP). Details of data sources used are contained in a previous breast cancer paper [5].

### 2.3. Costs associated with the diagnosis and treatment of stage IV and metastatic disease

Modelling the management of stage IV disease was especially challenging, because of the multiplicity of therapeutic options available and the variability of the natural history of this stage of the disease. Standard therapies for metastatic breast cancer may include systemic therapy (hormonal therapy or chemotherapy), surgery, radiotherapy, or any combination of these as first, second and third-line options [9–18]. There was little documentation of the treatment approaches used in provincial databases. To address this data gap, a retrospective review of 500 Saskatchewan charts was undertaken to determine the types and frequency of therapeutic interventions in breast cancer patients diagnosed with a recurrence. In addition, 100 charts were extracted by personnel from the Ottawa Regional Cancer Centre to obtain information on the types of surgery performed on patients with metastatic disease and to determine the length of hospital stay for women with metastatic breast cancer. Costs of therapy were extracted from the same sources cited above.

### 2.4. Costs associated with ongoing or continuing care

Costs for ongoing care are inclusive of all treatments initiated 3 months after the diagnosis and treatment of metastatic disease until 3 months prior to death (these last three months are considered to be the 'terminal care' phase of the illness). Ongoing care costs include those for hospitalisation, inpatient and outpatient medical services, and treatment with radiotherapy or chemotherapy. The costs of home care, oral medications, or out of pocket expenses resulting from visits to healthcare institutions are not included.

A monthly cost for ongoing care was estimated in the following fashion:

1. Patient records in the computerised database at the Manitoba Cancer Treatment and Research Foundation were linked to records from Manitoba Health (the provincial health ministry). This unique linked database, containing all cases of breast cancer diagnosed in the province in 1990, provided information on stage at diagnosis, treatment provided (including the type and frequency of palliative radiotherapy and chemotherapy), and date of death [19]. Each encounter with the healthcare system was recorded, either through a physician's claim or through hospitalisation. The fees paid by Manitoba Health were used in the model;

2. Statistics Canada's 1993/1994 national person-oriented database of hospital discharges was used to determine hospital length of stay for cancer-related causes (using ICD-9 codes) [7]; and
3. Data from the Ontario Case Cost Project (OCCP) (1993–1995) were used to determine the average cost of hospitalisation for the management of non-surgical malignant breast disorders (CMGs (Case Mix Groups) 443, 444 and 445).

Table 1  
List of data requirements and sources

Data required	Data sources
Incidence of female breast cancer	Canadian Cancer Registry, 1995
Population count	Demography Division, Statistics Canada Canada Health Survey
Risk factors	National Breast Screening Study
Stage at diagnosis	Saskatchewan Cancer Foundation, 1993 <sup>a</sup>
Standard diagnostic work-up	Saskatchewan Cancer Foundation, 1993 Surveys of Canadian Oncologists, 1994 <sup>b</sup> Breast Cancer Experts
Therapeutic algorithms at initial diagnosis	Saskatchewan Cancer Foundation, 1993 Surveys of Canadian Oncologists, 1994 Breast Cancer Experts
Follow-up after initial treatment	Surveys of Canadian Oncologists, 1994 Breast Cancer Experts
Diagnosis and treatment of recurrent or metastatic disease	Saskatchewan Cancer Foundation — Special Chart Reviews, 1985–1992 Ottawa Regional Cancer Centre — Special Chart Reviews, 1996–1997
Survival data	Northern Alberta Breast Cancer Registry, 1971–1988 Saskatchewan Cancer Foundation — Special Chart Reviews, 1985–1992 British Columbia Cancer Agency, 1989–1994
Fees for physicians' services, diagnostic and surgical tests and procedures	Ontario Fee Schedule, 1995 (reliability verified by Canadian Institute for Health Information)
Hospital per diem rates by case mix groups	Ontario Case Cost Project, 1993–1995
Hospital per diem rate for terminal care	Ontario Case Cost Project, 1993–1995
Hospital length of stay	Statistics Canada's National Person-oriented Database of Hospital Discharges, 1992–1994 Ottawa General Hospital
Radiotherapy costs	Earle [20]
Chemotherapy costs — drugs and administration	Ottawa Civic Hospital, 1995 Ottawa General Hospital, 1995
Facility overhead costs	Results of 1988 National Cancer Institute of Canada Clinical Trial — BR5 (updated with Consumer Price Index)
Hormonal therapy costs	Ottawa Pharmacies
Monthly costs of ongoing care	Manitoba Medical Services Foundation and Manitoba Cancer Treatment and Research Foundation (MCTRF), 1990 Manitoba Health Services Insurance Plan Statistics Canada's National Person-oriented Database of Hospital Discharges, 1992–1994 Ontario Case Cost Project, 1993–1995
Terminal care costs	Manitoba Medical Services Foundation and MCTRF, 1990 Manitoba Health Services Insurance Plan Statistics Canada's National Person-oriented Database of Hospital Discharges, 1992–1994 Ontario Case Cost Project, 1993–1995

It should be assumed that information from literature reviews and from breast cancer experts were sources for all data requirements.

<sup>a</sup> Special chart reviews of all patients diagnosed in 1993.

<sup>b</sup> 1994 surveys of Canadian oncologists (medical, surgical, and radiation) were for stages I, II and III only.

## 2.5. Costs associated with terminal care

Terminal care costs are those costs incurred by the healthcare system in the three months prior to death from breast cancer. The cost components are similar to those for ongoing care. Statistics Canada's 1993/1994 hospital discharge file was used to calculate the average number of days spent in hospital by breast cancer patients dying in hospital of a related cause. The average cost for these days was calculated from the OCCP by using the cost per encounter for patients who died between June 1993 and March 1995, according to Case Mix Groups (CMGs) 429–433, and 443–445. The Manitoba database provided the proportion of patients receiving palliative radiotherapy and the number of fractions per patient (five), at a cost per fraction of \$138 [20]. A consultation, a partial assessment and weekly blood work were added to the cost of radiotherapy treatment.

