The Cost of Managing Lung Cancer in Canada

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The POpulation HEalth Model (POHEM) lung cancer microsimulation model has provided a useful framework for calculating the cost of managing individual cases of lung cancer in Canada by stage, cell type, and treatment modality, as well as the total economic burden of managing all cases of lung cancer diagnosed in Canada. These data allow an estimation of the overall cost effectiveness of lung cancer therapy. The model also provides a framework for evaluating the cost effectiveness of new therapeutic strategies, such as combined modality therapy for stage III disease or new chemotherapy drugs for stage IV disease. By expressing the cost of lung cancer treatment as cost of life-years gained, such analyses allows useful comparisons of the cost effectiveness of these treatments with those of other costly but accepted medical therapies. [ONCOLOGY 9(Suppl):147-153, 1995]

Introduction

Lung cancer is a disease of epidemic proportions in North America and the leading cause of cancer mortality for both men and women in Canada and the United States [1,2]. There is a widely held view that the cost of treating patients with lung cancer places a large economic burden on the increasingly constrained health care resources of both countries. In reality, there have been few data available to show whether this belief is fact or fiction. To understand the extent of the economic burden of lung cancer in Canada, and to be better able to predict future costs, requires a careful analysis of the complex interaction among population demographics, smoking patterns, distribution of lung cancer cell types and stages, treatment options, and the actual cost of care.

The Social and Economics Study Division of Statistics Canada (the Canadian government statistical agency) is in the process of developing a comprehensive microsimulation model of Canadian health, incorporating population demographics, risk factors, the distribution of disease states, and treatment options for a number of common diseases affecting Canadians, including lung cancer [3]. Ultimately, this POpulation HEalth Model (POHEM) will also include breast cancer, cardiovascular disease, dementia, and arthritis. Using POHEM, it has been possible to estimate the cost of managing an individual case of lung cancer, according to its stage and cell type, and to determine the total economic burden of managing all cases of lung cancer diagnosed in Canada. From this information and data on the survival of patients with lung cancer, it is then possible to estimate the overall cost effectiveness of lung cancer therapy. In addition, the model allows for simulation of new treatment approaches, such as the use of combined modality therapy for stage III disease or of new chemotherapy drugs for stage IV disease, and estimation of their cost per case and cost effectiveness.

This manuscript will briefly describe the POHEM model and some of the key observations that have been made relating to the economic burden of lung cancer on the Canadian health care system. Some of this information has been presented previously [4,5].

Methods

The POpulation HEalth Model (POHEM) is a software framework that integrates data on risk factors, disease onset and outcomes, health care utilization, and direct medical care costs. The computer program generates a synthetic cohort of people with demographic and labor force characteristics, risk factors exposures, and health histories typical of Canadians [3].

The Lung Cancer Submodel

When an individual is assigned a diagnosis of lung cancer in the microsimulation model, the lung cancer submodel then assigns a particular histologic cell type and stage based on the distribution of these characteristics in the Canadian population. It further assigns treatment and subsequent progression of the disease using lung cancer survival rates from the medical literature. Finally, it assigns costs for the various components of care appropriate for the management of that cell type.
and stage of disease.

To construct the POHEM lung cancer submodel, we first obtained information on the distribution of lung cancer cases according to demographic characteristics and tumor cell types. These data were obtained from the National Cancer Incidence Reporting System (NCIRS), which is maintained by the Health Statistics Division of Statistics Canada. This information is collected annually from Canada's 10 provincial and two territorial cancer registries. Information in NCIRS is available on patient age, gender, and tumor cell type.

When this project began, only 1984 data were available from NCIRS. Subsequently, 1988 incident cases became available, and they are the database on which the model is currently structured. For that reason also, costing was done in 1988 Canadian dollars. In that year, 15,817 cases of lung cancer were reported, of which 15,624 were either non-small-cell lung cancer (NSCLC) or small-cell lung cancer (SCLC). Unfortunately, staging information was not available from the NCIRS database, and it was therefore necessary to retrospectively stage a cohort of lung cancer cases. This was done using the new international TNM staging system for NSCLC [6] and the Veterans Administration Lung Group Staging System for SCLC [7].

Statistics Canada contracted with the Alberta Cancer Board and the Ontario Cancer Registry to review the charts of all cases diagnosed in the Province of Alberta in 1984 and of 1,000 cases diagnosed in 1984 and 1985 in the Province of Ontario. Of the 856 cases from Alberta in 1984, 57% contained sufficient information for staging, as did 62% of the Ontario sample. The combined Alberta and Ontario staging data were then used to estimate the probability of the 1988 incident cases being at a particular stage given a particular cell type, gender, and age. We assumed that between 1984 and 1988 no new diagnostic approaches were introduced that might have caused stage migration.