## 2.6. Disease progression

Data from the cancer registries of Alberta and Saskatchewan were used to determine the patterns of breast cancer progression. A state transition approach was used. The transitions were derived separately for each stage at diagnosis [21]. For women diagnosed at stage I, II or III, the three most common transitions modelled were: diagnosis to local recurrence, diagnosis to distant recurrence (or metastasis), or diagnosis directly to progression and death.

Once a local recurrence occurs, transitions to distant recurrence or to death are possible. For those with distant metastases or stage IV disease at diagnosis, the only transition is to progressive disease and death. The time to death from distant metastasis is estimated separately for visceral and non-visceral metastases. Fig. 1 provides a schematic representation of disease progression. The Lifetest procedure from SAS [22] was used to estimate the parameters of the survival function.

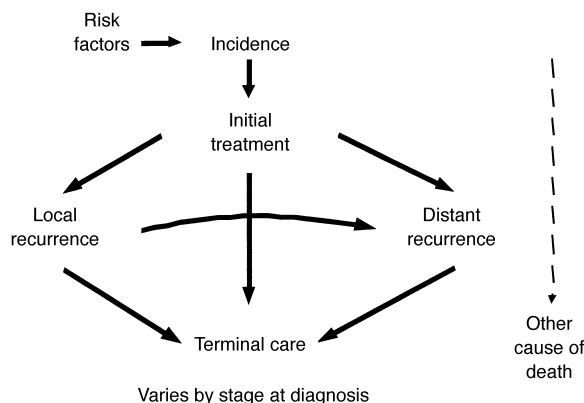


Fig. 1. Breast cancer progression.

## 2.7. The Population Health Model (POHEM)

POHEM is a health microsimulation model used to estimate quantitative patterns of disease incidence, progression and treatment consequences in a large population [2,21]. Microsimulation means that the unit of analysis is the individual. POHEM synthesises a sample of complete individual health and socio-economic biographies. Each synthetic individual is aged and subjected to the demographic and health characteristics, disease onset and progression parameters, healthcare resource utilisation and direct medical care costs of the Canadian population, using probabilistic methods.

The information collected on incidence, treatment modalities and disease progression is all incorporated into POHEM. The likelihood that a simulated individual would develop breast cancer is derived from the number of cases in the Canadian Cancer Registry divided by the population of Canadian women by age group. Each individual 'diagnosed' with breast cancer in the simulated population is assigned a stage at the time of that diagnosis, based on the stage distribution obtained from the Saskatchewan Cancer registry. The stage and age at diagnosis of the simulated women would determine the treatment modalities to be assigned, based on the distribution of initial treatment approaches, as described in the previous section. Subsequent progression of the disease and outcomes are determined by comparing random numbers with the estimate of the parameters of the survival function obtained from the SAS Lifetest procedure [22].

The distribution of type and site of recurrence and the treatment by metastatic site are built into the computer model, so that the costs over time can be estimated. All costs were determined in constant 1995 Canadian dollars and the economic analysis was carried out from the perspective of the government as payer in a universal healthcare system. Costs were discounted at 0, 3 and 5% rates, according to current convention [23,24]. To ensure the stability of the simulation results, a synthetic cohort of one million women was simulated.

## 3. Results

### 3.1. Estimated costs of initial treatment and follow-up

Fig. 2 shows the initial treatment algorithm for women aged 50 years and older diagnosed with stage I breast cancer. In current Canadian practice, the majority of these women are treated with breast conserving surgery followed by radiotherapy. A small proportion receives adjuvant therapy. Stage I women undergoing mastectomy generally do not receive radiotherapy. Treatment algorithms for the other stages by age are available on request. Because of the complexity of the

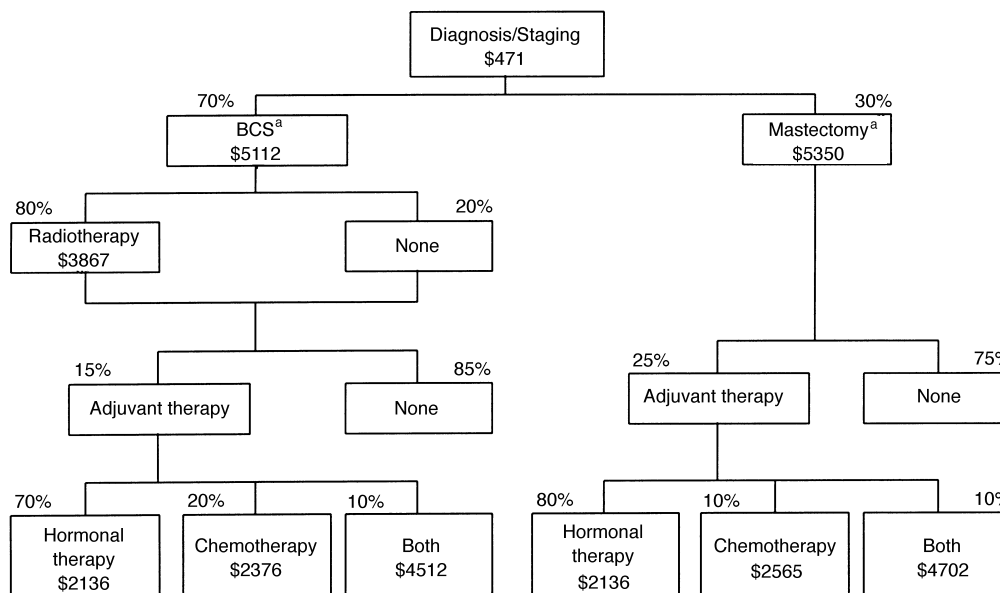


Fig. 2. Treatment algorithm with costs for stage I women  $\geq 50$  years of age ( $n = 6269$ ). <sup>a</sup>Includes cost of hospitalisation.

model, the results for the initial treatment of stages I–III breast cancer have been described in a separate report [5].

A summary of average costs associated with the diagnosis and initial treatment is presented in Table 2. These costs vary from a low of \$8214 for stage I women  $> 50$  years of age to a high of \$10985 for stage III women  $< 50$  years of age. The largest contributors to these costs are hospitalisation, for all stages and both age groups, except for stage III women  $< 50$  years, where chemotherapy is the most expensive component of care. Radiotherapy is the second most expensive component for most stages and age groups. As seen in Table 2, the costs associated with treating younger women are higher than those for treating women 50

years of age or older. This is attributed to the higher proportion of younger women who receive chemotherapy and radiotherapy, compared with older women, who are more commonly treated with hormonal therapy.

Follow-up regimens are dependent on stage, and are only incorporated into the model for the first 5 years following initial diagnosis. Follow-up activities include physician assessments, blood work and biochemistry tests, as well as specific procedures, such as mammograms, bone scans or liver ultrasounds. Total annual follow-up costs were estimated to decrease from \$467 in year 1 to \$286 by year 5 for early stage breast cancer patients, if the patient remained disease free. For stage III, follow-up costs were estimated to decrease progressively from \$482 in the first year to \$322 by year 5.

### 3.2. Estimated costs of diagnosis, treatment and follow-up of local recurrence

Fig. 3 shows the treatment algorithm for women aged 50 years and older who develop a local recurrence, with the proportions receiving local and/or systemic therapy. For ease of presentation, Table 3 summarises the tests and procedures used to diagnose locally recurrent disease, as well as their unit cost and frequency of use. Similar information is provided in Table 3 for stage IV disease at initial presentation and for patients developing metastatic breast cancer. It is assumed that all breast cancer patients undergo a diagnostic work-up at their first encounter with the healthcare system (weighted average of \$329), plus additional tests and procedures for recurrent disease. For those presenting for the first time with stage IV disease, the tests and procedures listed in Table 3 are added to the diagnostic work-up. The

Table 2  
Costs for diagnosis and initial treatment of breast cancer by stage (1995 Canadian \$)

Component	Stage I		Stage II		Stage III		Stage IV <sup>a</sup>	
Age group (yrs)	$< 50$	$\geq 50$	$< 50$	$\geq 50$	$< 50$	$\geq 50$	$< 50$	$\geq 50$
Diagnosis	329	329	329	329	329	329	387	385
Staging	142	142	257	257	334	334	370	386
Surgery	674	678	682	688	589	530	346	279
Hospital	3901	4505	3982	4556	3458	3488	3894	3941
Radiotherapy	2768	2177	2386	1529	2048	1640	1674	1268
Chemotherapy	382	116	2419	446	4091	1529	2650	1139
Hormonal therapy	123	267	331	897	136	624	1349	1801
Total <sup>b</sup>	8319	8214	10386	8701 <sup>c</sup>	10985	8475 <sup>c</sup>	10669 <sup>c</sup>	9200 <sup>c</sup>

<sup>a</sup> Stage IV costs include the diagnosis and initial treatment of stage IV cases at presentation and of metastatic disease.

<sup>b</sup> Survival is taken into consideration in totals.

<sup>c</sup> Numbers may not add up due to rounding off of figures.

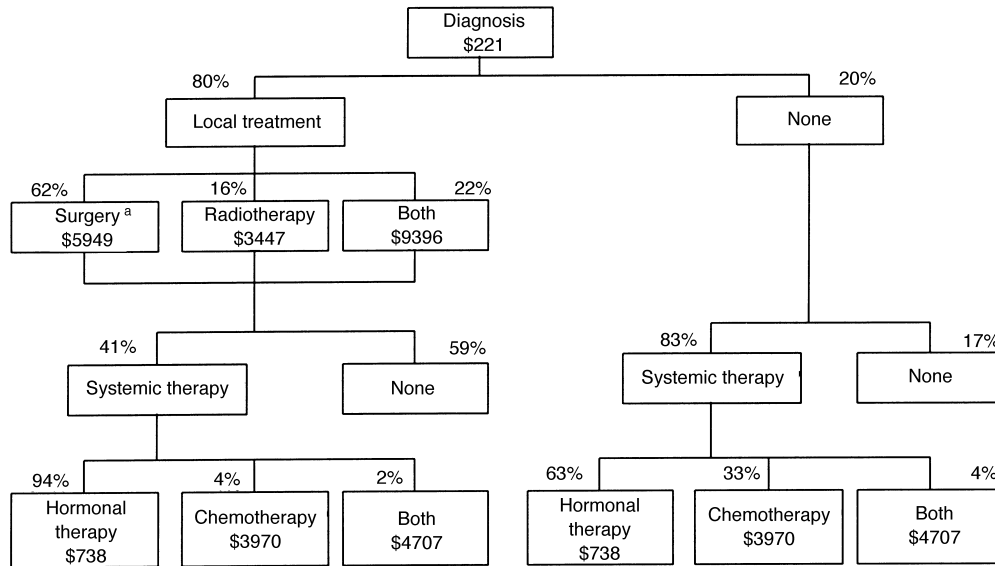


Fig. 3. Treatment algorithm with costs for locally recurrent breast cancer, women  $\geq 50$  years of age. <sup>a</sup>Surgery (includes hospitalisation): excisional biopsy (41%, 7.3 days); simple mastectomy (33%, 6.7 days); excision of single malignant lesion (26%, 11.1 days).

average cost of diagnosing a local recurrence is estimated to be \$221.