**Clinical Algorithms**

Simplified clinical algorithms of lung cancer management were constructed. Those knowledgeable of lung cancer will appreciate from the example shown in the Figure of stages I and II NSCLC that the model does not address all potential diagnostic and therapeutic interventions. Nonetheless, it was constructed taking into account the practice recommendations within the US National Cancer Institute's Patient Data Query (PDQ) database, with modifications for Canadian practice according to a lung cancer expert panel made up of physicians working at the Ottawa Regional Cancer Centre. In addition, Canadian thoracic surgeons and radiation oncologists completed a national questionnaire survey of practice patterns, and this was used in estimating the proportion of patients that Canadian physicians would refer for treatment and, in the case of radiation therapy, the dose and number of fractions that would be administered.

In determining the makeup of the diagnostic submodel, only essential diagnostic tests were included, with the understanding that this would tend to underestimate the costs of diagnosis. In practice, some tests are repeated as a patient is referred from one physician to another, and lung cancer does not always present in a straightforward fashion. In addition, investigations for paraneoplastic syndromes can add considerably to the cost of the diagnostic workup, but these factors were ignored in the diagnostic test module. Similarly, tests were only repeated in the model when they were considered essential to monitor therapy. It was assumed that diagnostic procedures and surgical/radiotherapy treatment interventions were uncomplicated. These decisions were necessary because of the lack of available data on resource utilization for lung cancer management through provincial data information systems. However, valuable information was obtained from the Ontario Cancer Registry about the average duration of hospitalization during diagnostic workup and initial therapy. The extent of outpatient clinic utilization and hospitalization for chemotherapy delivery or best supportive care was obtained from previously reported lung cancer studies done by the National Cancer Institute of Canada (NCIC) (BR.4 and BR.5) [8,9].

Patient survival was based on data in the medical literature and was assigned, as appropriate, for cell type and stage. The data sources used included Lung Cancer Study Group data on the survival of surgically resected NSCLC patients [10,11]; Radiation Therapy Oncology Group (RTOG) data on the survival of stage III NSCLC patients [12]; NCIC clinical trial data on best supportive care versus chemotherapy (BR.5) in stage IV NSCLC patients [9]; and NCIC clinical trials (BR.3 and BR.4) of therapy for patients with limited and extensive SCLC [8,13]. When incorporating survival information into the model, it was assumed that if a patient survived 5 years from the diagnosis of lung cancer, he or she was cured, and no additional costs for lung cancer management were incurred.

**Cost Determination**

The perspective of this economic analysis was that of the Canadian government as payer in a universal health care system. As such, the analysis specifically excludes indirect costs, such as out-of-pocket costs to patients for oral medications, travel to a treatment center, parking, and lost
wages. All costs were determined in 1988 Canadian dollars. Although each province and territory has a different schedule of benefits for medical assessments, procedures, and laboratory tests, we assumed that these benefits would be similar to those paid in Ontario under its Health Insurance Plan (OHIP).

The cost of hospitalization for the surgical management of NSCLC patients was based on a per diem rate of $545.19, which was obtained from Statistics Canada's Annual Return of Hospitals-Hospital Indicators: 1988 to 1989[14]. This per diem rate was the average cost per day of care in a tertiary health care facility where, presumably, most thoracic surgery is performed. The cost of hospitalization for the inpatient care of patients with SCLC and for the provision of supportive care was extracted from the economic analyses done previously by the NCIC during its BR.4 and BR.5 studies[15,16]. This average per diem was $361.00. The cost of a radiotherapy treatment fraction was based on a study by Wodinsky and Jenkin in which they determined the cost of operating a radiotherapy treatment facility in Ontario[17].

Results

Of the 15,624 cases of bronchogenic carcinoma diagnosed in 1988 in Canada, the majority (80.3%) were NSCLC histologies, and the remaining 19.7% were SCLC. Non-small-cell lung cancer cases were almost equally split between squamous and nonsquamous histologies, and 63% of cases presented in an advanced stage, either stage III or IV.

Lung Cancer Treatment Costs

The costs of treating NSCLC by stage and treatment modality are summarized in Table 1. For those with stage I or II lung cancer treated by surgery alone, the initial management cost is $14,110. Postoperative radiotherapy, as recommended in up to 20% of cases by Canadian radiation oncologists, adds an additional $3,779, assuming that 25 fractions of radiotherapy are given. Management of patients with stage IIIa disease with "radical" radiotherapy (45 Gy in 20 fractions) has an initial cost of $11,714. Palliative radiotherapy for stage IIIb disease (35 Gy in 10 fractions) costs $1,600, and the total cost of care is $9,347. The initial management of stage IV disease, including hospitalization for diagnosis and subsequent administration of palliative radiotherapy according to observations made in the BR.5 protocol, leads to costs of $6,333. However, stage IV patients generally also incur terminal care costs within 1 year of diagnosis, and these costs were calculated to be $10,331. In the model, patients who relapse with metastatic disease are assigned the cost of terminal care ($10,331) in the year of their death.