Table 4 provides the average cost of treating a local recurrence, according to the patient's age and type of therapeutic intervention required. This cost varies from \$6907 for women less than 50 years to \$5903 for women

aged 50 years and older. As indicated in Fig. 3, 80% of older women receive local treatment for a local recurrence. Because higher proportions of younger women (88%) receive local treatment than those over 50 years of age, the cost associated with their treatment is higher. Follow-up after treatment of a local recurrence is assumed to continue for the rest of the patient's life. Follow-up includes physician assessments, clinic costs

Table 3  
Costs for the diagnosis of local recurrence, stage IV and recurrent/metastatic breast cancer

Tests/procedures	Unit cost (\$)	Local recurrence (%) <sup>b</sup>	Stage IV at presentation (%) <sup>b</sup>	Metastatic disease (visceral) (%) <sup>b</sup>
General assessment	53.60	100	100	100
Biochemistry	38.25	77	100	87
Bone scan	151.90	53	100	60
Complete blood count	10.34	78	100	87
CT scan abdomen	102.60	16	0	73
Abdominal ultrasound	77.90	0	100	0
Chest X-ray	30.71	67	100	82
Bilateral mammogram	57.34	21	0	10
Skeletal survey	101.30	0	25	0
Diagnostic work-up (\$) <sup>a,c</sup>	0	329	0	
Weighted cost <sup>c</sup>	221	334	292	
Total weighted cost <sup>c</sup>	221	663	292	

<sup>a</sup> Diagnostic work-up at the time of initial diagnosis of stage IV breast cancer. For local recurrence and metastatic disease, the diagnostic work-up was completed at initial presentation.

<sup>b</sup> (%) indicates proportion of patients actually receiving test/procedure. The weighted cost is the sum of the unit cost times the proportions in the columns.

<sup>c</sup> Numbers may not add up due to rounding off to nearest dollar.

Table 4  
Cost of treating a patient who develops a local recurrence

Care component	Average cost per patient	
	Women < 50 years \$	Women $\geq 50$ years \$
Diagnostic work-up	221	221
Local treatment:		
surgery	257	240
hospitalisation	4036	3758
radiotherapy	1325	1048
Total-local treatment	5618	5046
Systemic therapy after local treatment:		
chemotherapy	965	322
hormonal therapy	103	314
chemotherapy + hormonal therapy	<sup>a</sup>	<sup>a</sup>
Total-systemic therapy <sup>b</sup>	1068	636
Average cost <sup>b</sup>	6907	5903

<sup>a</sup> Number included in above calculations.

<sup>b</sup> Numbers may not add up due to rounding off to nearest dollar.

(including overhead), haematology, biochemistry, a bone scan, chest X-ray, liver ultrasound, and a mammogram once a year, for a total cost of \$827 in years 1 and 2, \$612 in years 3 and 4, and \$497 for year 5 and after.

### 3.3. Estimated costs of diagnosis and treatment of stage IV and metastatic disease

Fig. 4 summarises the wide variety of therapeutic options available for stage IV or metastatic breast cancer, and their costs for patients with visceral metastases.

Similar algorithms have been developed for bone and soft tissue metastases, and are available upon request. The algorithm has been compartmentalised into 'local treatment', which includes surgery and/or radiotherapy to the breast (for women diagnosed with stage IV disease), or 'treatment of metastases', which includes diagnostic surgery or other outpatient procedures, therapeutic surgery and/or radiotherapy, and systemic therapy, such as chemotherapy, hormonal therapy or combinations of both. The model considers only the most prevalent chemotherapeutic and/or hormonal interventions currently in practice.

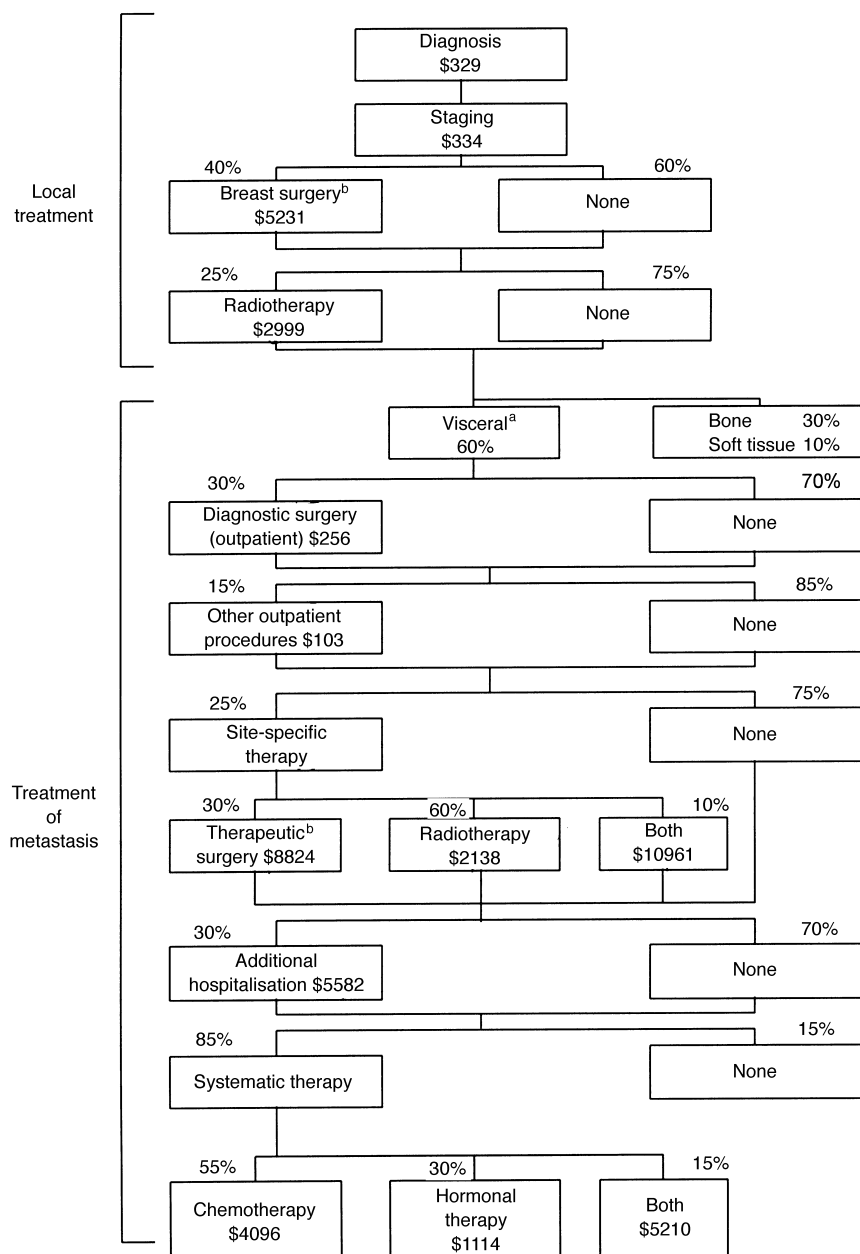


Fig. 4. Treatment algorithm with costs for stage IV women  $\geq 50$  years of age, diagnosed with visceral metastases. <sup>a</sup>Women with breast cancer diagnosed with distant metastasis would undergo a different diagnostic work-up (average \$285). <sup>b</sup>Surgery (includes hospitalisation). <sup>c</sup>Algorithms for bone and soft tissue metastases are available upon request, as are algorithms by age group for other stages of disease.

### 3.3.1. Costs of diagnostic work-up and staging investigations

Women presenting with stage IV disease represent only approximately 6% of all breast cancer patients. The average cost for the initial diagnosis and staging of stage IV patients totals \$663 (see Table 3 for details).

When metastatic disease is suspected, the diagnostic investigation varies according to the site of presumed metastasis. As an example, based on our retrospective review of charts, when patients were suspected of having bone, soft tissue or visceral metastases, bone scans were ordered in 84, 56 and 60% of cases, respectively. For all three sites, the average total diagnostic cost was \$285.

### 3.3.2. Costs of local treatment of stage IV disease

Fig. 4 provides details regarding the costs associated with the local treatment of stage IV disease. By adding the costs associated with the diagnostic work-up, staging procedures, surgery, hospitalisation and radiotherapy, it can be determined that the cost of local treatment for premenopausal women was \$3894, compared with \$3506 for postmenopausal patients.

### 3.3.3. Costs of metastatic breast cancer treatment

Fig. 4 shows the costs for women aged 50 years and older associated with the diagnosis and initial treatment of visceral metastatic breast cancer. These costs are inclusive of all treatments initiated in the first three months following the diagnosis of metastases. A hospitalisation of 12.5 days duration was associated with therapeutic and/or ancillary surgery, based on registry data. Assuming the same average cost per day of hospitalisation for older women as for mastectomy at diagnosis (\$674), the total cost, including the cost of surgery and physician visits, would be \$8824. The 1993–1995 non-surgical average cost per day of hospitalisation was \$400, based on the Ontario Case Cost Project (Case Mix Groups 443, 444, and 445) and this was used to calculate the cost of the 13.4 days of additional hospitalisation and physician assessments required to treat complications or disease progression (\$5582) [25].

Fifteen fractions totalling 40 Gy of radiotherapy were included as part of the site-specific palliative therapy, at a cost of \$2138. For patients requiring chemotherapy, the majority received CAF (cyclophosphamide, doxor-

ubicin and 5-fluorouracil) or CMF (cyclophosphamide, methotrexate and 5-fluorouracil). Further details regarding the calculations involved in determining the cost of systemic therapy can be provided on request. The average cost associated with the diagnosis and treatment of a woman with visceral metastases from breast cancer was estimated to be \$5545, compared with \$3801 for bone metastases, and \$4172 for soft tissue metastases.

### 3.4. Estimated costs of ongoing or continuing care

On average, \$400 per month per patient was spent on hospitalisation. Monthly medical services in and out of hospital were estimated to be \$29 and \$33 per case, respectively. Finally, the Manitoba database was used to determine the average number of fractions of palliative radiotherapy, at a cost of \$138 per fraction [19,20]. Additional costs were added for a physician consultation, partial assessments and weekly blood work, for a total palliative radiotherapy cost of \$1977. From the Manitoba database, we estimated that during each month, 2.2% of patients received palliative radiotherapy, resulting in a monthly per patient cost of \$43. The addition of the hospital *per diem*, hospital service charges and radiotherapy resulted in an average monthly cost for ongoing care of \$506.

### 3.5. Estimated costs associated with terminal care

Statistics Canada's national hospital discharge file indicated that the average length of stay for terminal care was 27 days in 1993/1994. An average cost per day of hospitalisation of \$565 was calculated from data on the cost per encounter for patients who died between June 1993 and March 1995, according to Case Mix Groups (CMGs) 429–433, and 443–445. The cost of radiotherapy was based upon five fractions of palliative radiotherapy at a cost per fraction of \$138. When a radiation oncology consultation, a partial assessment and weekly blood work were added, the total cost of palliative radiotherapy amounted to \$839.

Since the Manitoba records indicated that only 10% of terminal care patients received palliative radiotherapy, the average cost per patient for radiotherapy

Table 5  
Summary of breast cancer disease progression

Stage at diagnosis	Number diagnosed (1995)	Per cent developing local recurrence	Per cent developing metastatic disease	Per cent dying of breast cancer	Number of years alive following diagnosis
I	8142	16.8	32.8	31.6	15.4
II	7257	14.9	46.1	46.2	13.4
III	1239	21.1	70.6	76.3	6.4
IV	1062	N/A	100	91.2	2.6
All stages	17 700	15.3	44.9	44.3	13.2



Table 6  
Components of cost and lifetime cost by stage at presentation (1995 Canadian \$)

Cost component	Stage I \$	Stage II \$	Stage III \$	Stage IV <sup>d</sup> \$	Average all stages \$	Per cent
Initial treatment	8238	9089	9052	9538	8722	34.0
Local recurrence	1399	1109	1404	—	1197	4.7
Follow-up	2313	1841	1429	—	1918	7.5
Rx of metastases <sup>a</sup>	2026	2603	3820	—	2267	8.8
Ongoing care	4395	3840	4643	12 634	4679	18.2
Terminal care <sup>b</sup>	4905	7177	11 849	14 169	6878	26.8
Average cost/case <sup>c</sup>	23 275	25 658	32 197	36 340	25 661	100.0
No. of patients	8142	7257	1239	1062	17 700	—
Lifetime cost (\$,000)	189 508	186 200	39 892	38 593	454 193	—
Per cent (%)	41.7	41.0	8.8	8.5	100.0	

Numbers may not add up due to rounding off of figures.