Table 2 shows a similar analysis for SCLC according to disease stage. Patients with limited stage disease receiving combined modality therapy incur costs of approximately $18,500. Those with extensive disease, who receive less radiotherapy, incur costs of $13,325. Terminal care costs for extensive disease patients were estimated at $9,387 and would be added to the above costs in the model during the year of the patient's death.

Total Burden of Health Care Costs

Table 3 summarizes the burden of health care costs for the treatment of all 1988 incident cases of NSCLC during the first year of care, the cumulative 5-year costs of care, and the average cost per case over 5 years by tumor stage. For all stages combined, the total first year cost of managing NSCLC in Canada was $203 million. Stage IV NSCLC patients accounted for almost one third of the total first year costs. Over 5 years, the total expenditure for the 12,549 NSCLC patients was estimated to be $248.2 million. The average cost per case over 5 years varied according to disease stage and treatment but ranged from $16,501 to $23,881.

Table 4 shows the total burden of cost incurred in managing the 1988 incident cases of SCLC during the first year, as well as the cumulative 5-year costs and the average cost per case over 5 years by disease extent. To manage the 1,113 cases of limited SCLC in the first year, the estimated cost was $26.4 million. For extensive disease, the first year management of 1,962 cases cost $40 million. Total 5-year costs were estimated at $79.7 million. The average cost per case ranged from $23,789 for extensive disease to $29,864 for limited disease.

Cost Per Life-Year Gained

Non-Small-Cell Lung Cancer—Although the information on the total cost of care is of interest, particularly to policymakers, the cost per life-year gained is of greater interest and usefulness to health care practitioners. The cost per life-year gained is the cost of all care provided divided by the total life-years gained by the treatment intervention. It is most conveniently determined by comparing the survival of treated patients with that of an untreated patient population. However, in NSCLC, it is difficult to identify a no treatment group, particularly for patients with stages I and II.
disease who are almost universally treated by surgery unless medically unsuitable. A few patients refuse surgery, but they are sufficiently rare that it was not possible to find a survival curve in the medical literature for these untreated, but otherwise medically suitable, early stage lung cancer patients. The literature does contain reports of patients with stages III and IV disease who are untreated, but since current therapeutic interventions add modestly at best to the survival of these patients, we assumed that for the purposes of determining overall cost effectiveness of treatment in NSCLC, there is no survival gain from treatments for stage III or IV disease. This may, in fact, underestimate the true number of life-years gained by treatment.

In doing the calculations of cost effectiveness, we also assumed that any stage I and II surgically resected patients who survived 5 years were cured and therefore would have a normal life expectancy conditional on age, gender, and other risk factors. Since relapse from lung cancer can occur after 5 years, the number of life-years gained based on this assumption is, no doubt, overestimated.

To estimate the survival gained by surgically treated patients with NSCLC, we used as the "untreated" control group two different groups of stage I and II patients managed by radiotherapy: One group consisted of those individuals who were medically unsuitable for surgery and who did not achieve a complete response to radiotherapy [18], and a second group was made up of medically inoperable patients treated with radiotherapy only when pulmonary symptoms developed [19]. The former group was chosen because it was a patient population that did not benefit from the effects of radiotherapy. However, since they were medically inoperable, they may have had a poor overall outcome because of comorbid diseases. The second group of medically inoperable patients had the potential to derive a survival benefit, but since the radiotherapy was delayed until the disease was symptomatic, presumably the intervention was less effective. A true natural history survival curve for untreated stage I and II lung cancer might possibly lie somewhere between these two survival curves. Based on these assumptions, we determined the total number of life-years gained by finding the product of the number of patients in stages I and II in 1988 times the difference between the survival of the standard treatment arms and the "no treatment" controls. The estimated life-years gained ranged from 21,044 to 24,763 years, and the cost per life-year gained ranged from $10,024 to $11,796.

Small-Cell Lung Cancer—For SCLC, we used survival curves for untreated limited and extensive disease reported in the literature [20]. For combined modality therapy for limited disease, patients gained 2,880 life-years at a cost per life-year gained of $11,543. The benefits of therapy for extensive disease were less and were incurred at a greater cost. We estimated 1,206 life-years gained at a cost per life-year gained of $38,750.