<sup>a</sup> Rx of metastases includes treatment initiated within 3 months of diagnosis of metastases.

<sup>b</sup> Terminal care includes costs in the last 3 months of life.

<sup>c</sup> Average lifetime cost per case.

<sup>d</sup> For stage IV, initial treatment includes treatment of stage IV at presentation and of metastatic disease.

amounted to \$84. Similarly, the average expenditure per case for medical services in and out of hospital was calculated to be \$132 and \$56, respectively. In total, the cost of terminal care (for those dying of breast cancer) was \$15 531, of which \$15 259 (98%) was attributable to the cost of hospitalisation.

### 3.6. Disease progression

The results of the Lifetest procedure identified that progression of breast cancer is best estimated by a piecewise Weibull survival function [21,22]. Table 5 provides a brief summary of disease progression. Using women with stage I breast cancer as an example, the life expectancy would be 15.4 years following diagnosis; 16.8% of these stage I women would experience a local recurrence; and 32.8% would progress to the metastatic phase of the disease; 31.6% of stage I women would be expected to die of breast cancer, compared with 44.3% of all women with the disease.

### 3.7. Summary of estimated lifetime costs of breast cancer therapy in Canada

Table 6 provides the individual cost components which make up the lifetime costs of providing care to 17 700 women diagnosed with breast cancer in 1995. The average cost per case for all stages of breast cancer was \$25 661 and ranged from \$23 275 for stage I women to \$36 340 for those with stage IV. By phase of illness, initial treatment (34%) and terminal care (26.8%) comprised 60.8% of the total cost, mainly because of the large amount of hospitalisation in these phases. Fig. 5 presents the cost components for all stages of breast cancer in pie chart format, and shows that hospitalisation comprised 63% of the lifetime costs of breast cancer treatment. Table 7 provides more detail on the cost of breast cancer by phase of illness for stage I women  $\geq 50$  years of age. The total lifetime cost of treatment for all women with breast cancer (stages I–IV) was over \$454 million. Discounted lifetime costs at 3% and

Table 7  
Lifetime cost per case for stage I women  $\geq 50$  years<sup>z</sup>

	Initial Rx \$	Local recurrence \$	Metastasis \$	Ongoing care \$	Terminal care \$	Lifetime costs \$	Per cent (%)
Diagnosis	329	33	94	—	—	456	2.2
Stagings	142	—	—	—	—	142	0.7
Surgery	678	36	14	—	—	727	3.6
Hospital	4505	560	569	2591	3976	12 201	59.7
Radio therapy	2177	160	151	282	22	2791	13.6
Chemotherapy	116	50	322	—	—	488	2.4
Hormonal therapy	267	364	488	—	—	1120	5.5
Other medical	—	—	—	401	49	450	2.2
Sub-total	8214	1202	1639	3274	4047	18 375	89.8
Follow-up	1420	658	—	—	—	2079	10.2
Total	9634	1860	1639	3274	4047	20 454	100.0
Per cent	47.1%	9.1%	8.0%	16.0%	19.8%	100.0%	100.0

Numbers may not add up due to rounding off of figures.

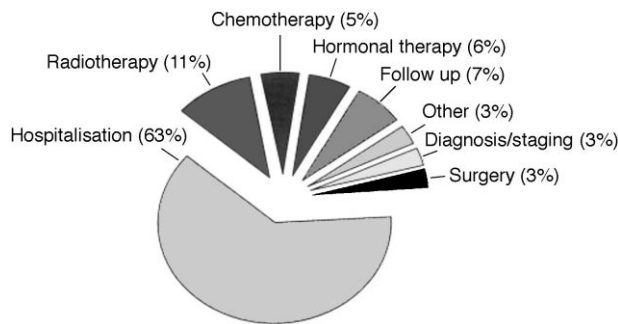


Fig. 5. Components of per patient lifetime costs of breast cancer by intervention, all stages. Total cost = \$25 661. Per cents do not add up due to rounding-off of figures.

5% would be almost \$390 million and \$362 million, respectively.

#### 4. Discussion

This disease-specific microsimulation costing model is a beginning to the complicated process of understanding healthcare costs. To our knowledge, the breast cancer model that we have developed is the most comprehensive one available, because it incorporates information on risk factors, incidence, staging, treatment costs and survival.

Our breast cancer model is based on Canadian risk, incidence, treatment and disease progression data. The results of the Canadian model cannot be directly applied to other countries, due to different incidence rates, treatment patterns and healthcare systems. However, international comparisons of treatment patterns and costs provide a mechanism for countries to understand better the strengths and weaknesses of their healthcare delivery system. We have compared our results with those of other countries who have attempted to determine the cost of breast cancer care [26–29]. Different methodologies regarding the length of time for ‘initial’ and ‘terminal’ care, different comparator years, as well as different healthcare systems and currencies make such comparisons difficult. For example, in our study, initial treatment included all costs associated with treatment initiated in the first 3 months following diagnosis, as was the case for Baker and colleagues [26]. Riley and associates used a longer phase for initial treatment (1 month before diagnosis to 6 months after) [27] and Taplin and colleagues used 6 months [28]. We arbitrarily used 3 months to define the terminal care phase, whereas the other three authors all used 6 months. British researchers, Wolstenholme and coworkers, estimated the mean costs of diagnosis, treatment and follow-up by stage of a sample of 137 breast cancer patients over a period of 4 years, but did not define phases of disease [29].

Using the Continuous Medicare History Sample File and national surveys, Baker and colleagues estimated the lifetime direct medical expenses attributable to breast cancer to be US\$36 926 in 1984. Taplin and associates evaluated the costs of breast cancer treatment in the US by stage, age and comorbidity, but did not evaluate the impact of these differences over the patient’s lifetime subsequent to diagnosis. In addition, their analysis was based on the costs in a Health Maintenance Organisation (HMO), and not a universal healthcare setting. Their average costs of care of breast cancer and all other conditions in 1992 US dollars during the initial, continuing and terminal care phases were \$10 813, \$1084 and \$17 686, respectively. Taplin and associates also increased the estimates of Baker and colleagues to 1992 dollars, using the medical care CPI. This resulted in total costs for breast cancer patients during initial, continuing, and terminal care of \$13 521, \$2576 and \$26 908, respectively. Riley and colleagues calculated the costs of breast cancer treatment from diagnosis to death to be US\$50 448 in 1992. Their calculations were based on Medicare payments, which include only those charges allowed for Americans aged 65 years and older. Based on 4 years of data, Wolstenholme and coworkers predicted lifetime breast cancer treatment costs by stage at diagnosis, in the UK in 1991. Their average lifetime cost was £5269 (approximately US\$11 000).

The considerable variation in costs of breast cancer treatment between the three countries may seem surprising. However, there are several plausible reasons for the differences in costs, including differences in the aggressiveness of treatment approaches, the nature of the healthcare systems themselves, and the patient populations included in the analyses. The cost estimates derived for the US, Canada and the UK are also consistent with each country’s pattern of healthcare spending. In 1990, the proportion of gross domestic product devoted to healthcare was 12.7, 9.4 and 6.0% for the US, Canada and the UK, respectively [30].

Despite the methodological differences stated above, similarities between the study results were identified. Researchers have generally found that hospitalisation is the major contributor to the total cost of treatment, and that hospitalisation occurs predominantly in the first year after diagnosis and soon before death [31–34]. Our analysis indicates that hospitalisation is the major contributor to the lifetime costs of breast cancer therapy, being responsible for 63% of total costs (Fig. 5). Table 6 reinforces this observation that the greatest amount of hospitalisation is associated with initial diagnosis and treatment, and with the terminal care phase.

This report could be criticised for not including the direct costs to patients and caregivers, community care costs, the cost of lost productivity and the impact of

treatment on quality of life. It is acknowledged that such data are important in understanding the costs of a disease from a societal perspective. It is also acknowledged by those who have attempted to determine the costs associated with treating complex diseases such as breast cancer, that it is difficult to obtain such data [35]. In addition, the methodology used to calculate indirect costs as a cost to society is controversial [36]. However, as studies are done which can provide this information, it can readily be integrated into the breast cancer module in POHEM.

The main limitation of studies based upon simulation modeling is that the model is only as good as the data that are available to be incorporated into it. Even though we used nationally representative data when they were available, there are many data sources that do not have a national coverage. It is implicitly assumed that these data sources are nationally representative. As an example, whilst we have an excellent national registry for cancer incidence, this registry does not contain staging data. The staging data were obtained from a population-based registry representing approximately 3% of the Canadian population. In some instances, there were no available databases and we had to rely on expert opinion. This was the case, for example, for breast cancer diagnostic tests. Another limitation is that the results are for an hypothetical cohort and not for real patients.

The major strength of an approach using a simulation model is that it can be used as a policy analysis tool to answer 'what if' questions that go beyond cost issues and can incorporate outcome measures. The availability of information on disease costing is crucial, since it forms the basis against which cost reduction strategies and cost-effectiveness analyses can be evaluated. This becomes particularly pertinent in an era of fiscal restraint, where new therapies are generally expensive and difficult policy decisions may need to be made before such new therapies can be generally adopted.

Recently, we have used the model to assess the cost impact and the cost-effectiveness of the introduction of three different therapeutic approaches that could be adopted into medical practice. We have estimated the economic impact of reducing the length of in-patient stay (LOS) from current levels in Canada to benchmark levels, for patients undergoing breast conserving surgery (BCS) and mastectomy (M), whilst providing optimised home-based care services [37]. We have evaluated the economic and survival impact of loco-regional radiotherapy (LRRT) applied to all postsurgical node-positive stage II breast cancer patients [38]. Finally, we have evaluated the population health impact of providing preventative tamoxifen to Canadian women at high risk of breast cancer [39].

As demonstrated in the cost-effectiveness studies cited above, having detailed documentation of current treatment modalities and costs of treating a disease like

breast cancer, combined with an integrating framework like POHEM, provides a valuable tool to guide health policymakers in decisions related to the introduction of new therapies and on strategies to improve the efficiency of the healthcare system to make care delivery more efficient and less costly.

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## References

1. National Cancer Institute of Canada. *Canadian Cancer Statistics 1995*. Toronto, Canada, 1995.
2. Wolfson MC. POHEM — a framework for understanding and modelling the health of human populations. *World Health Statist Quart* 1994, **47**, 157–176.
3. Will BP, Berthelot J-M, Houle C, Verma S, Tomiak E, Evans WK. A model for estimating the costs and burdens of breast cancer diagnosis and treatment in Canada. *Health Rep* 1993, **5**, 399–408.
4. Drummond MF. Cost-of-illness studies: a major headache. *PharmaEconomics* 1992, **2**, 1–4.