Cost Effectiveness of New Therapies for Stage III and IV Disease

Combined modality approaches are increasingly being advocated based on the results of trials of neoadjuvant therapy for stage IIIa disease [21,22] and of combined modality therapy for stage IIIb disease [23-26]. Furthermore, there is evidence of a small but definite survival improvement for chemotherapy over supportive care alone from seven randomized trials [9,27-33] and three metaanalyses of chemotherapy in stage IV disease [34-36]. There has been some reluctance to adopt these newer approaches in Canada, because the magnitude of the survival gain relative to the treatment-related toxicity and impact on quality of life is perceived to be small, particularly for stage IV disease. Concerns have also been raised that these combined modality or chemotherapy interventions are costly and presumably not cost effective.

We have used POHEM to simulate the impact of the new combined modality approaches that have been reported for stage III disease. For stage IIIa, we modeled the impact of using the approach reported by Pisters et al [21], which consisted of two preoperative and two postoperative cycles of mitomycin (Mutamycin), vindesine, and cisplatin (Platinol) plus postoperative radiotherapy in patients with clinically evident N2 disease. We have also modeled the cost of delivering two cycles of vinblastine and cisplatin followed by radical radiotherapy (60 cGy in 30 fractions) for patients with stage IIIb disease, as originally reported by Dillman et al [23] and confirmed by RTOG 8808 [25]. Although the incremental cost per case was high, particularly for combined modality therapy in stage IIIa disease ($23,512 vs $9,599 for standard radiotherapy), the estimated life-years gained were also substantial (2,116) and equated to a cost per life-year gained of $6,638. Similarly, the combined modality approach of vinblastine-cisplatin followed by radical radiotherapy for stage IIIb patients was more expensive ($13,886) than standard Canadian radiotherapy ($7,229). However, the estimated life-years gained with combined modality therapy was 2,274 years and equated to a cost per life-year gained of $2,898 [5].

For stage IV disease, we have modeled etoposide (VePesid) and cisplatin given in the outpatient...
department, as well as vindesine plus high-dose cisplatin administered in the hospital (the best arm of the BR.5 NCIC study). It was assumed that survival with both regimens was similar and equivalent to that observed in the NCIC clinical trial. Based on these assumptions, the cost per life-year gained for etoposide-cisplatin was a very modest $2,000. On the other hand, the vindesine-cisplatin combination was much more expensive and translated to a cost per life-year gained of $9,402.

**Discussion**

The accuracy of the data on cost per case, total cost burden, and cost effectiveness is dependent on the assumptions used in constructing the lung cancer model. The fact that we costing only essential tests and assumed that any diagnostic and therapeutic interventions were free of complications would clearly tend to underestimate the total burden of health care costs. On the other hand, we assumed that all incident cases diagnosed in 1988 were, in fact, treated according to the clinical algorithms described in this manuscript. The reality is that lung cancer is a disease of elderly people, many of whom are simply too frail to treat or have other comorbid conditions that preclude any active intervention. In addition, other factors may act as a barrier to care, including distance from health care facilities and language and cultural barriers. Weighing these various factors in the balance, it seems likely that we have modestly underestimated the cost per case but overestimated the total direct care costs to the Canadian health care system. A further factor that may contribute to our model's overestimating cost, but which is impossible to quantify, is the prevailing view of many health care practitioners that lung cancer is a lifestyle disease with a very poor outcome and therefore warrants little active intervention. Unfortunately, there is no national database that sheds any light on the proportions of patients who actually receive treatment.

Undoubtedly, the burden of health care costs will increase beyond the estimates described for the 1988 incident cases. Not only are there increasing numbers of lung cancer patients but also there is growing evidence of treatment efficacy for patients presenting with more advanced disease. As these treatment practices become established, they will add to the total burden of lung cancer treatment costs. However, it is reassuring to note that these new treatment approaches are, in fact, cost effective and competitive with many other health care strategies that are accepted as worthwhile by society. The overall cost effectiveness of treating NSCLC was estimated to be on the order of $10,000 to $12,000 per life-year gained, even though we assumed that only survival gain was attributable to surgery. Estimates of the cost effectiveness of combined modality approaches for stage III disease, and for chemotherapy alone in stage IV disease, demonstrate a cost per life-year gained of less than $10,000. Although these costs were determined based on the Canadian health care system, they nonetheless compare favorably with the cost per life-year gained of common procedures performed in the United States, such as renal dialysis ($46,249 in 1988 US$) and coronary artery bypass surgery [$113,087 in 1988 US$] [37].

The POHEM lung cancer microsimulation model has provided a useful framework for determining the cost of lung cancer management in Canada by stage and treatment modality. It also provides a framework in which the cost effectiveness of new therapeutic strategies can be evaluated. Although the total burden of health care costs in Canada attributable to lung cancer is large and rising, an analysis of the distribution of the costs incurred in managing lung cancer can be used to direct the reengineering of our health care system in a constructive fashion. All of this information will be helpful in the ongoing debate about the appropriate distribution of health care resources for this and other diseases.

**References:**


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