5. Will BP, Le Petit C, Berthelot J-M, Tomiak EM, Verma S, Evans WK. Diagnostic and therapeutic approaches for non-metastatic breast cancer in Canada, and their associated costs. *Br J Cancer* 1999, **79**, 1428–1436.
6. Sobin LH, Wittekind Ch, eds. UICC International Union Against Cancer. TNM Classification of Malignant Tumours, 5th edn. New York, Wiley-Liss, 1997.
7. Statistics Canada. National person-oriented database of hospital discharges, 1993–1994.
8. Tomiak EM, Diverty B, Verma S, et al. Follow-up practices for patients with early stage breast cancer: a survey of Canadian oncologists. *Cancer Prev and Control* 1998, **2**, 62–71.
9. Aisner J, Moossa AR, Schimpff SC, Robson MC, eds. *Management of advanced disseminated breast cancer. Comprehensive Textbook of Oncology*, 2nd edn. Baltimore, Williams & Wilkins, 1991, **85**, 836–844.
10. Hayes DF, Henderson IC, Shapiro CL. Treatment of metastatic breast cancer: present and future prospects. *Semin Oncol* 1995, **22**(Suppl. 5), 5–19.
11. Hillner BE. Economic and cost-effectiveness issues in breast cancer treatment. *Semin Oncol* 1996, **23**(Suppl. 2), 98–104.
12. Hortobagyi GN. Multidisciplinary management of advanced primary and metastatic breast cancer. *Cancer* 1994, **74**(Suppl.), 416–423.
13. Leonard RCF, Rodger A, Dixon JM. Metastatic breast cancer. *Br Med J* 1994, **309**, 1501–1504.
14. Quiet CA, Ferguson DJ, Weichselbaum RR, Hellman S. Natural history of node-negative breast cancer: a study of 826 patients with long-term follow-up. *J Clin Oncol* 1995, **13**, 1144–1151.
15. Seidman AD. Chemotherapy for advanced breast cancer: a current perspective. *Semin Oncol* 1996, **23**(Suppl. 2), 55–59.
16. Vandenberg TA. New developments in chemotherapy for metastatic breast cancer. *Anticancer Drugs* 1994, **5**, 251–259.
17. Verma S. Metastatic breast cancer: deciding on treatment. *Contemporary Oncol* 1994, **4**, 14.
18. Harris JR, Morrow M, Bonadonna G. Cancer of the breast. In De Vita VT, Hellman S, Rosenberg SA, eds. *Cancer: Principles & Practice of Oncology*, 4th edn., Philadelphia, J.B. Lippincott, 1993, 1264–1332.
19. Sloan J, Nemecek A. Experiences in constructing cancer patient trajectories through the Manitoba health care system. Final report to the Manitoba Medical Services Foundation, July 1995.
20. Earle C, Coyle D, Smith A, Agboola O, Evans WK. The cost of radiotherapy at an Ontario regional cancer centre. *Crit Rev Oncol/Hematol* 1999, **32**, 87–93.
21. Berthelot J-M, Le Petit C, Flanagan W. Use of longitudinal data in health policy simulation models. In *1997 Proceedings of the Government Statistics Section*. American Statistical Association, 1997, 120–129.
22. SAS/STAT User's Guide, Version 6, 4th edn, Volume 2.
23. Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the panel on cost-effectiveness in health and medicine. *J Am Med Assoc* 1996, **276**, 1253–1258.
24. Canadian Coordinating Office for Health Technology Assessment. Guidelines for economic evaluation of pharmaceuticals: Canada, 2nd edn. November 1997.
25. Ontario Case Cost Project (OCCP). Special Retrieval from April 1993 to March 1995 database of 13 Ontario hospitals.
26. Baker MS, Kessler LG, Urban N, Smucker RC. Estimating the treatment costs of breast and lung cancer. *Med Care* 1991, **29**, 40–49.
27. Riley GF, Potosky AL, Lubitz JD, Kessler LG. Medicare payments from diagnosis to death for elderly patients by stage at diagnosis. *Med Care* 1995, **33**, 828–841.
28. Taplin SH, Barlow W, Urban N, et al. Stage, age, comorbidity, and direct costs of colon, prostate, and breast cancer care. *J Natl Cancer Inst* 1995, **87**, 417–426.
29. Wolstenholme JL, Smith SJ, Whynes DK. The costs of treating breast cancer in the United Kingdom: implications for screening. *Int J Technol Assess Health Care* 1998, **14**, 277–289.
30. Organization for Economic Co-operation and Development (OECD) Health Data 3.6 version. 2, rue Andre Pascal, 75775, Paris, CEDEX 16, France.
31. Hurley SF, Huggins RM, Snyder RD, Bishop JF. The cost of breast cancer recurrences. *Br J Cancer* 1992, **65**, 449–455.
32. Butler JR, Furnival CM, Hart RF. The costs of treating breast cancer in Australia and the implications for breast cancer screening. *Aust N Z J Surg* 1995, **65**, 485–491.
33. Geddes M, Carli S, Ercolanelli M, Forno G, Capelli M, Barchielli A. Colorectal, lung, and breast cancer care during the three years following the diagnosis: a population-based study. *Tumori* 1996, **82**, 210–214.
34. Richards MA, Braysher S, Gregory WM, Rubens RD. Advanced breast cancer: use of resources and cost implications. *Br J Cancer* 1993, **67**, 856–860.
35. Hillner BE. Financial costs, benefits, and patient risk preferences in node-negative breast cancer: insights from a decision analysis model. *Recent Results Cancer Res* 1993, **127**, 277–284.
36. Koopmanschap MA, Rutten FFH. Indirect costs in economics studies: confronting the confusion. *Pharmacoeconomics* 1993, **4**, 446–454.
37. Evans WK, Le Petit C, Will BP, et al. Strategies to reduce the costs of care for breast cancer in Canada. Oral presentation — International Society for Technology Assessment in Health Care — Ottawa, June 1998.
38. Will BP, Berthelot J-M, Houle C, Tomiak EM, Verma S, Evans WK. The economic impact of locoregional radiotherapy (LRRT) on all post-surgical stage II breast cancer patients in Canada. Poster presentation — International Society for Technology Assessment in Health Care — Ottawa, June 1998.
39. Logan D, Will BP, Berthelot J-M, et al. Economic and health impacts of administering preventative tamoxifen to women at high risk of breast cancer in Canada. Oral presentation — American Society of Clinical Oncology annual meeting, Atlanta, Georgia, USA, May 1999. *Proc Am Soc Clin Oncol* 1999, **18**, abstract 1605.